

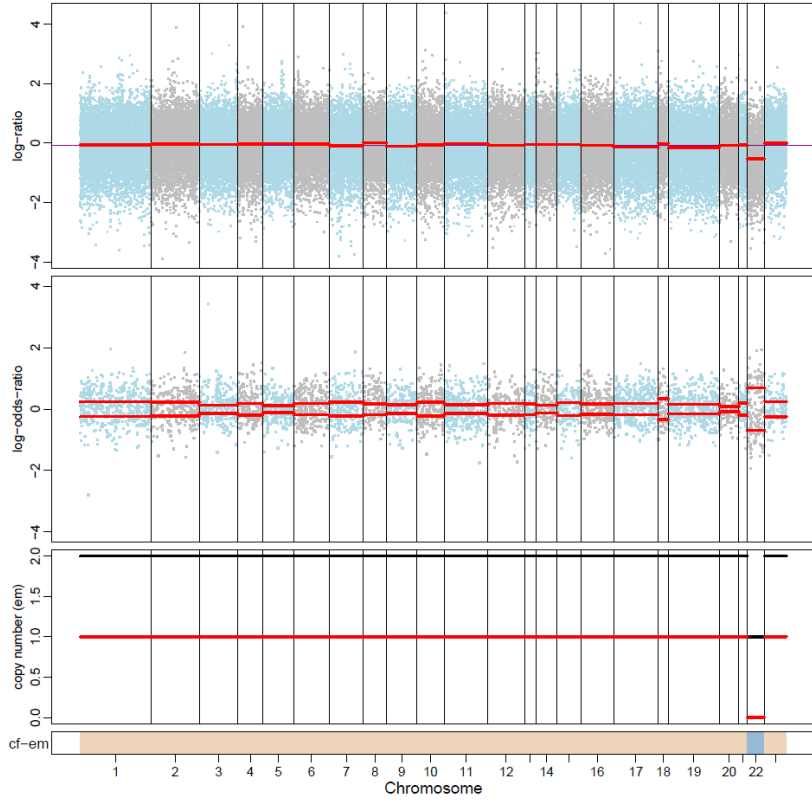
The American Journal of Human Genetics, Volume 105

Supplemental Data

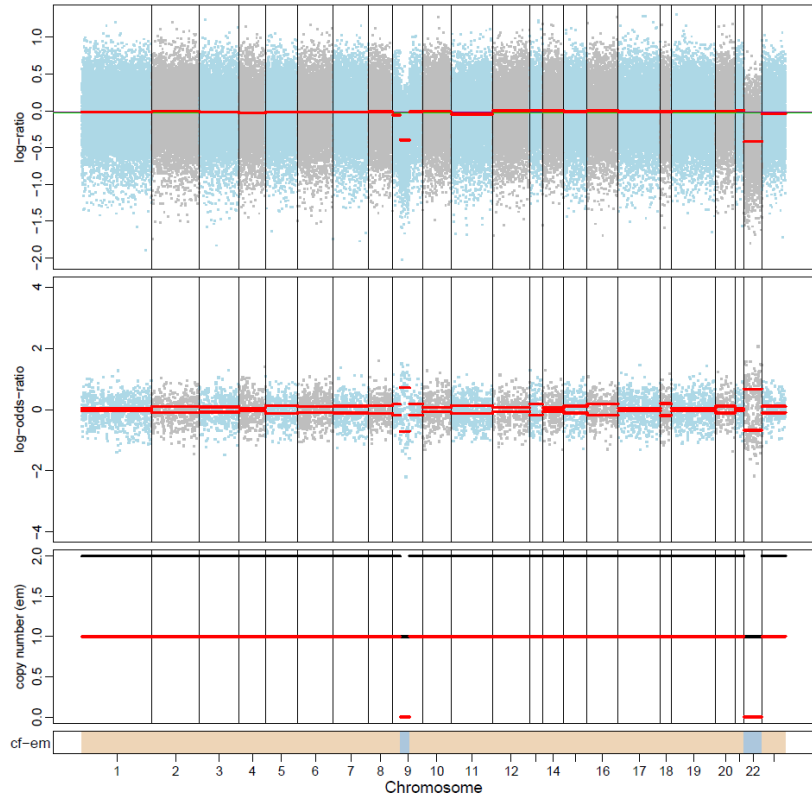
Evolution and Impact of Subclonal Mutations in Papillary Thyroid Cancer

Tariq Masoodi, Abdul K. Siraj, Sarah Siraj, Saud Azam, Zeeshan Qadri, Sandeep K. Parvathareddy, Saif S. Al-Sobhi, Mohammed AlDawish, Fowzan S. Alkuraya, and Khawla S. Al-Kuraya

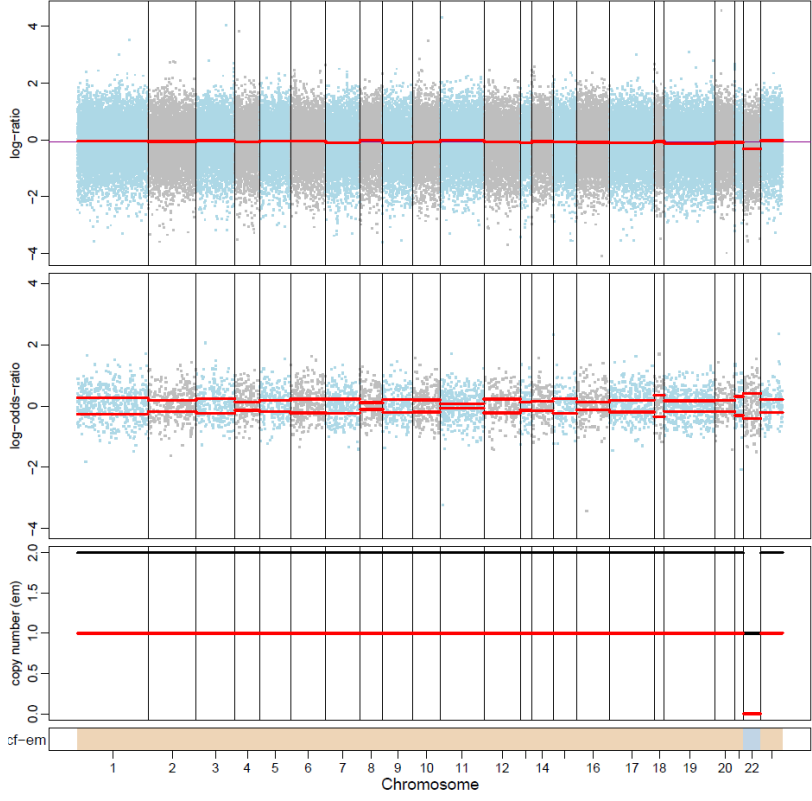
429-P



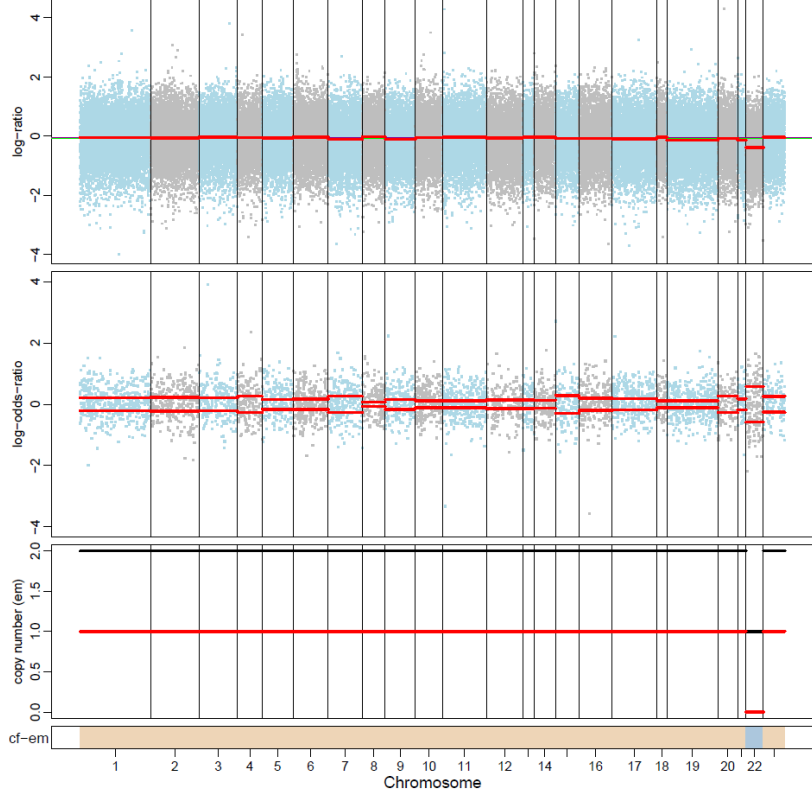
429-P0



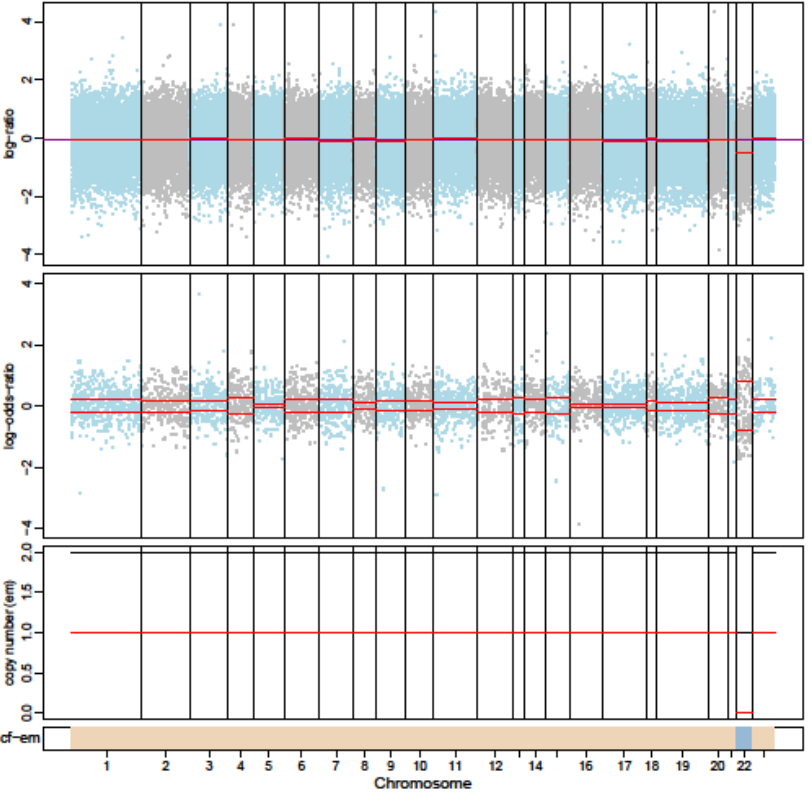
429-P1



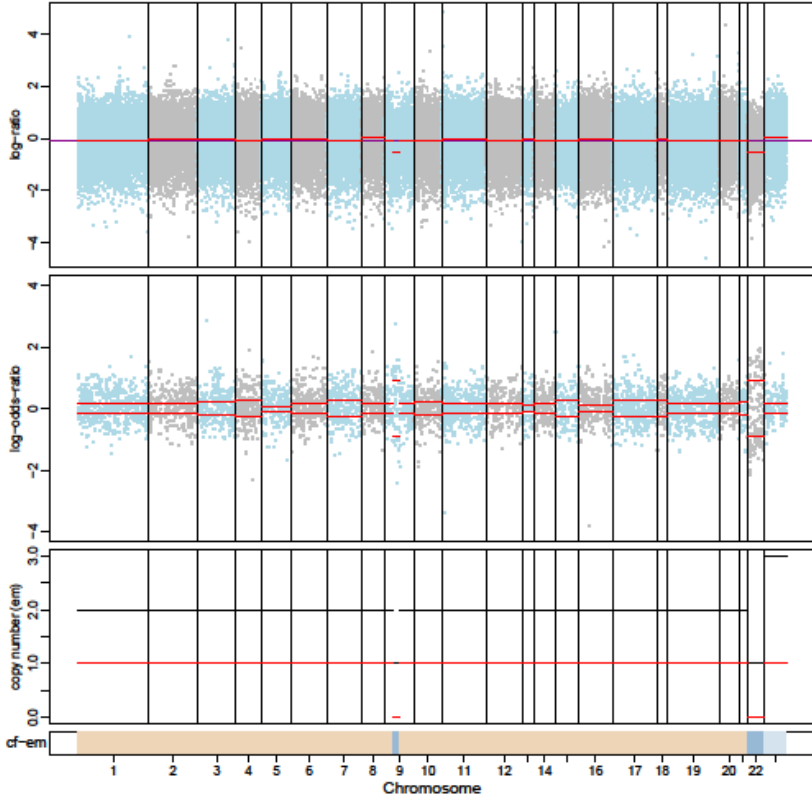
429-P2



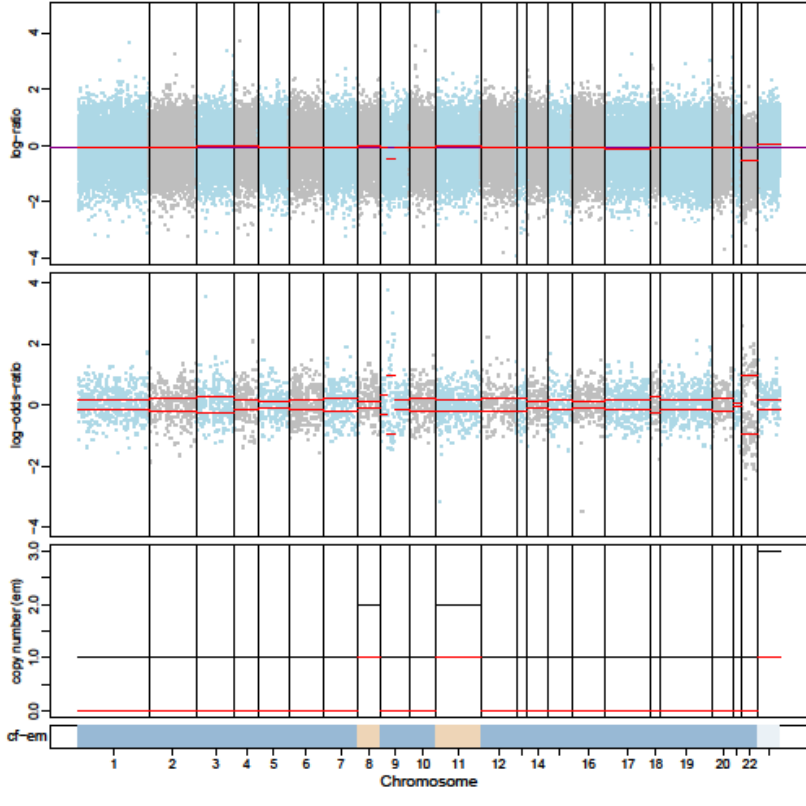
429-P3



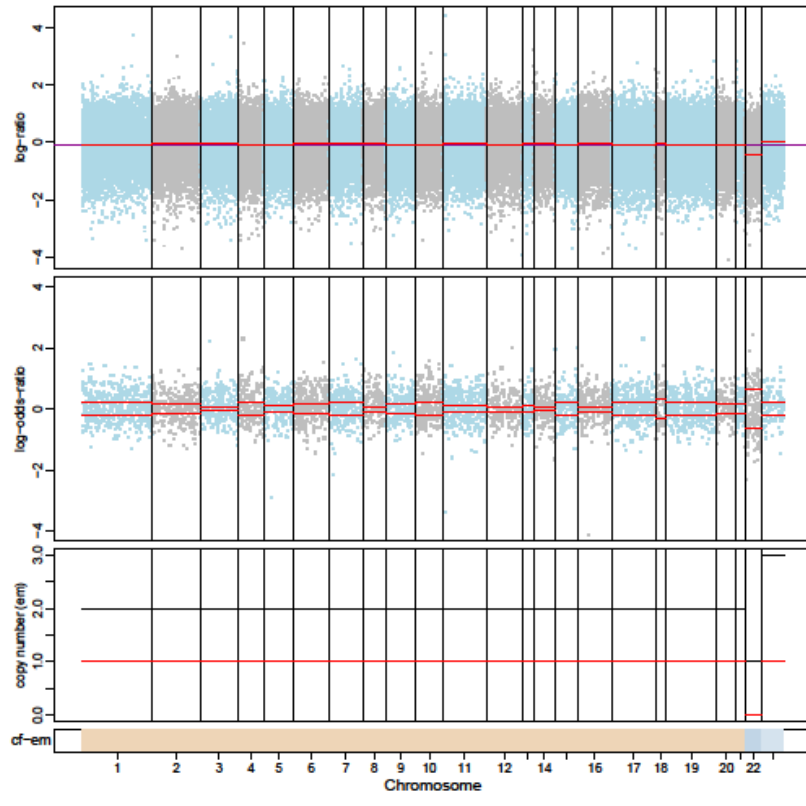
429-LR1



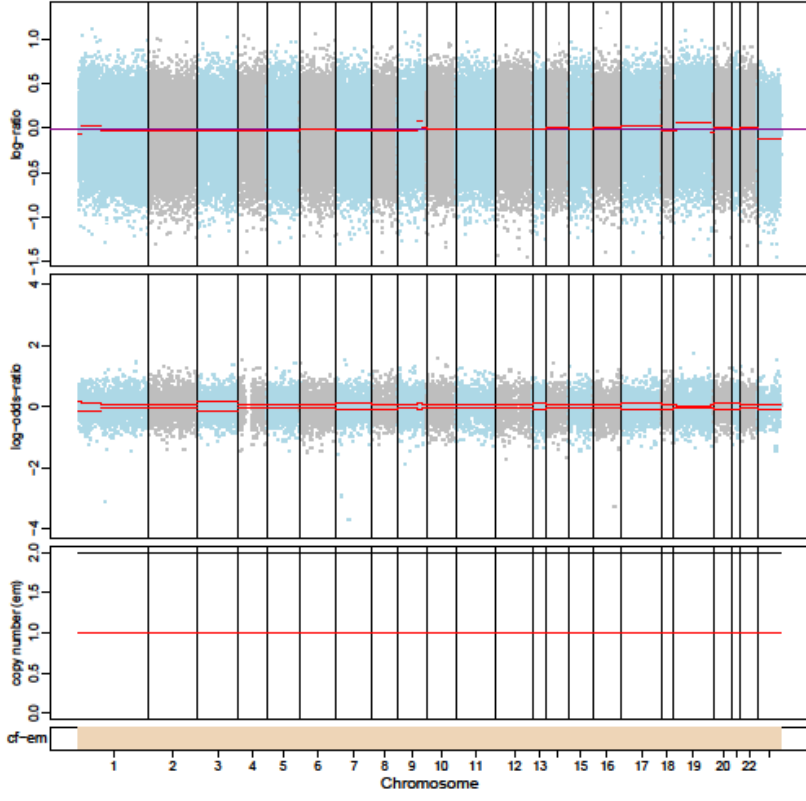
429-LR2



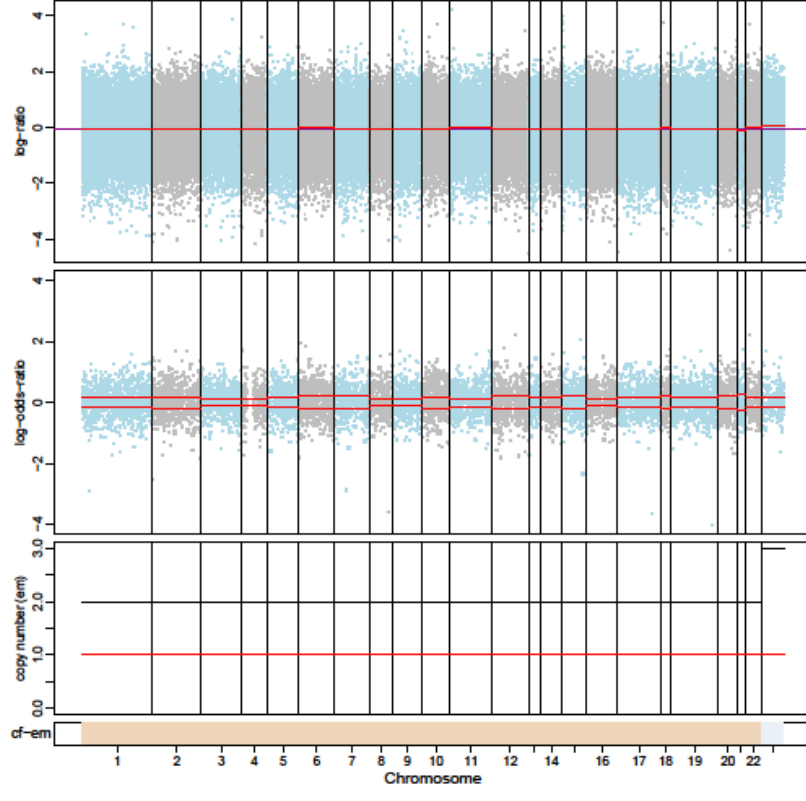
429-LR3



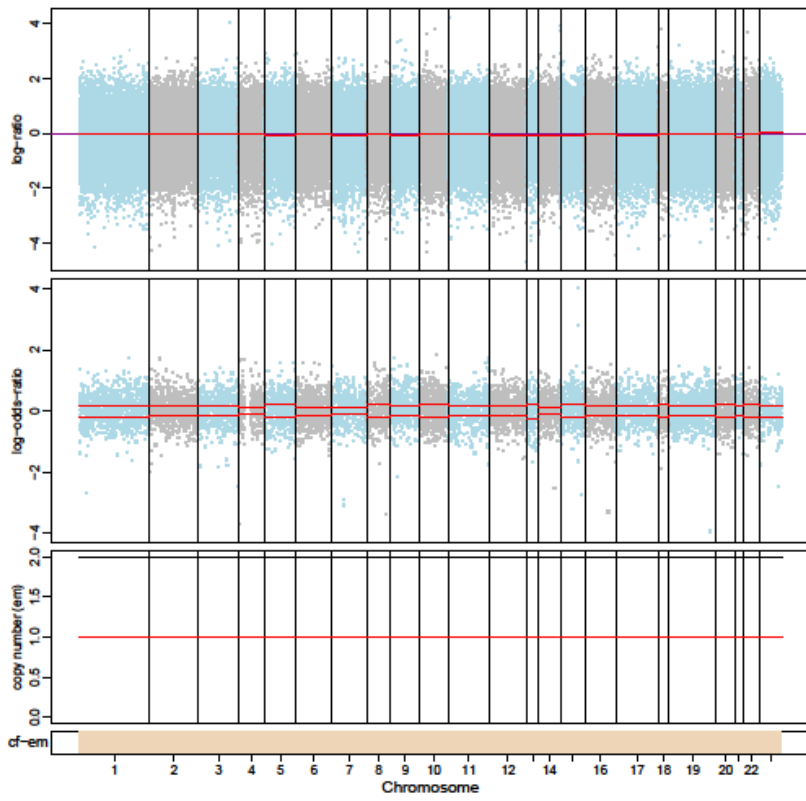
696-P0



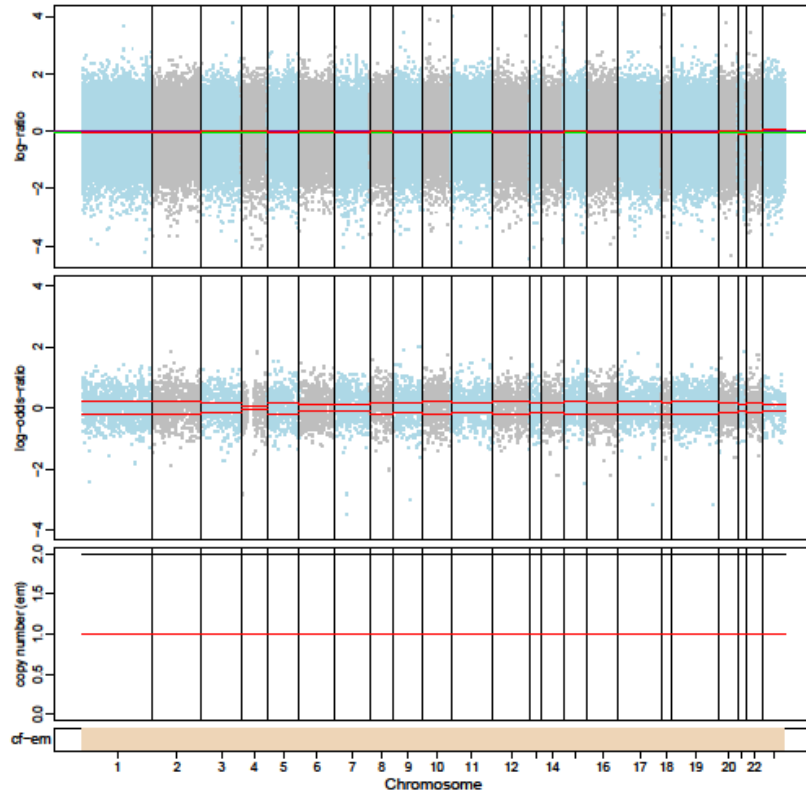
696-P1



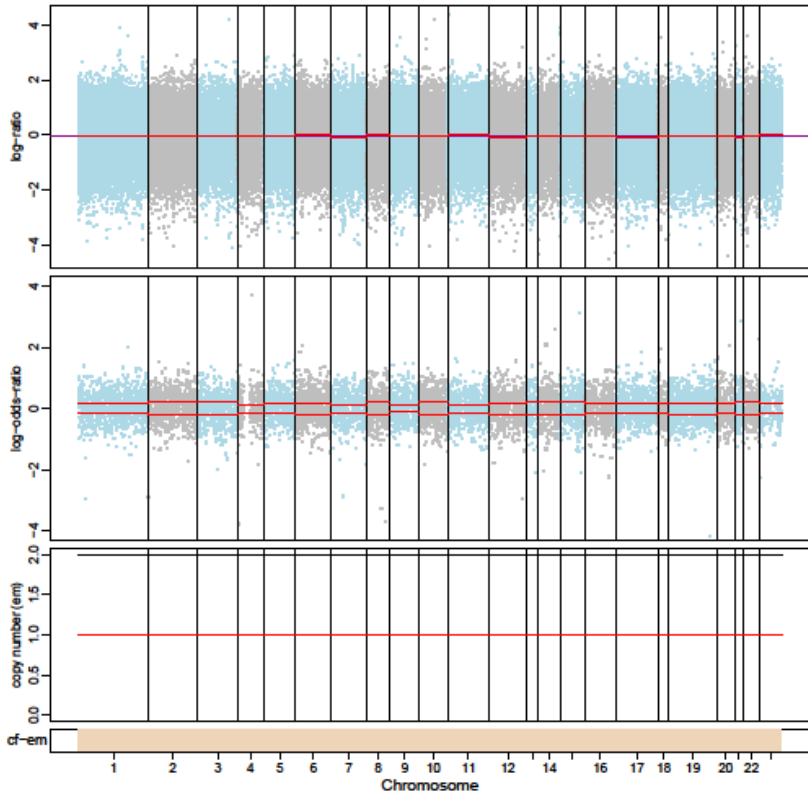
696-P2



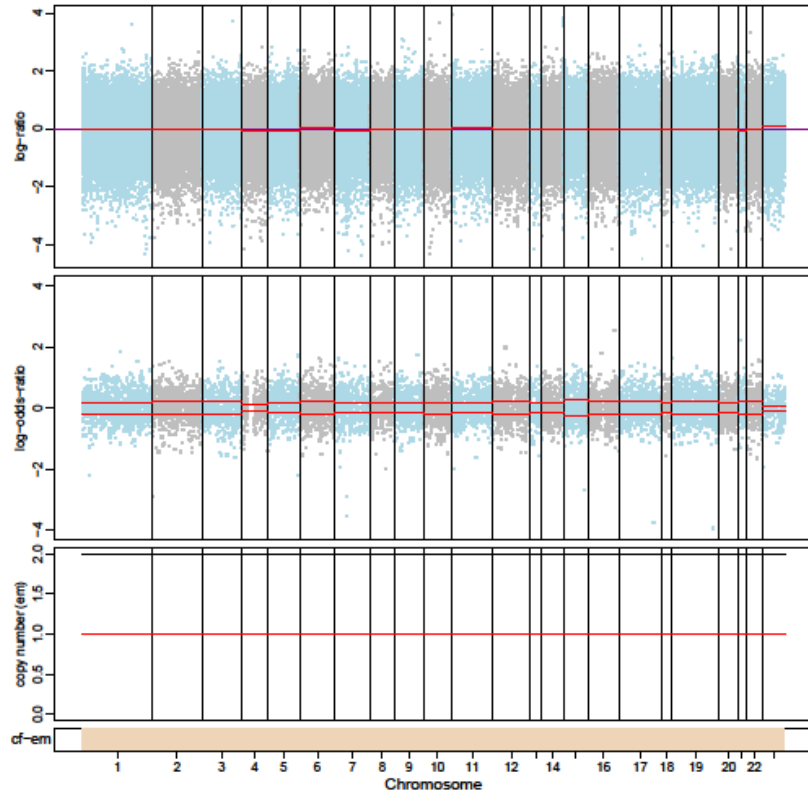
696-P3



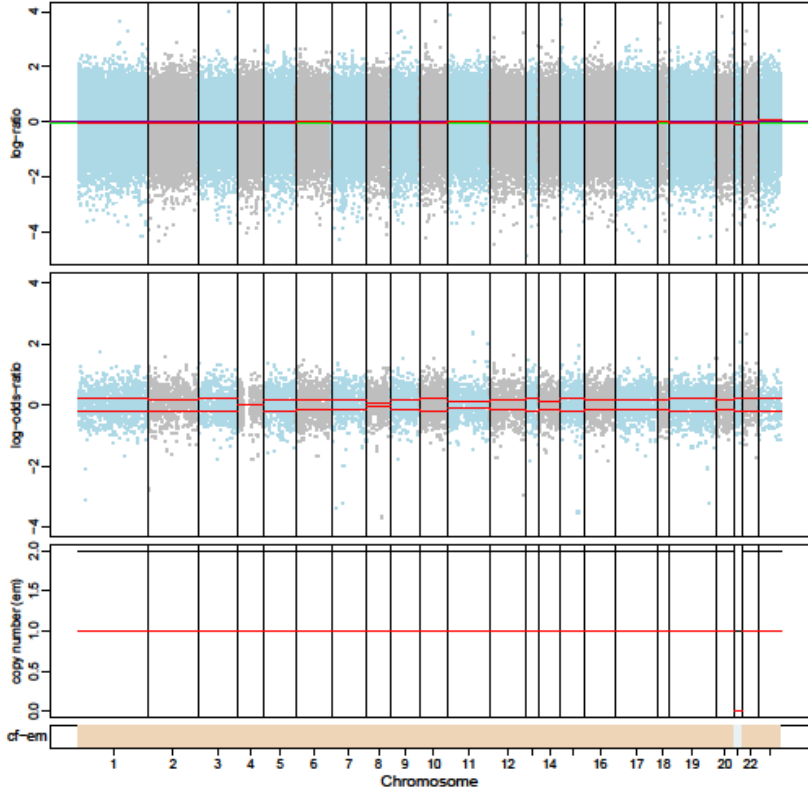
696-P4



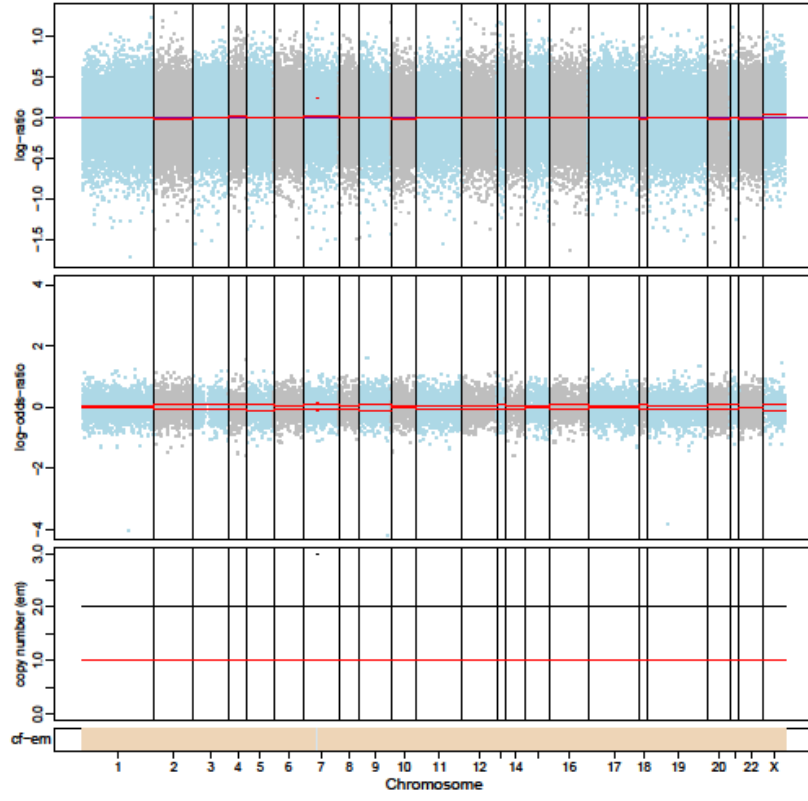
696-LR1



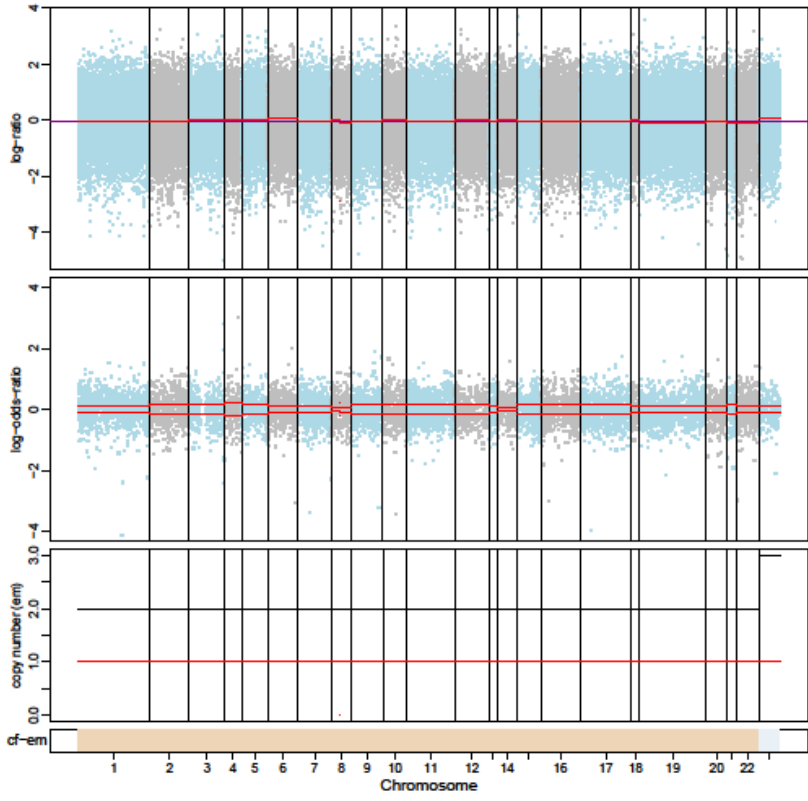
696-LR2



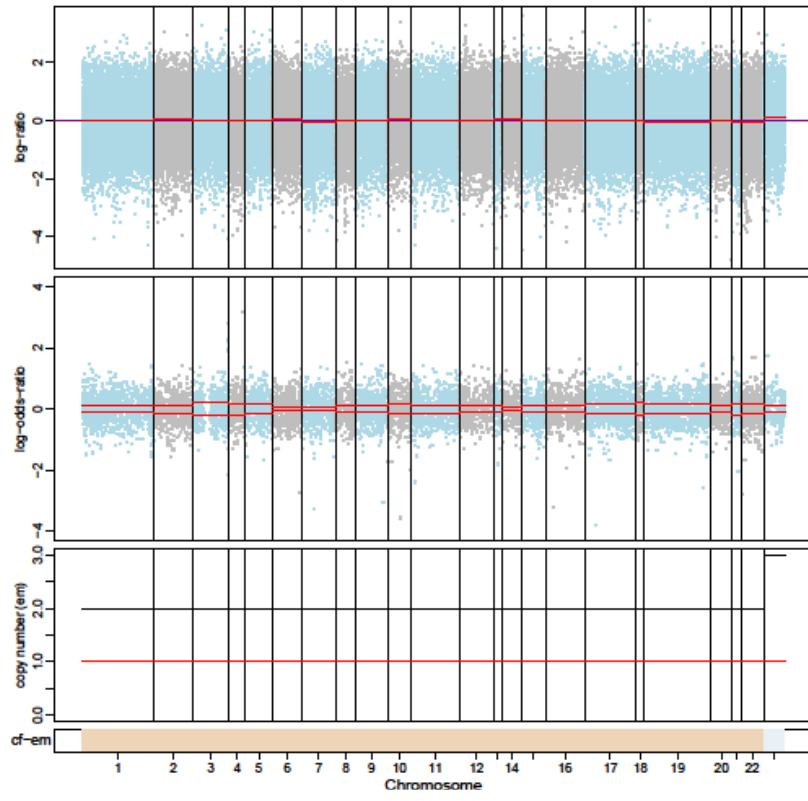
697-P0



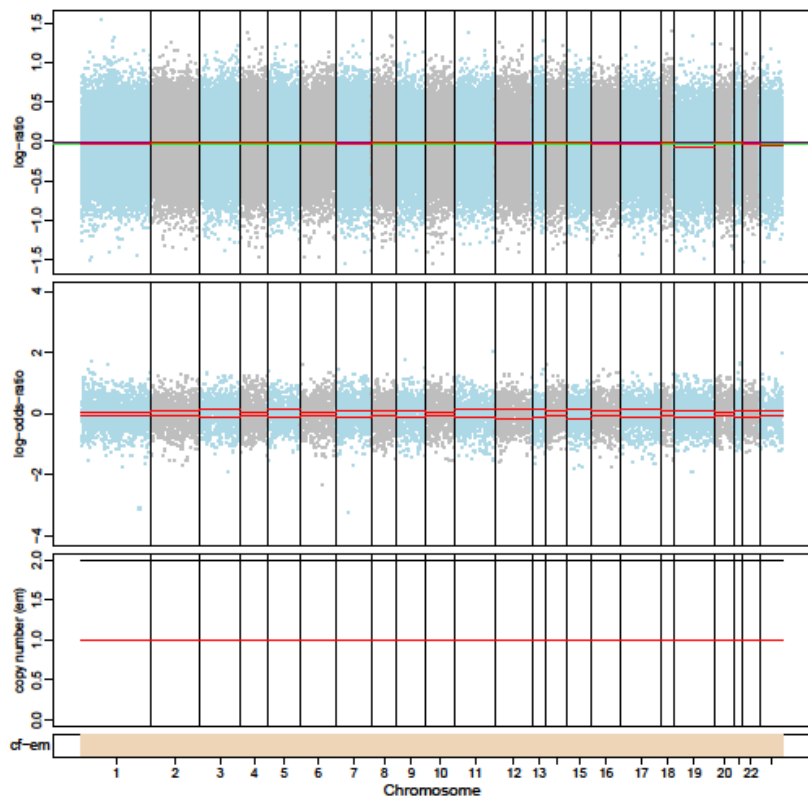
697-P1



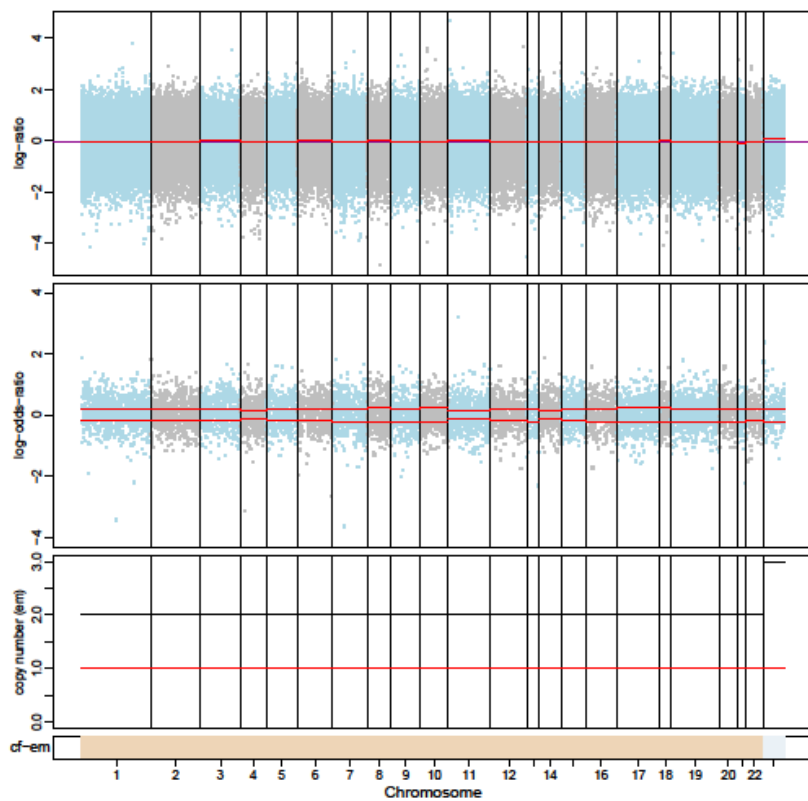
697-P2



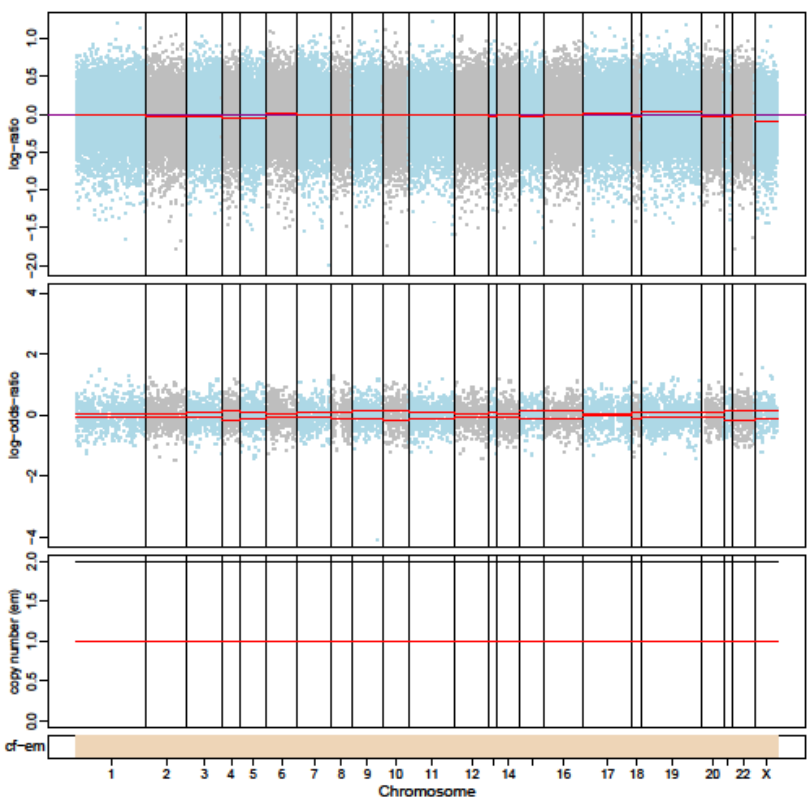
728-P0



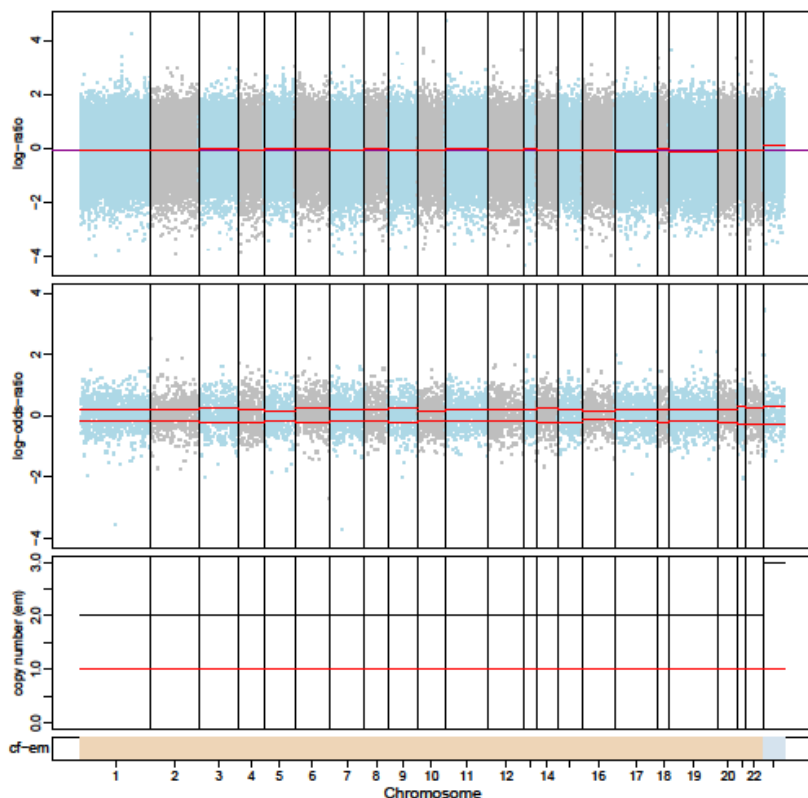
728-P2



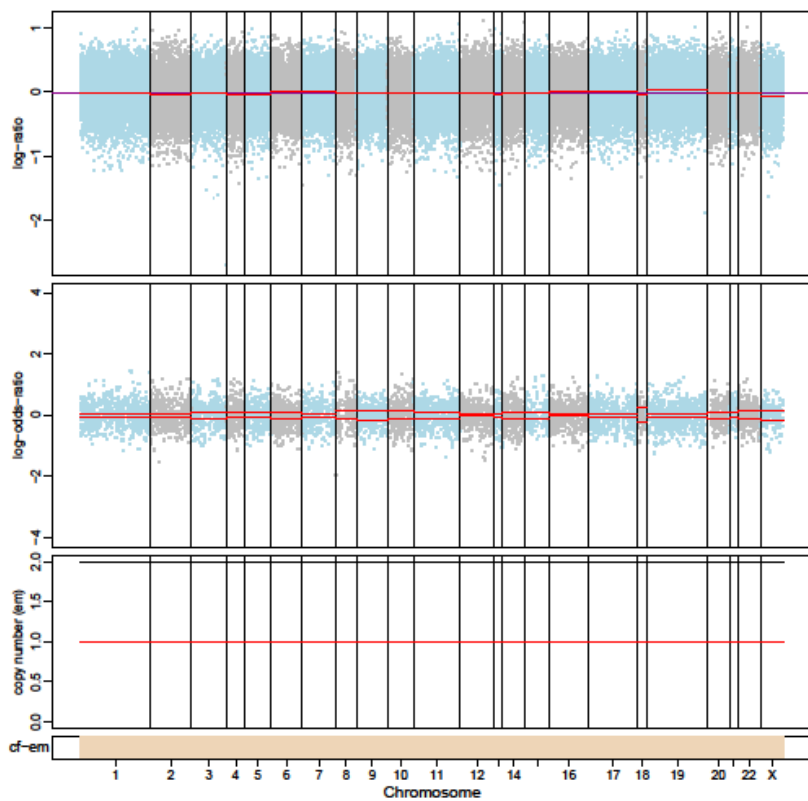
733-P2



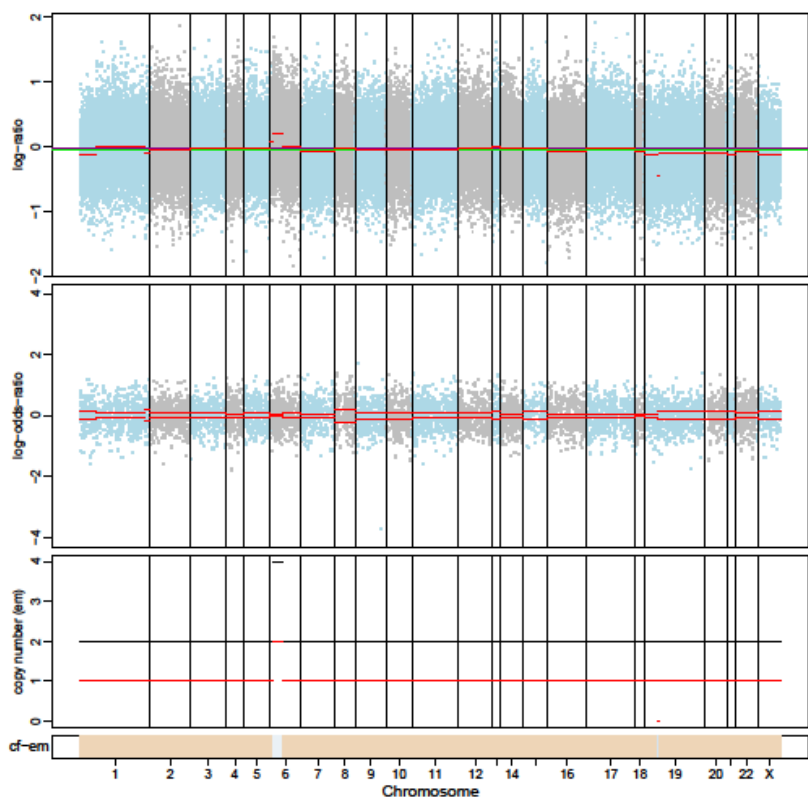
728-P1



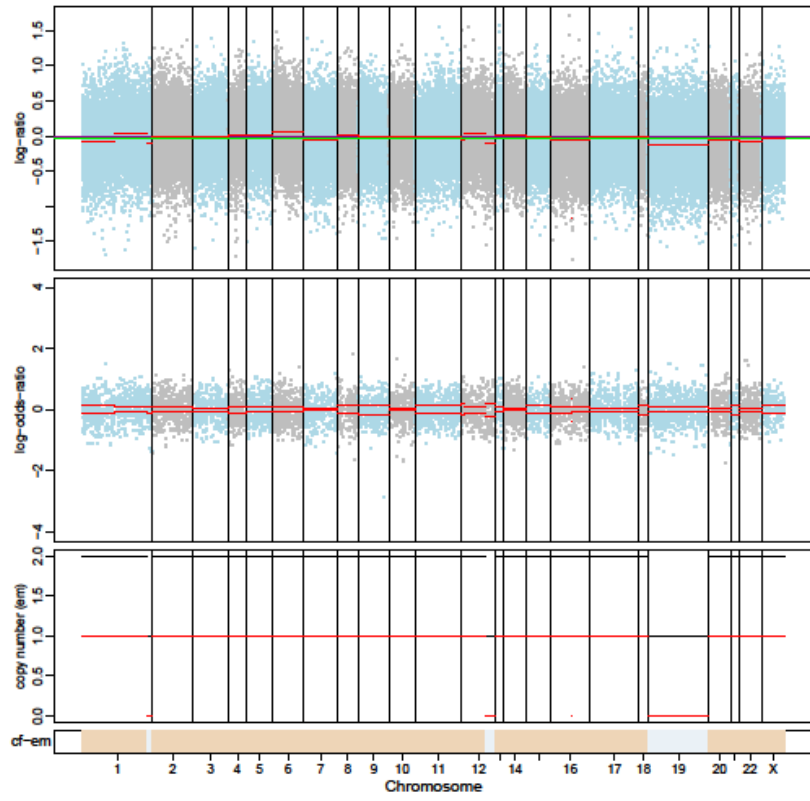
733-P1



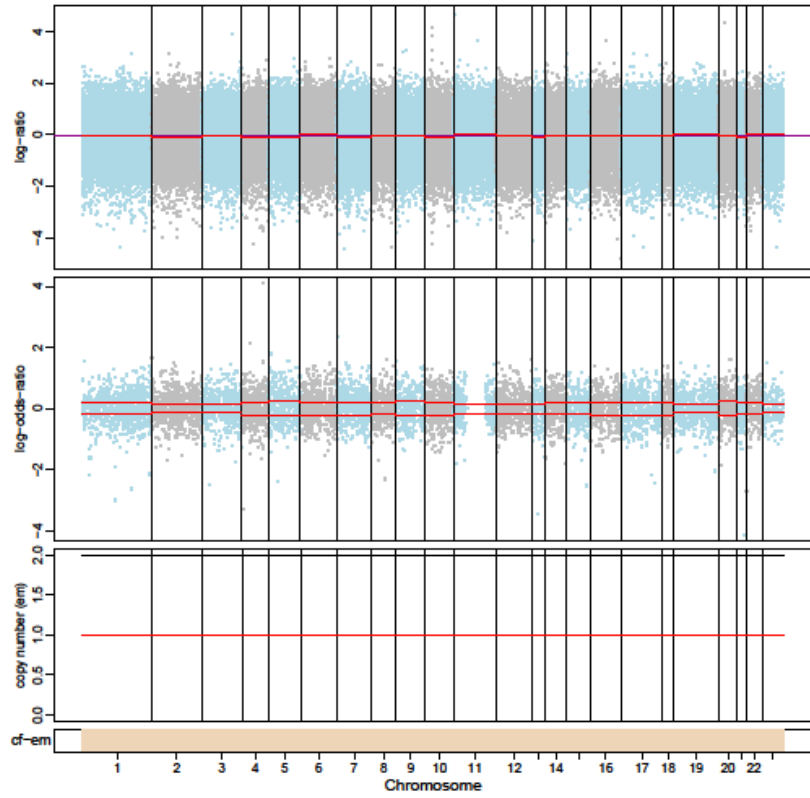
733-LR1



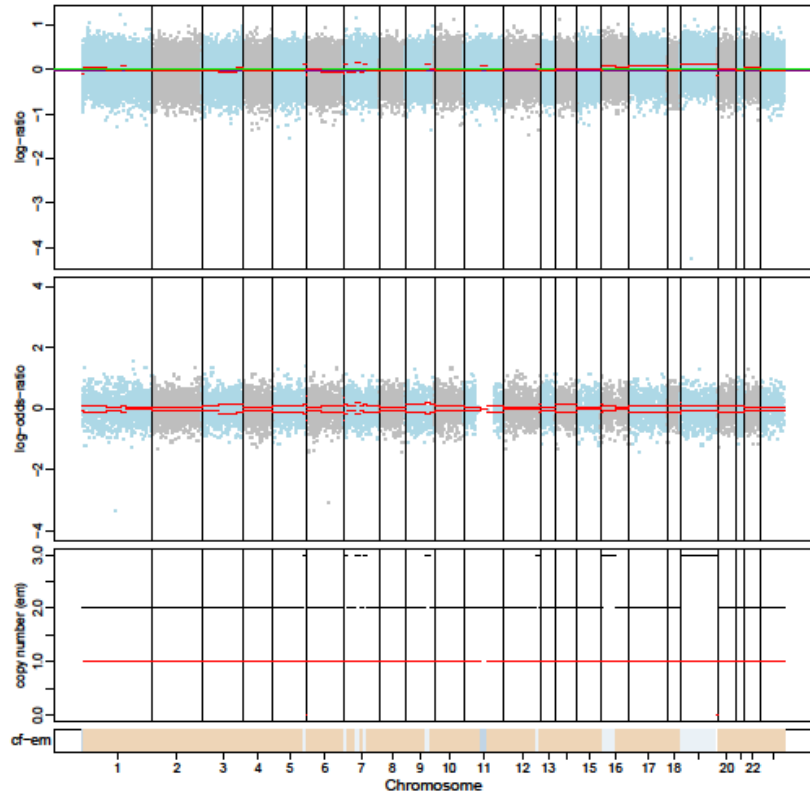
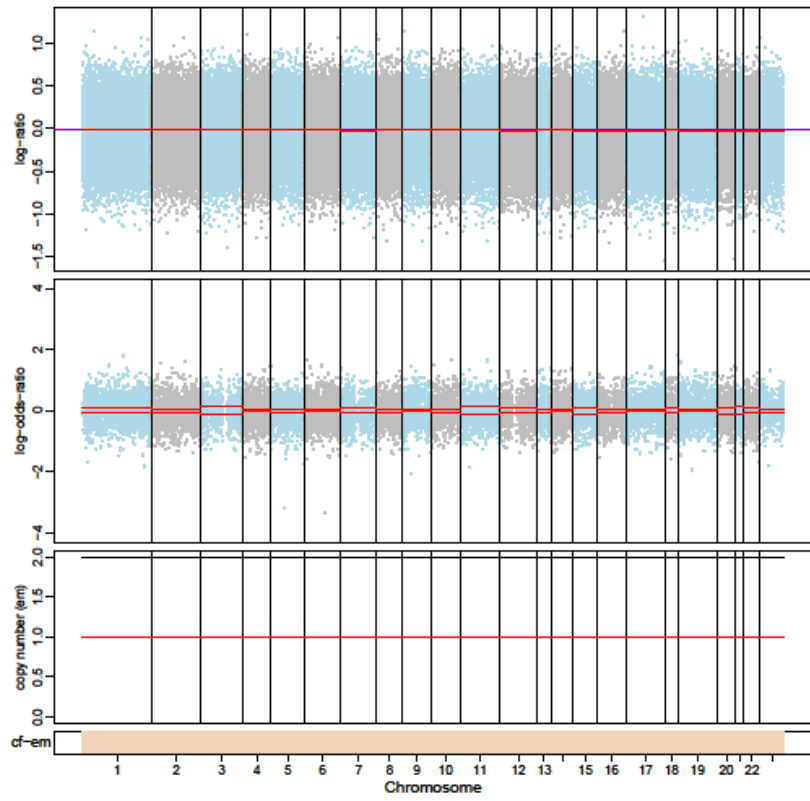
733-LR2



752-P1

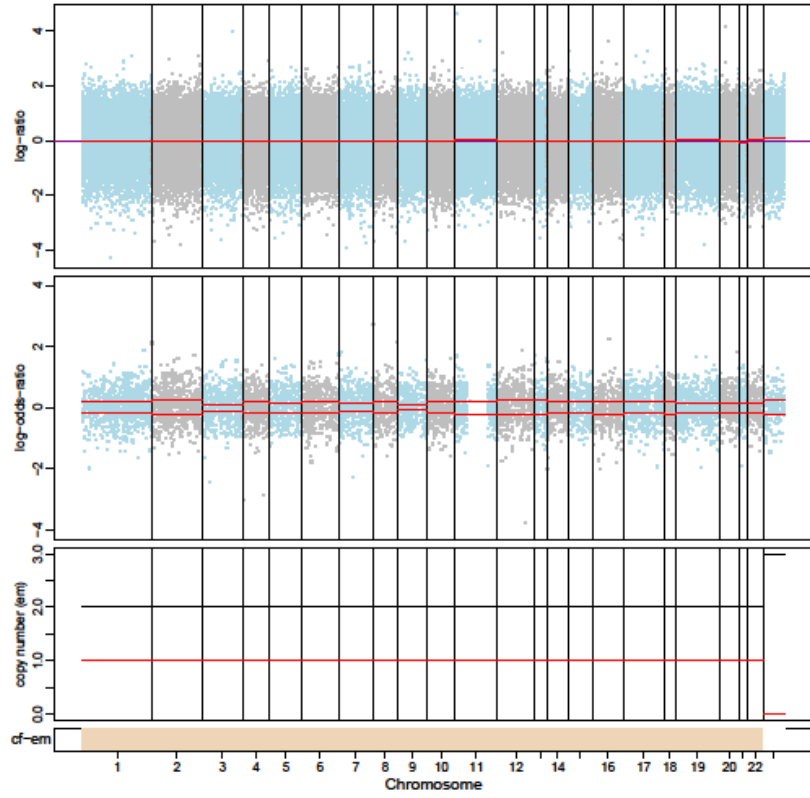


928-P0

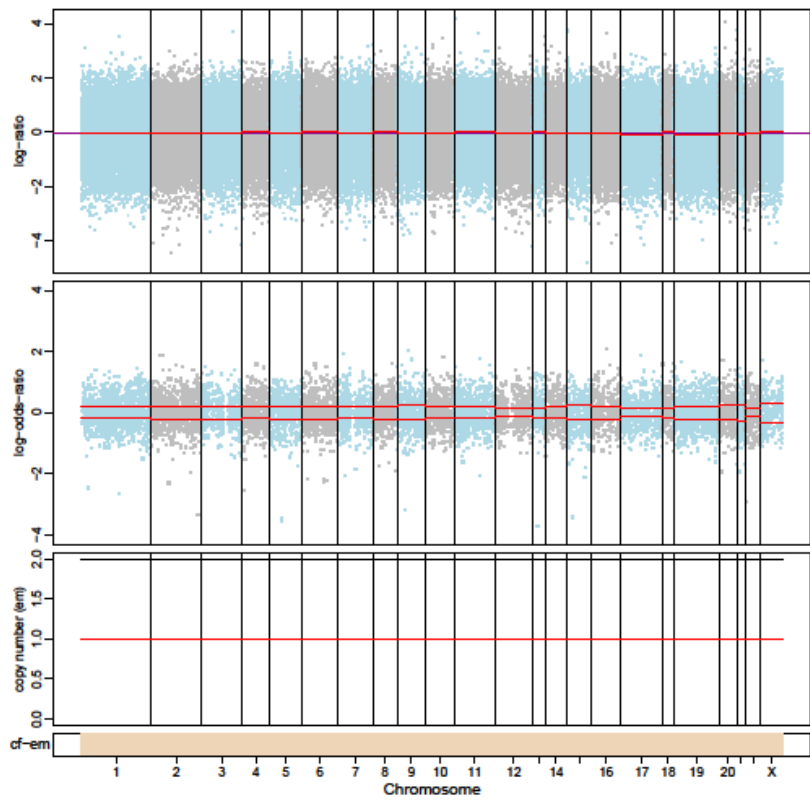


752-P0

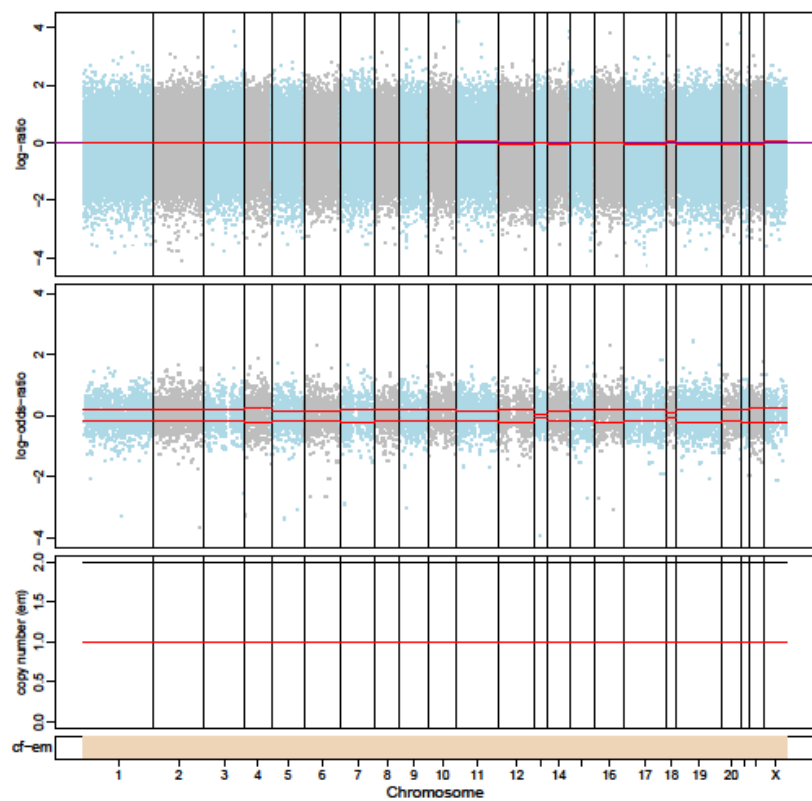
752-P2



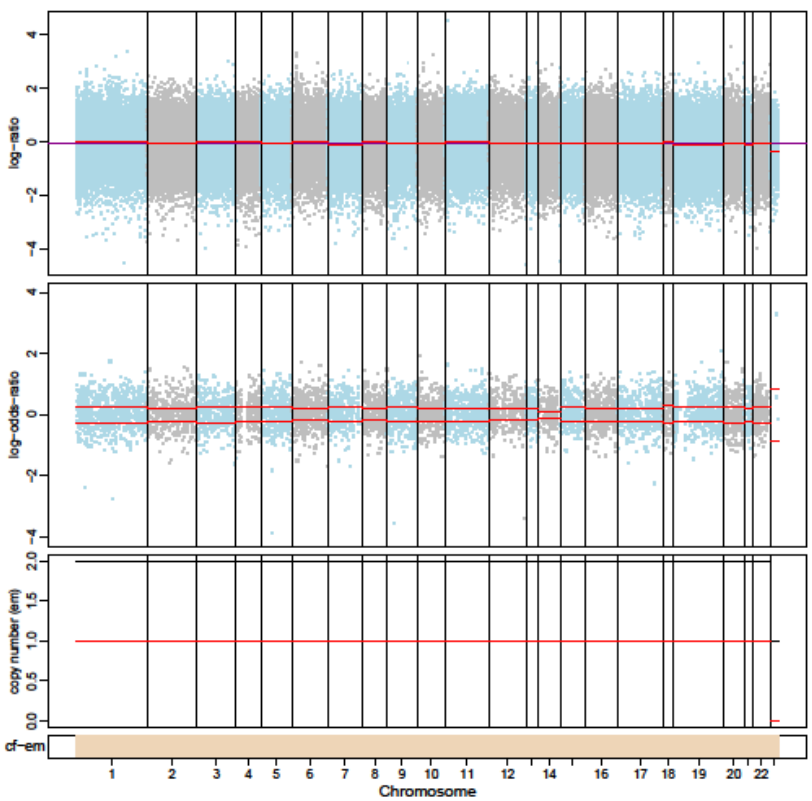
928-P1



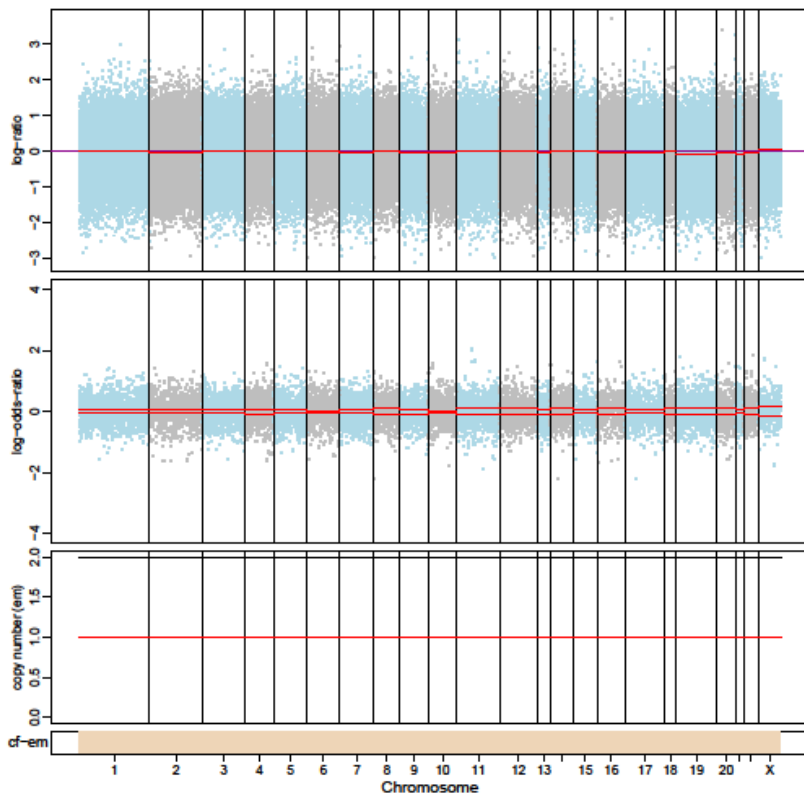
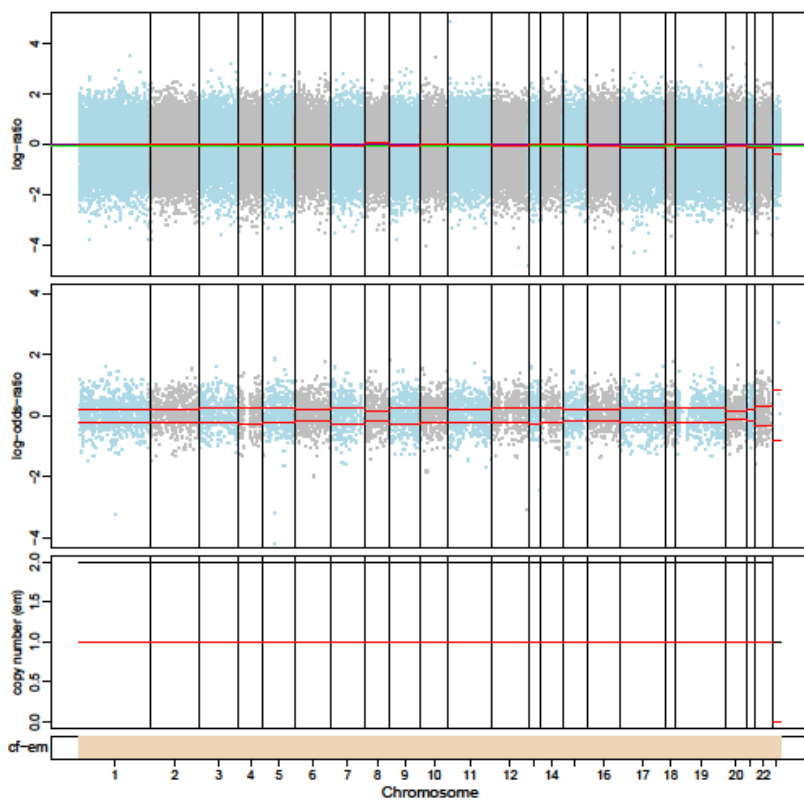
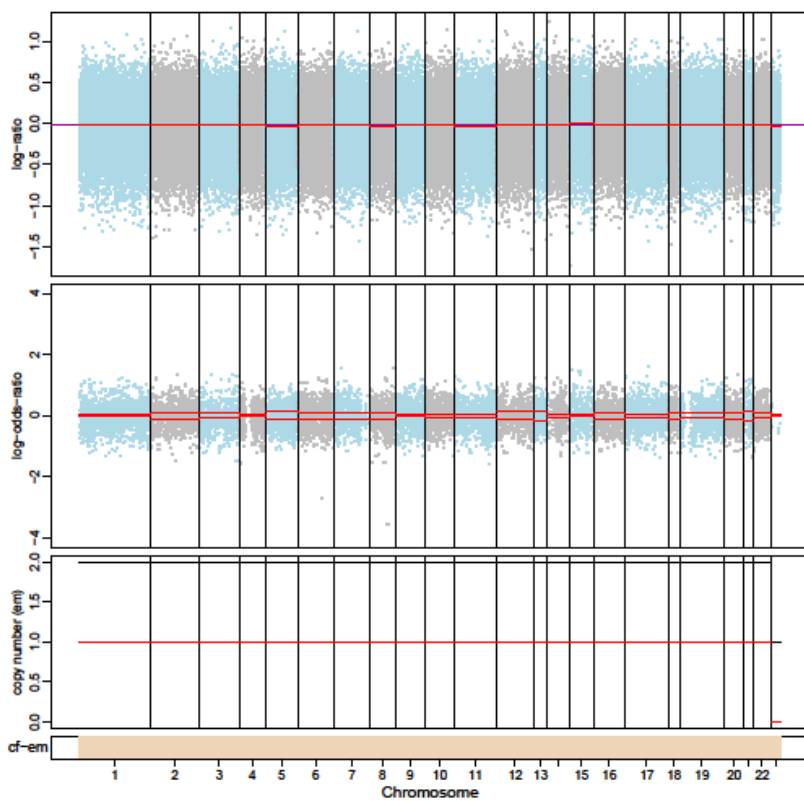
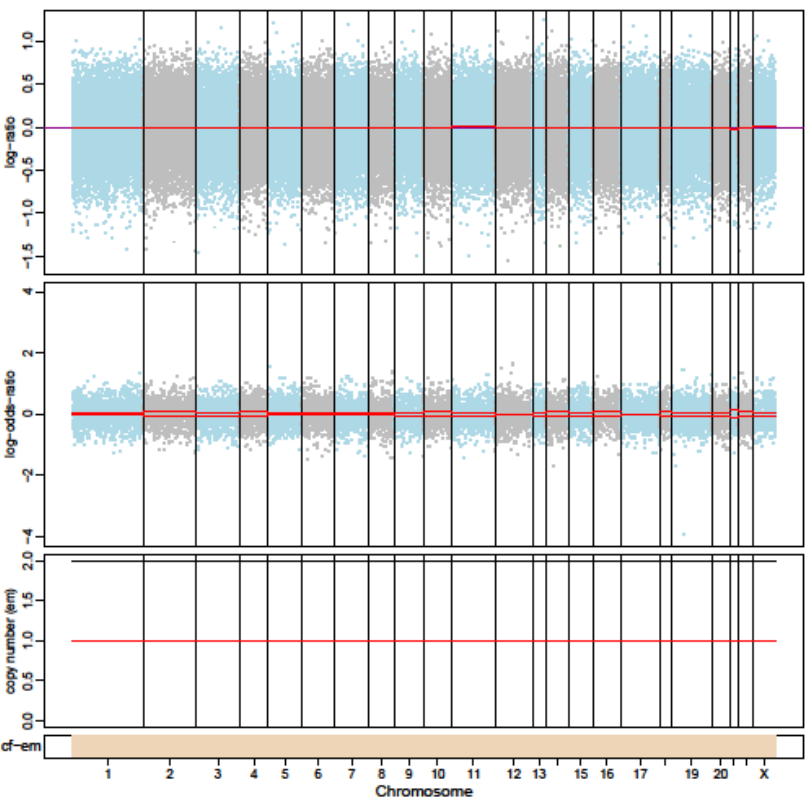
928-P2



929-P1



930-P0

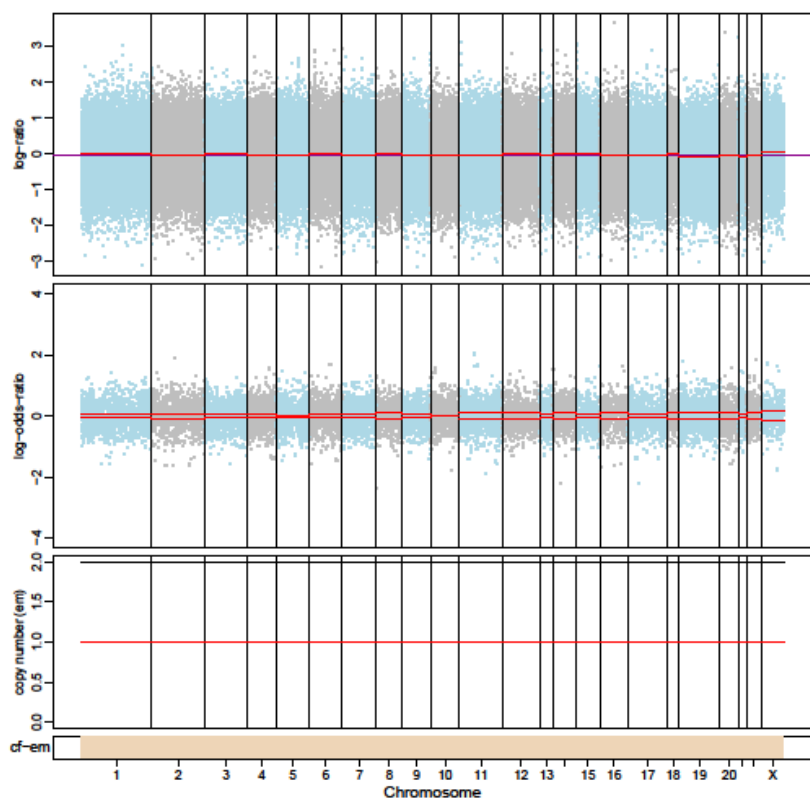


929-P0

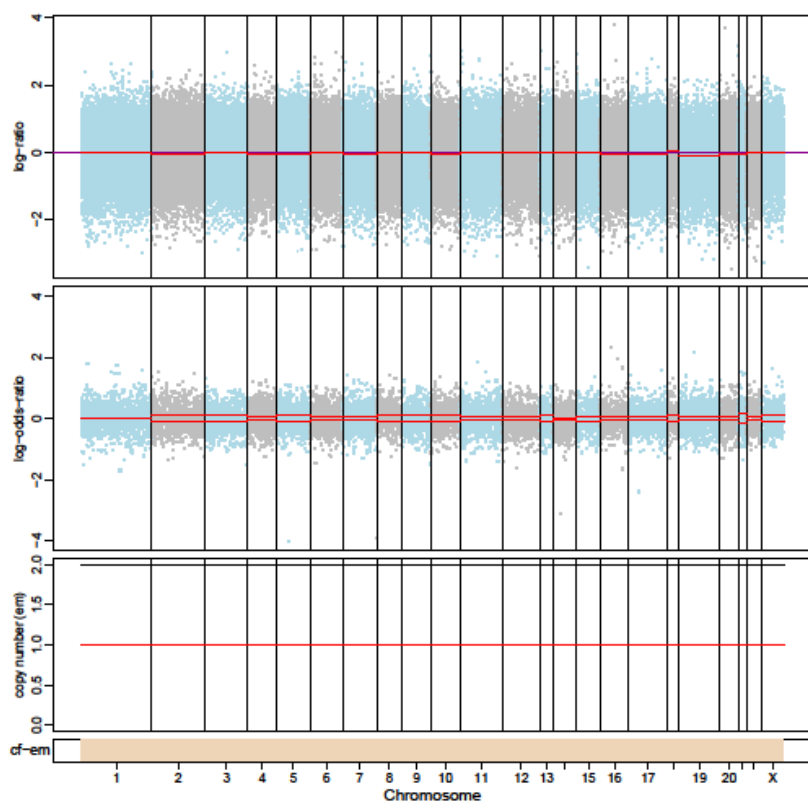
929-P2

930-P1

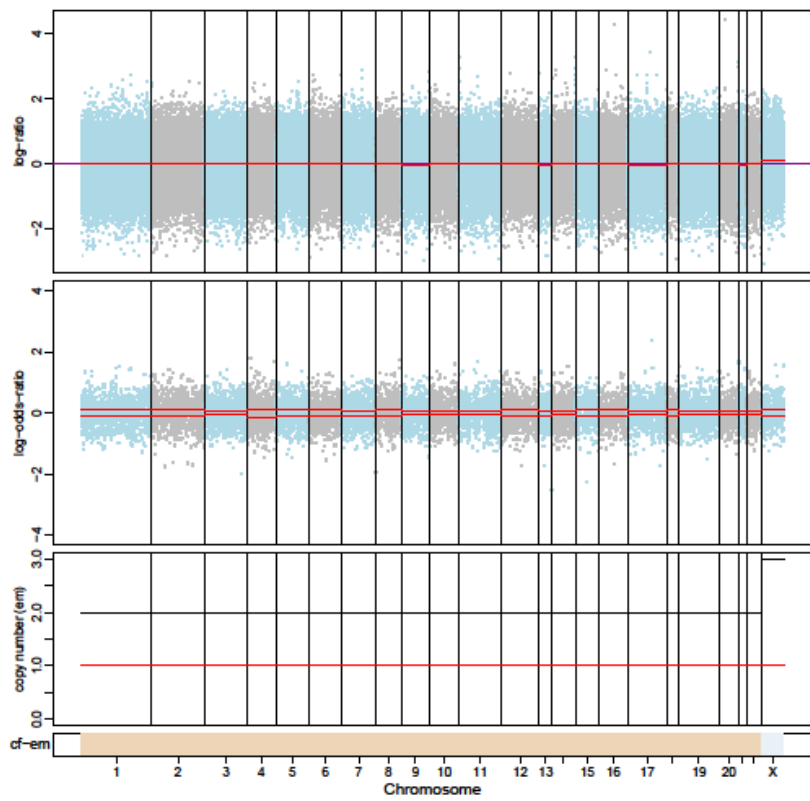
930-P2



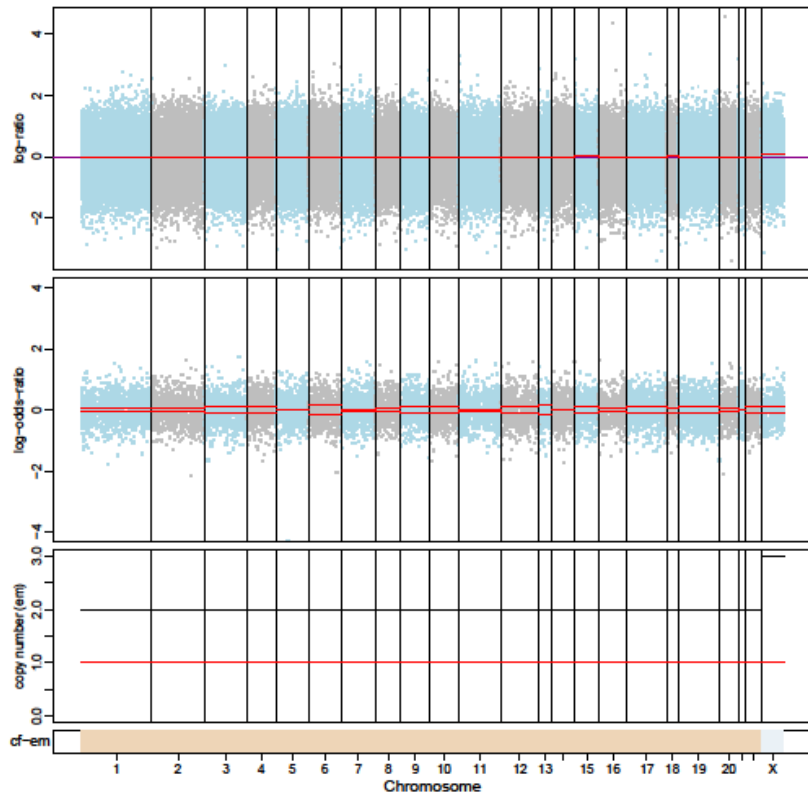
930-P3



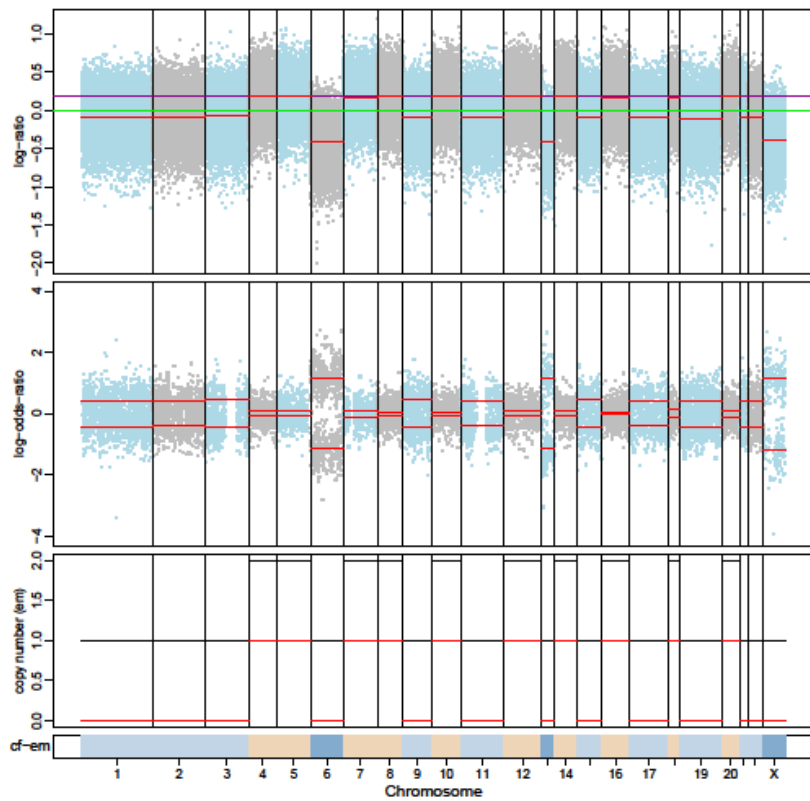
930-LR1



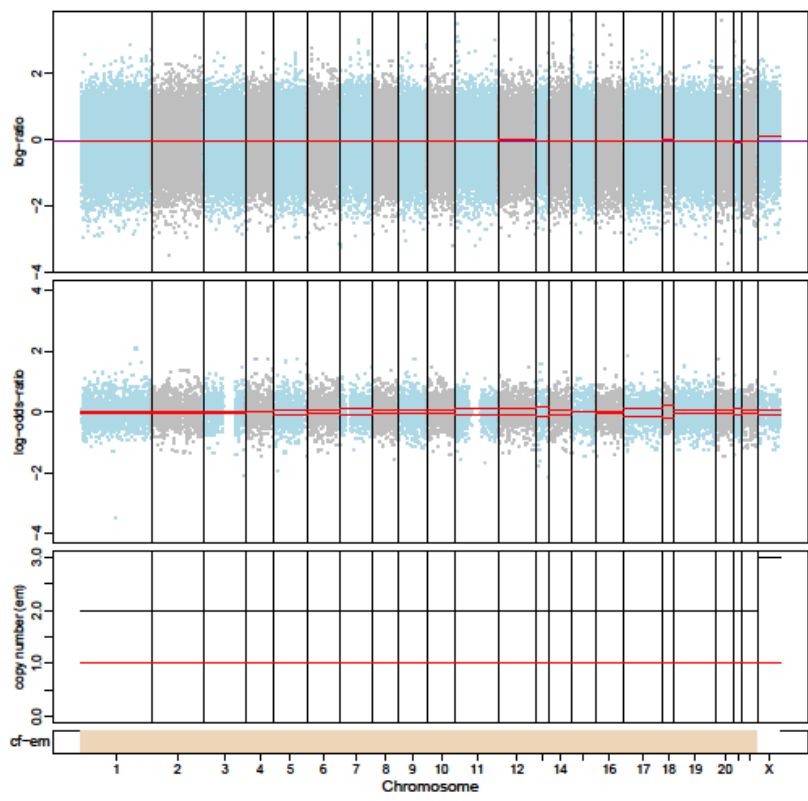
930-LR2



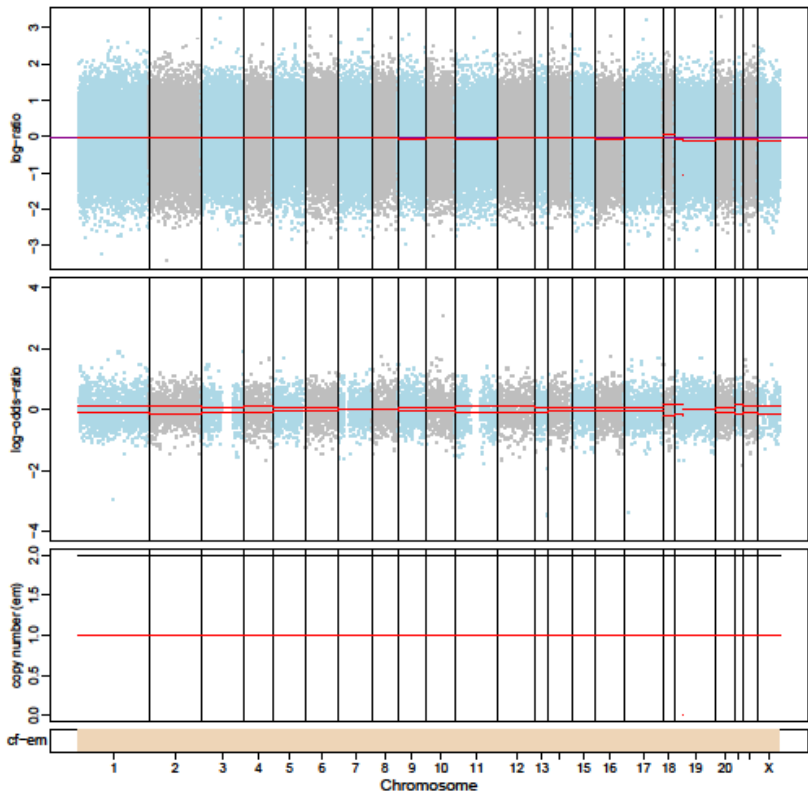
931-P0



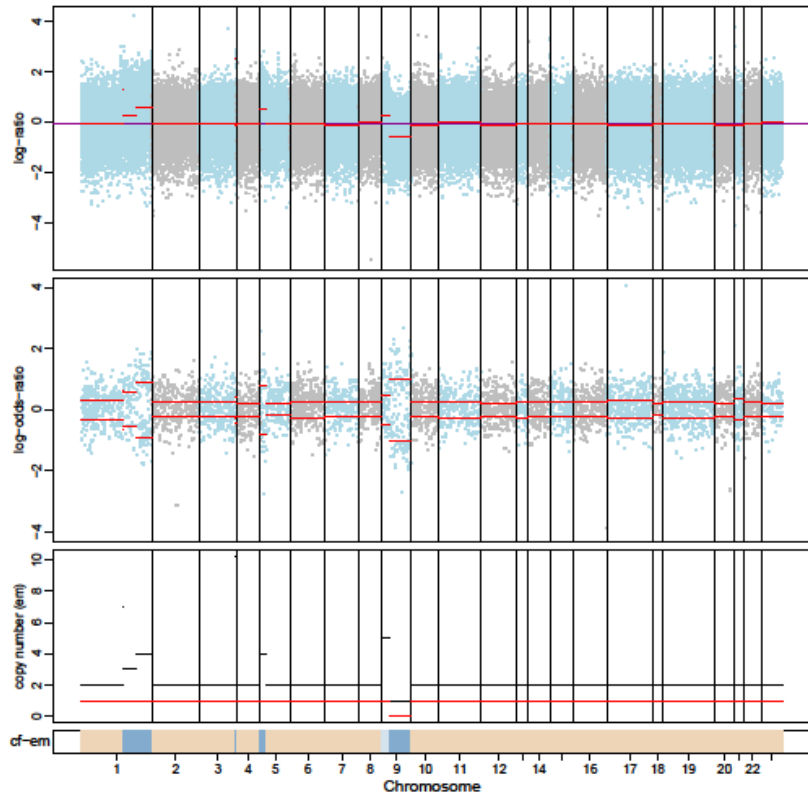
931-P1



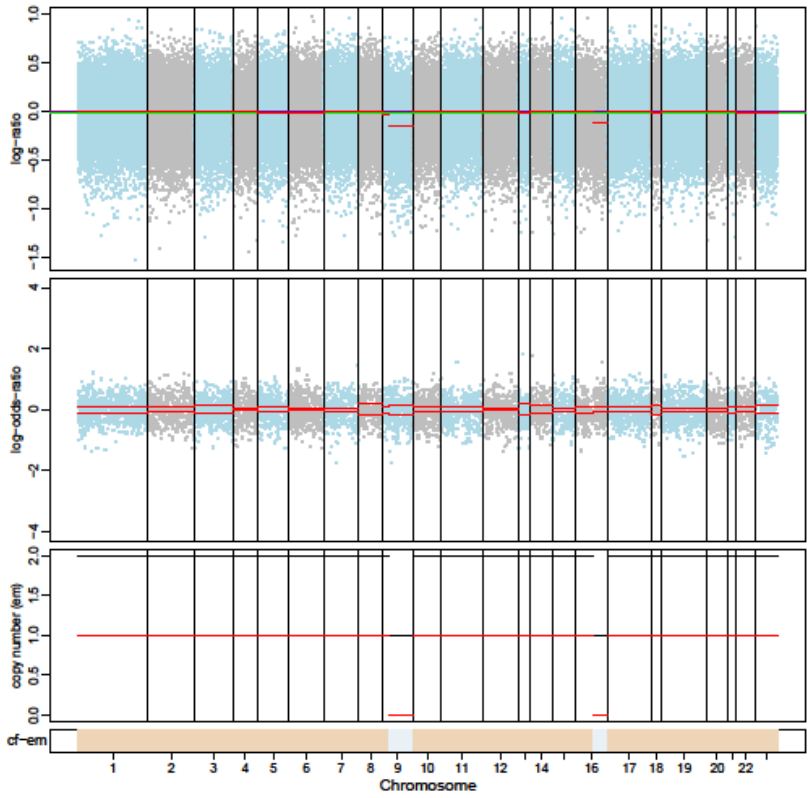
931-P2



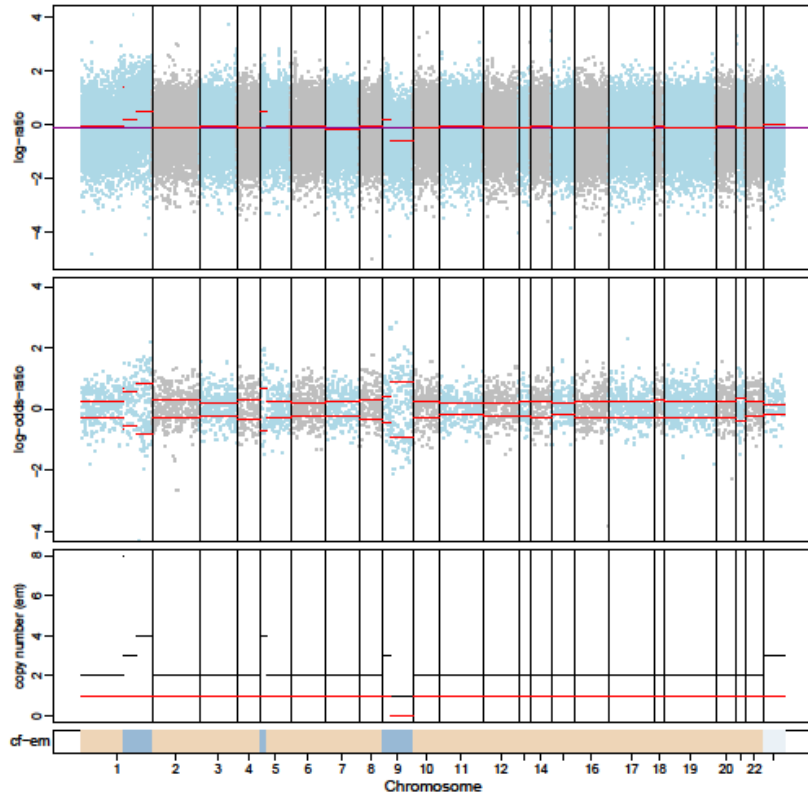
962-P



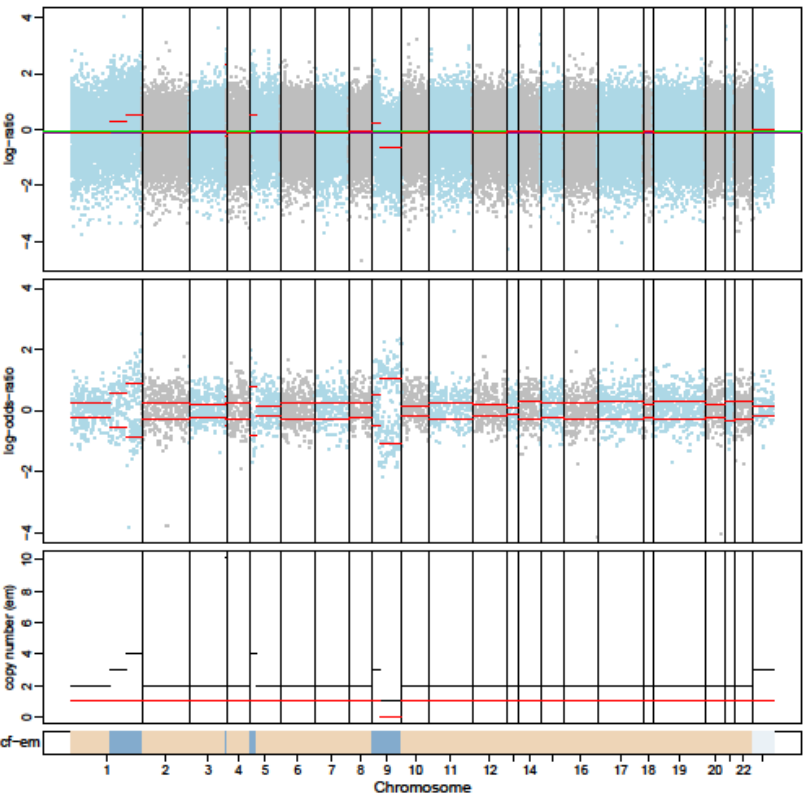
962-P0



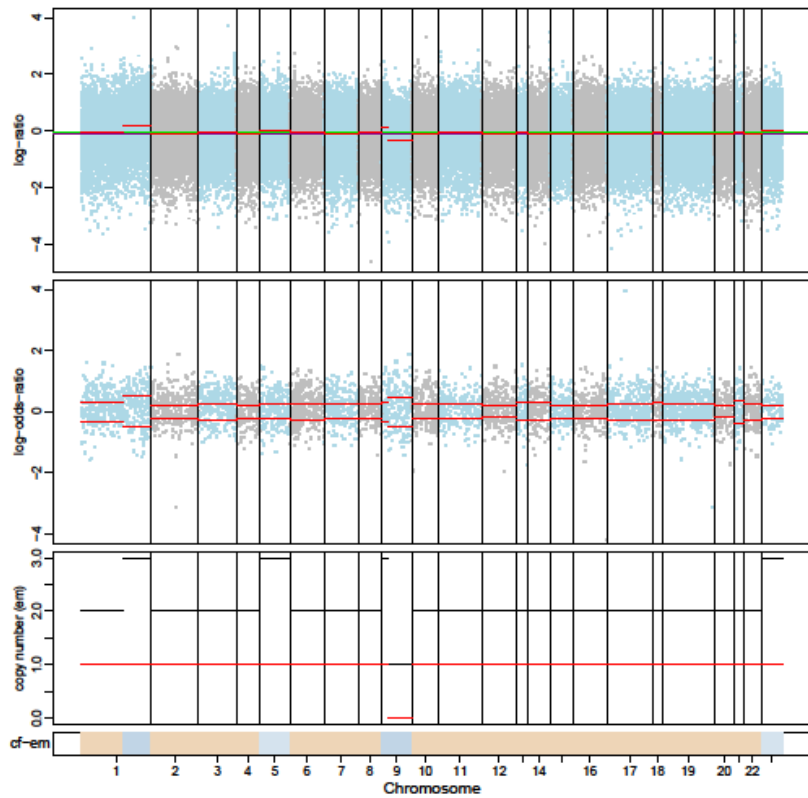
962-P1



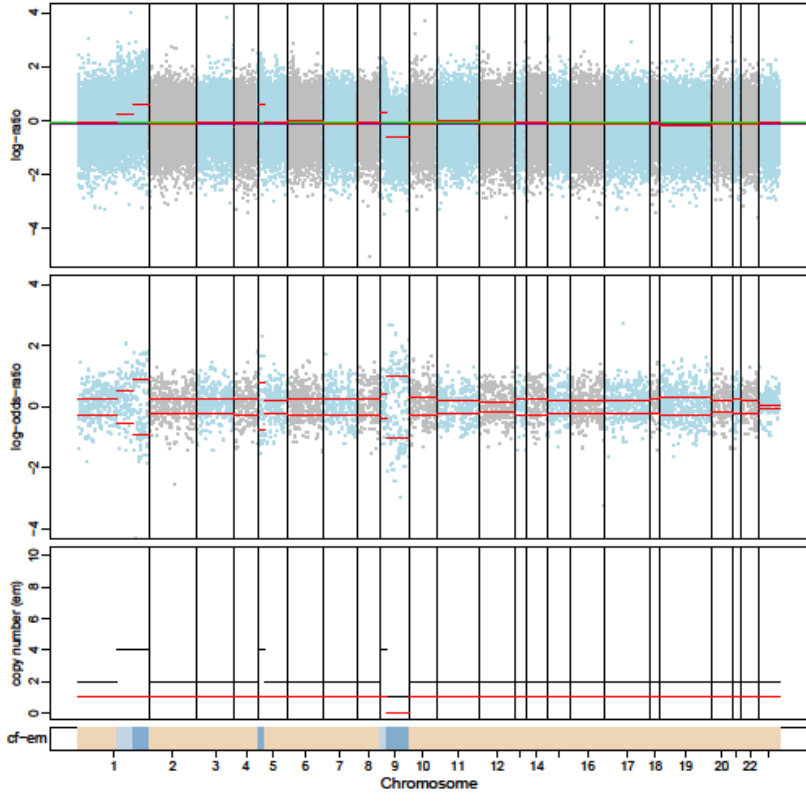
962-P2



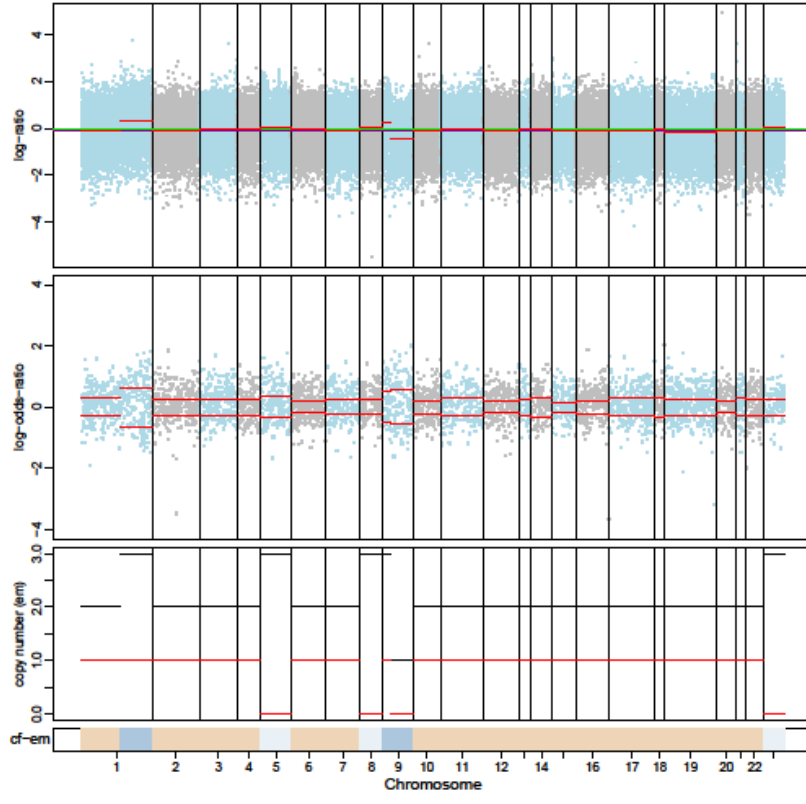
962-P3



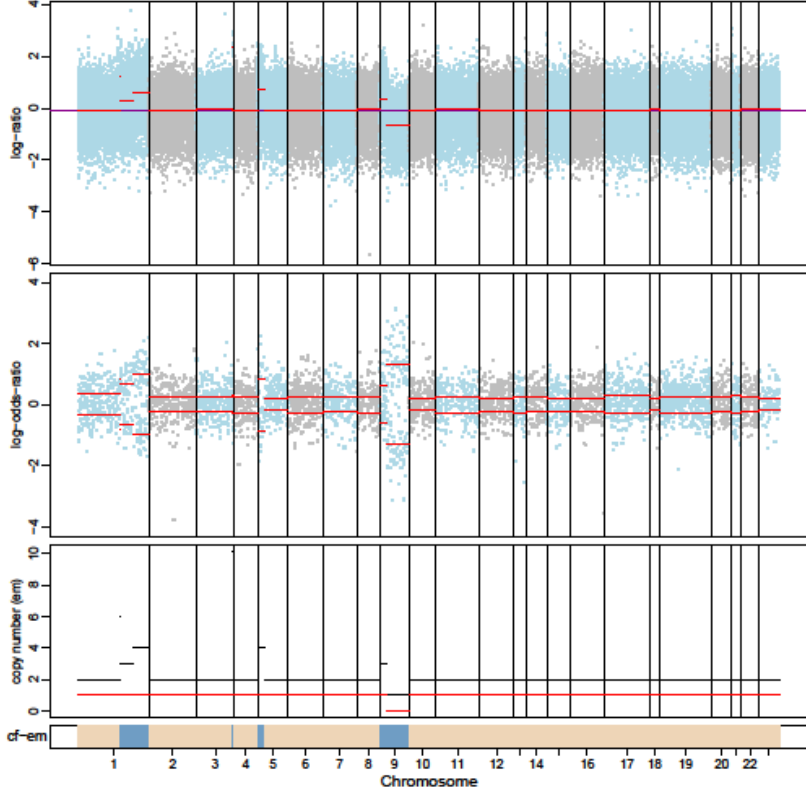
962-P4



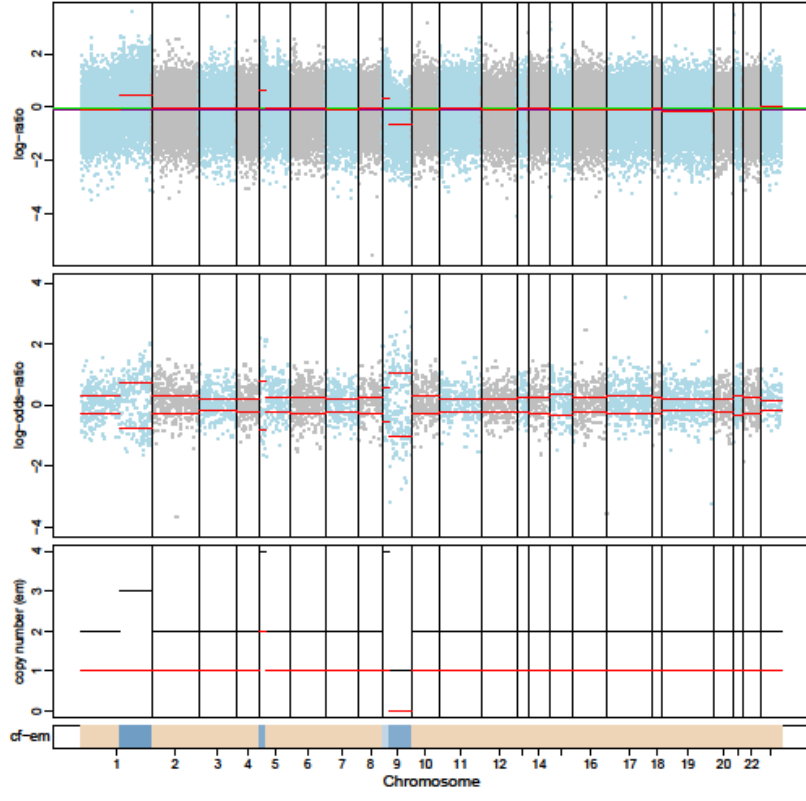
962-P5



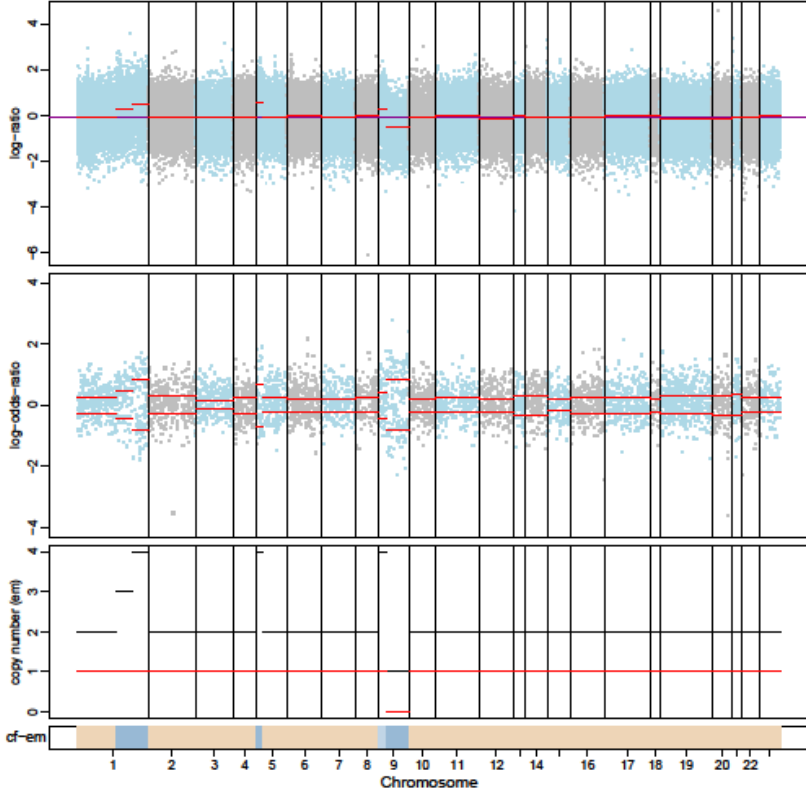
962-LR



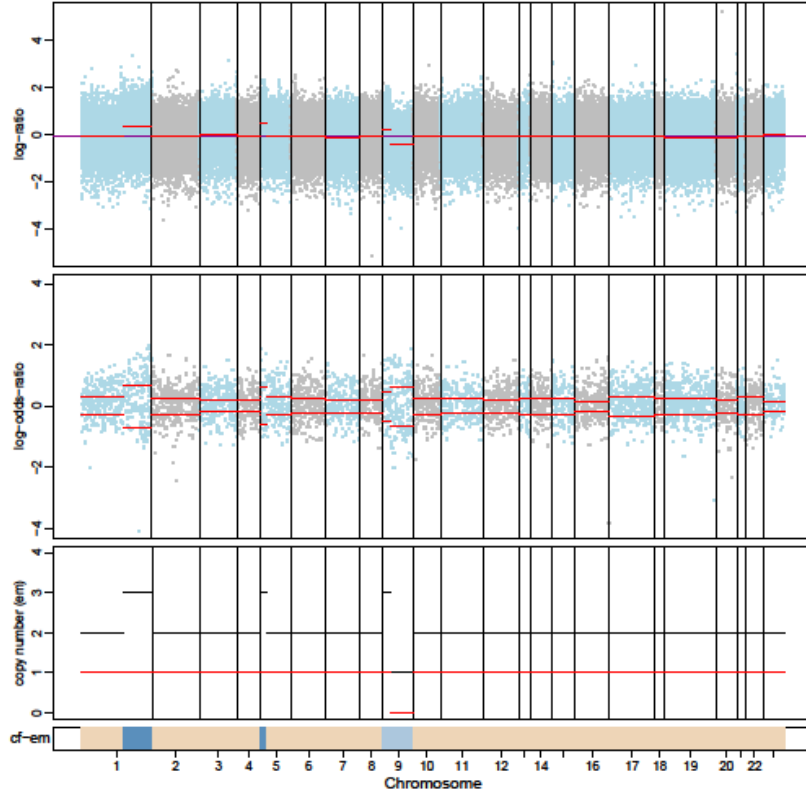
962-LR1



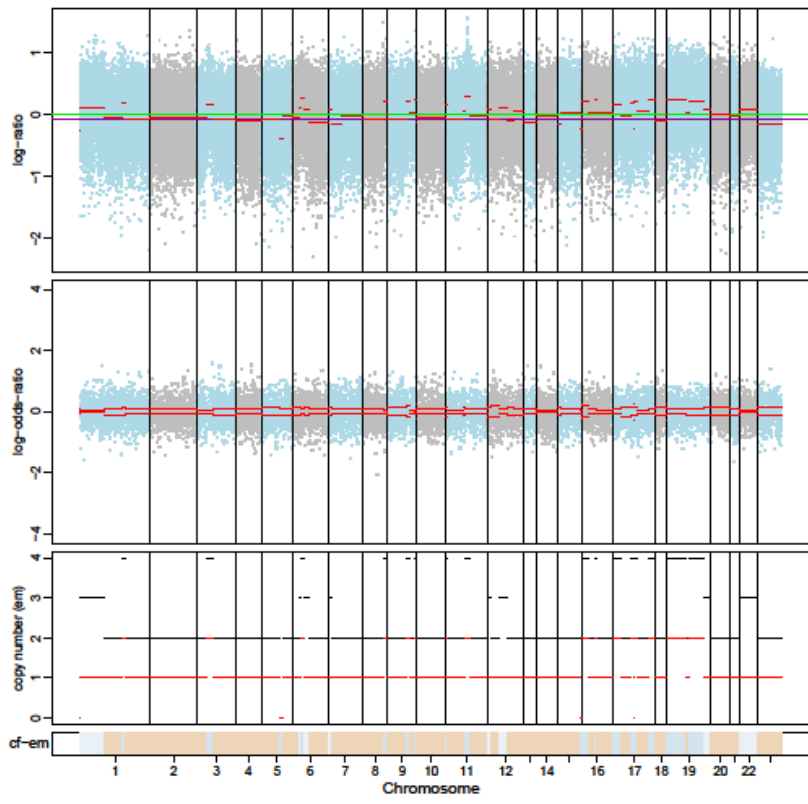
962-LR2



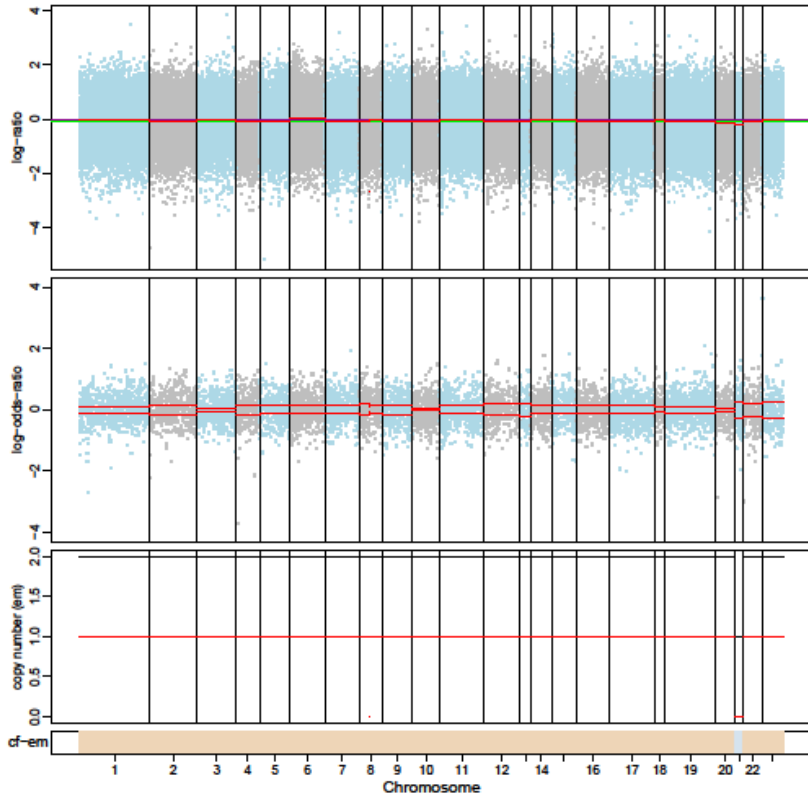
962-LR3



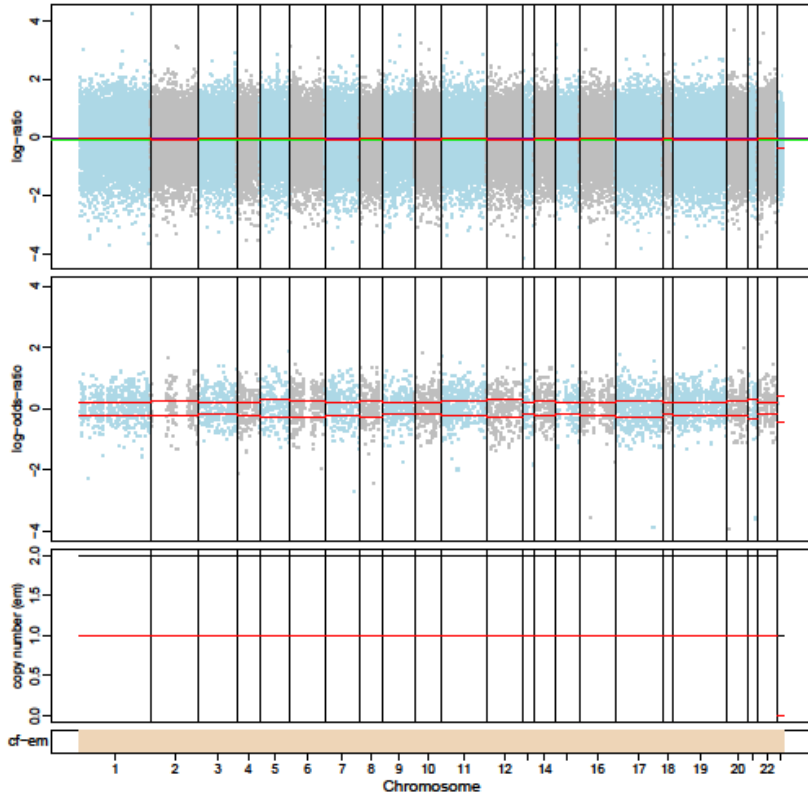
972-P0



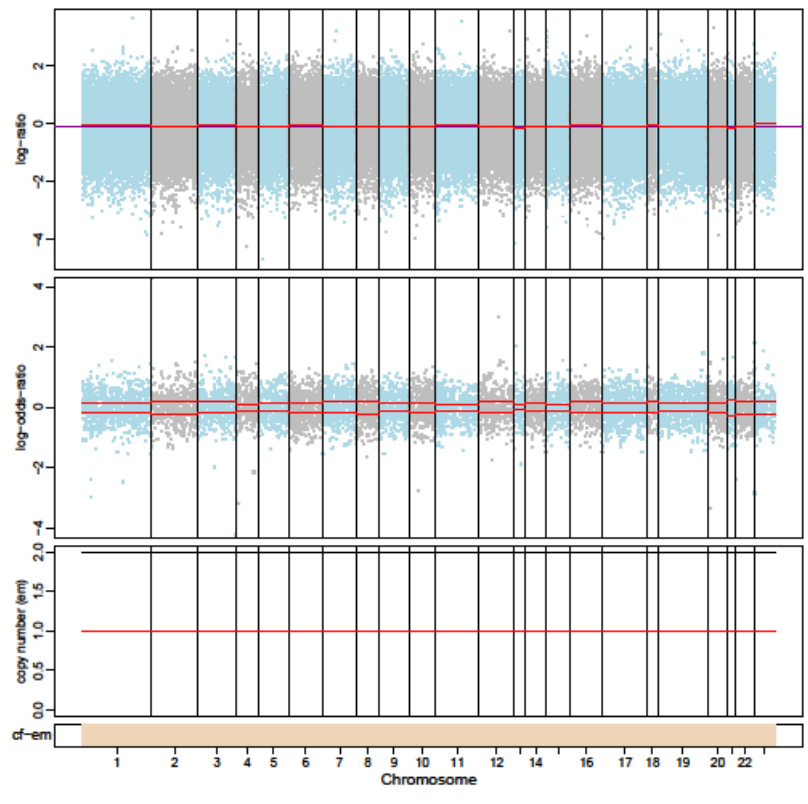
972-P2



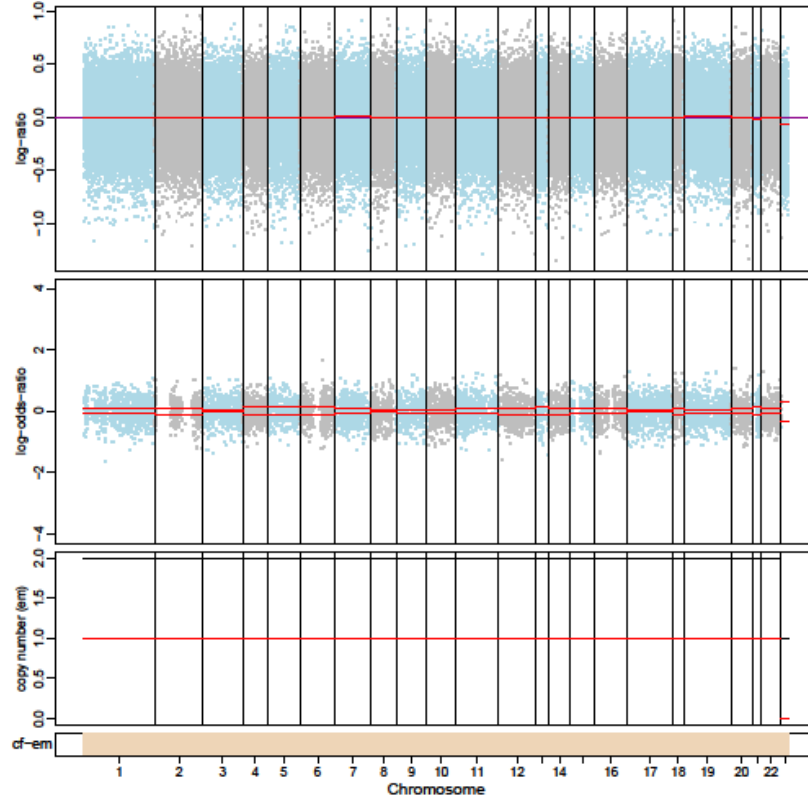
973-P1



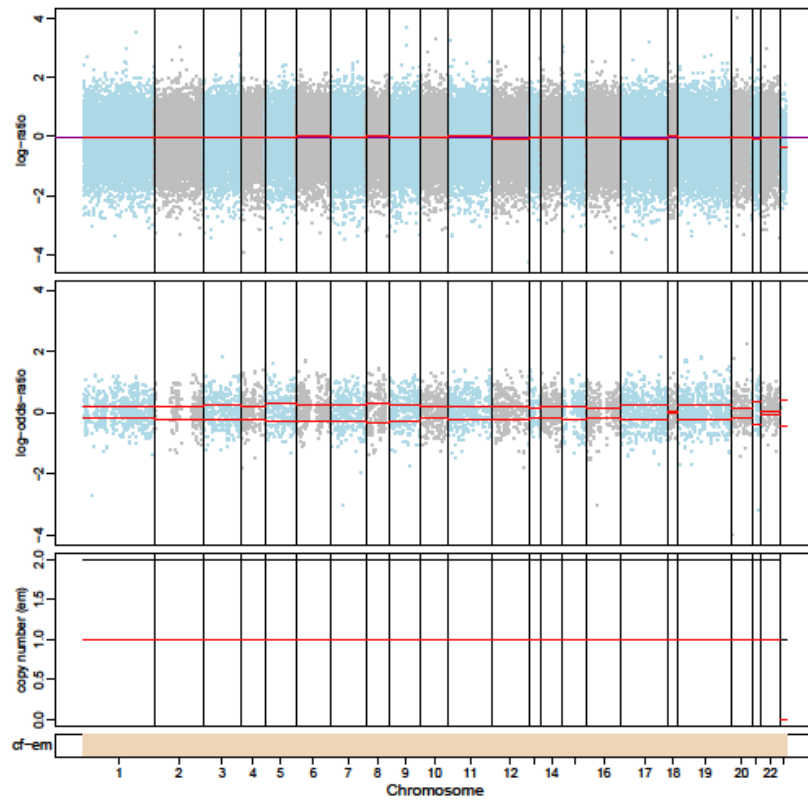
972-P1



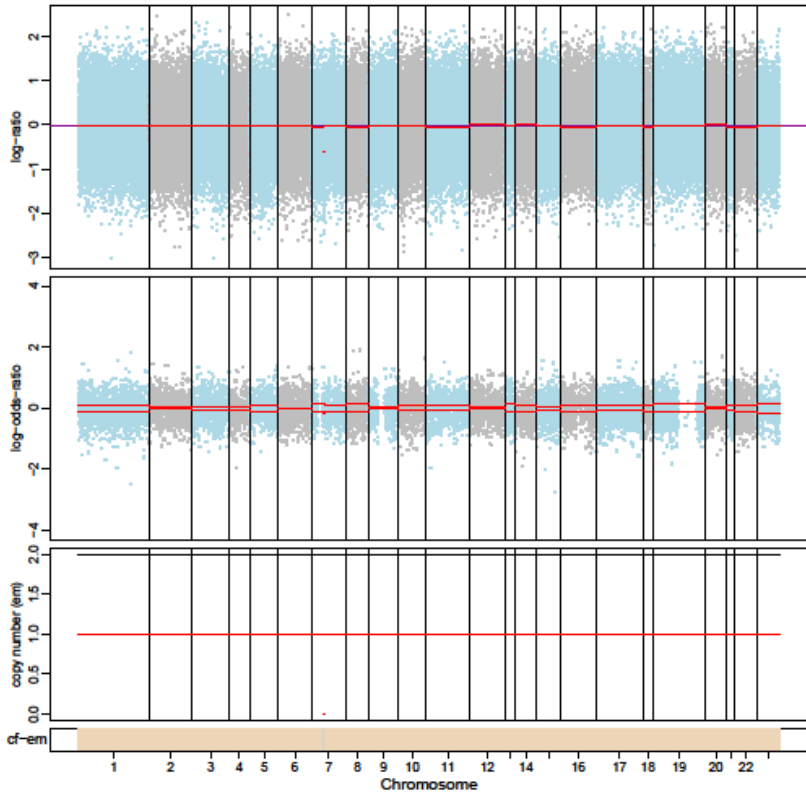
973-P0



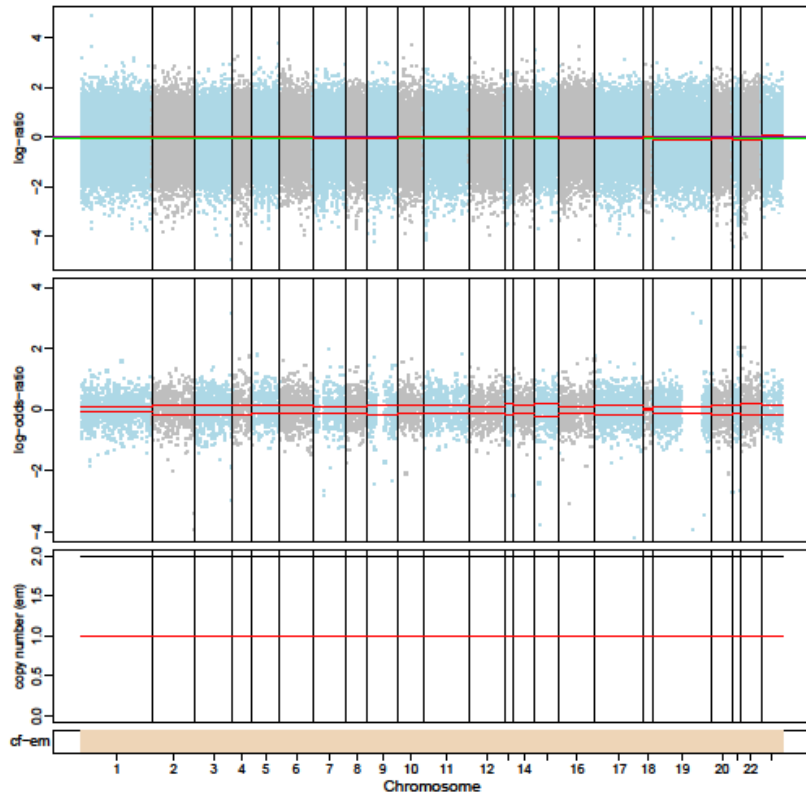
973-P2



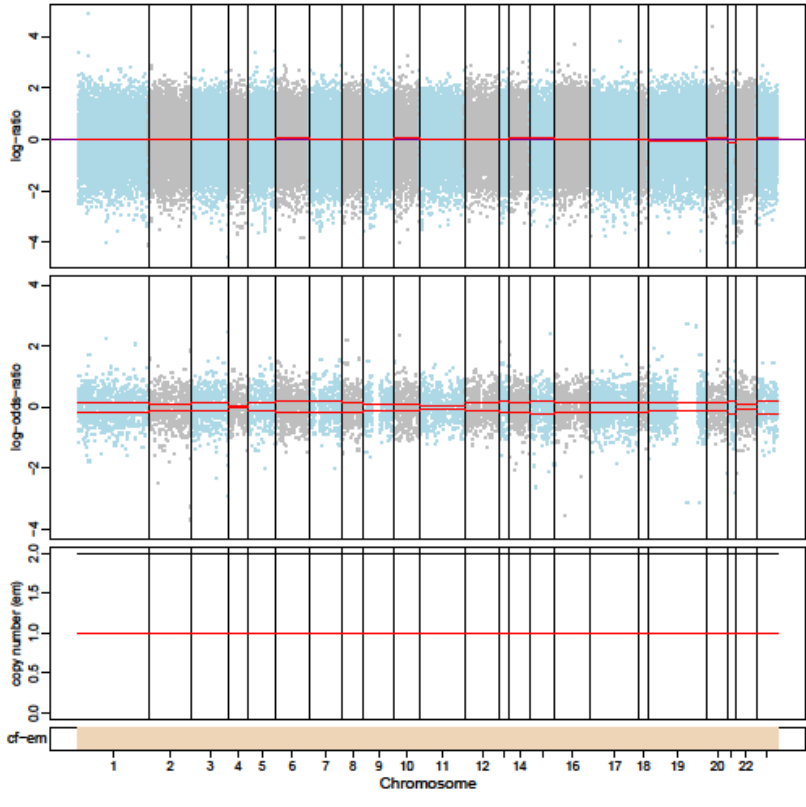
1182-P0



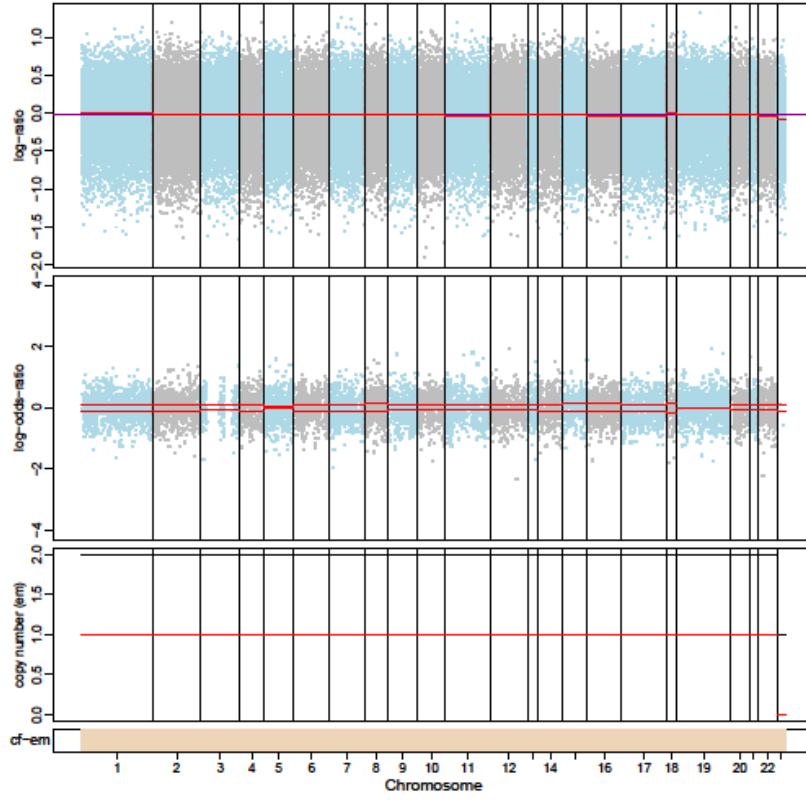
1182-P1



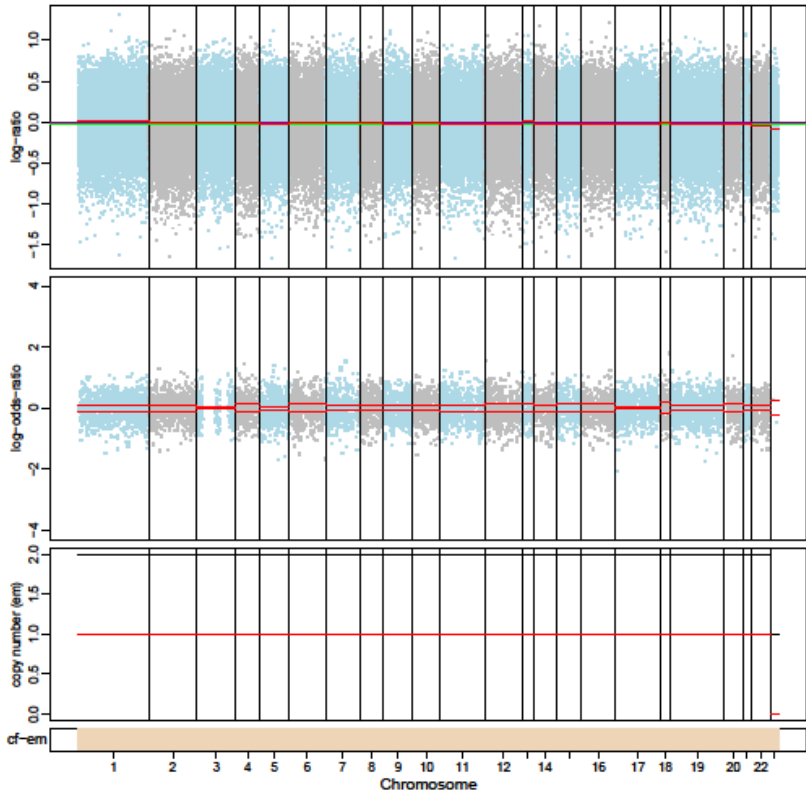
1182-P2



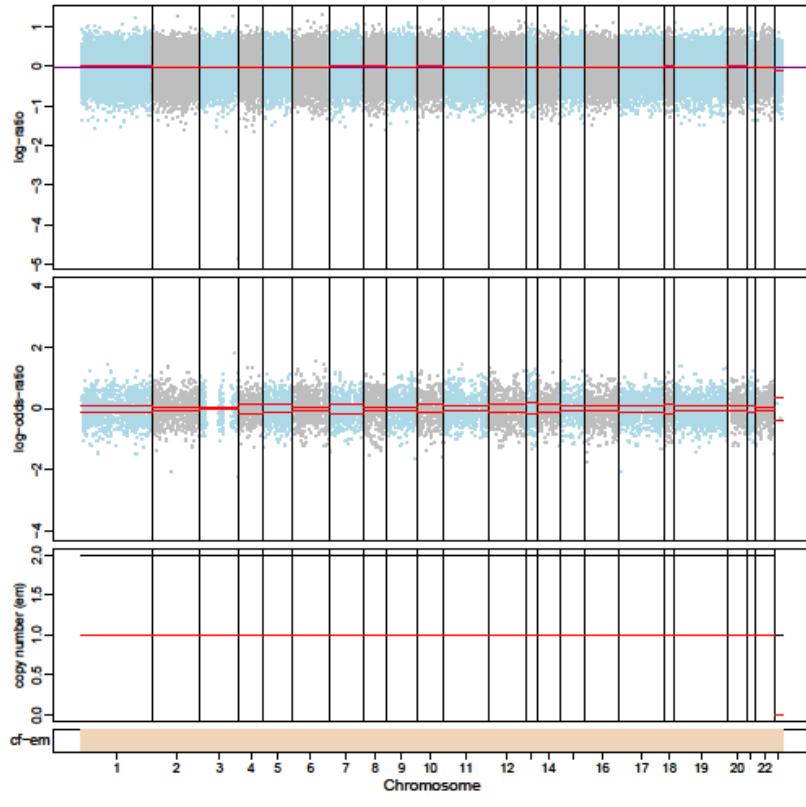
1002-P



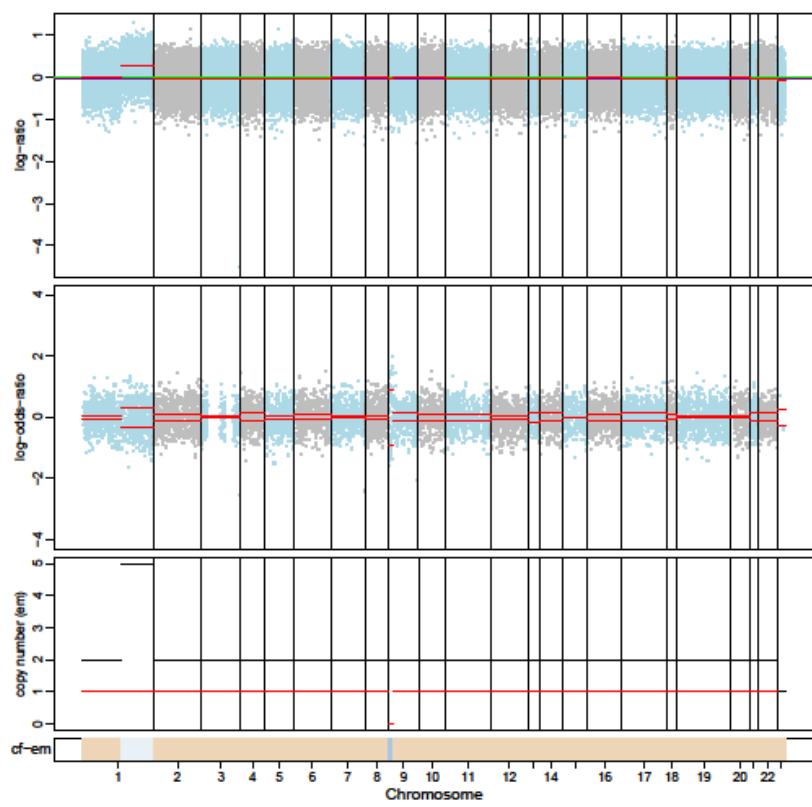
1002-P1



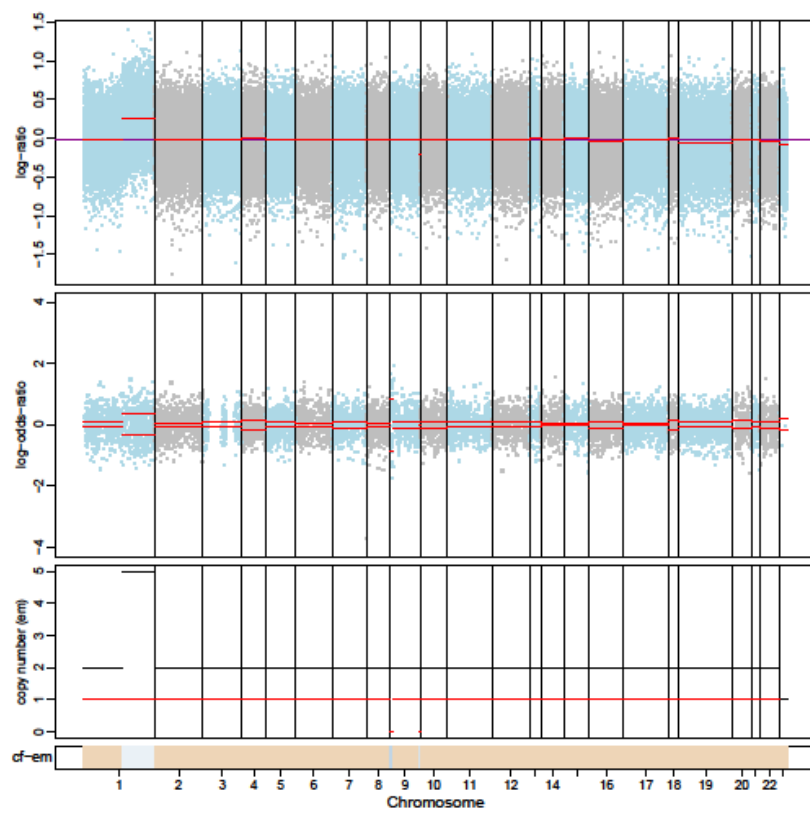
1002-P2



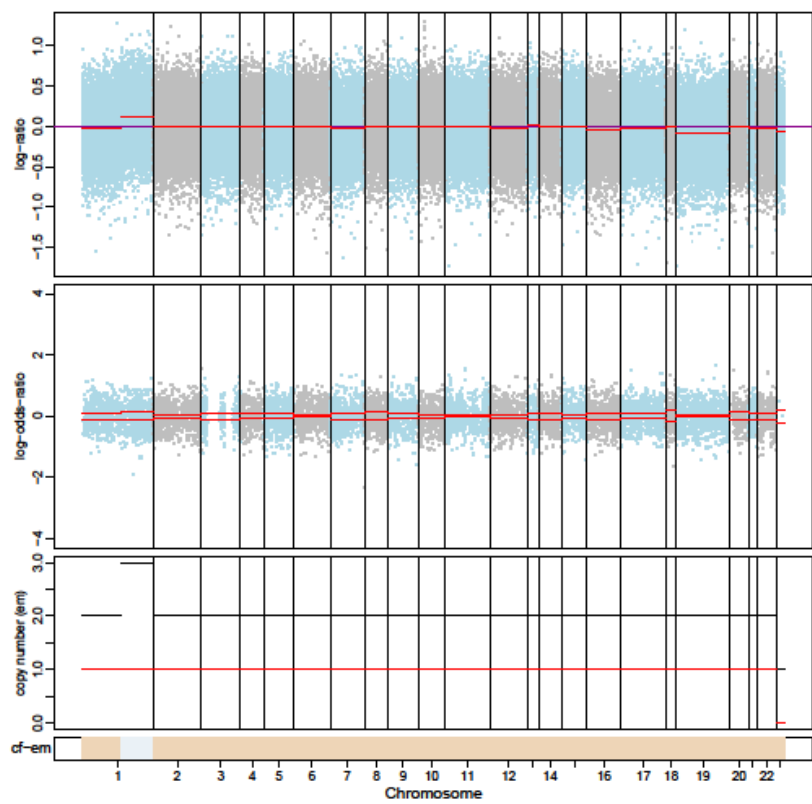
1002-LR



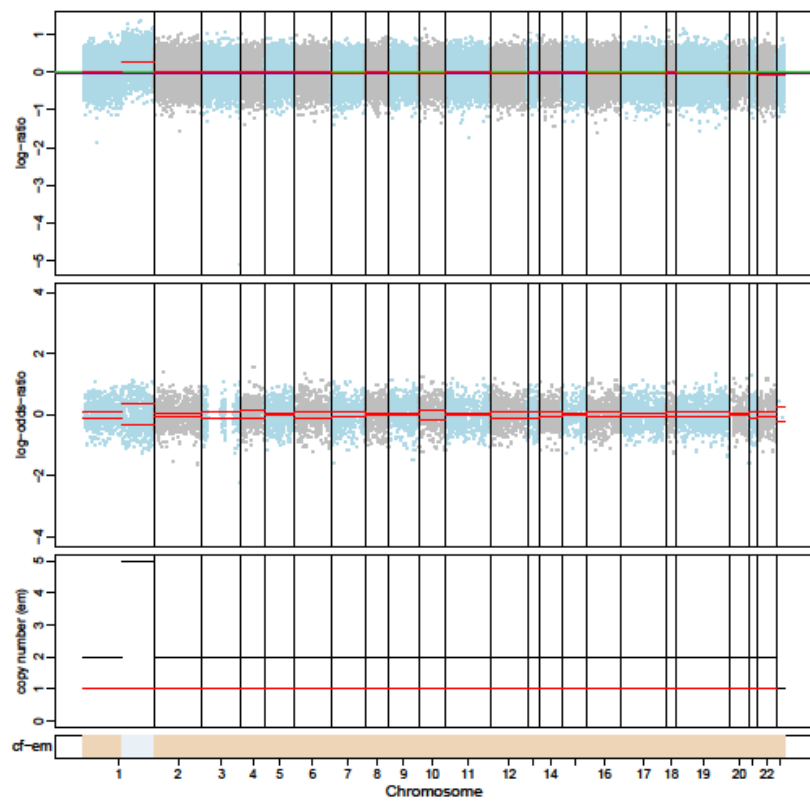
1002-LR1



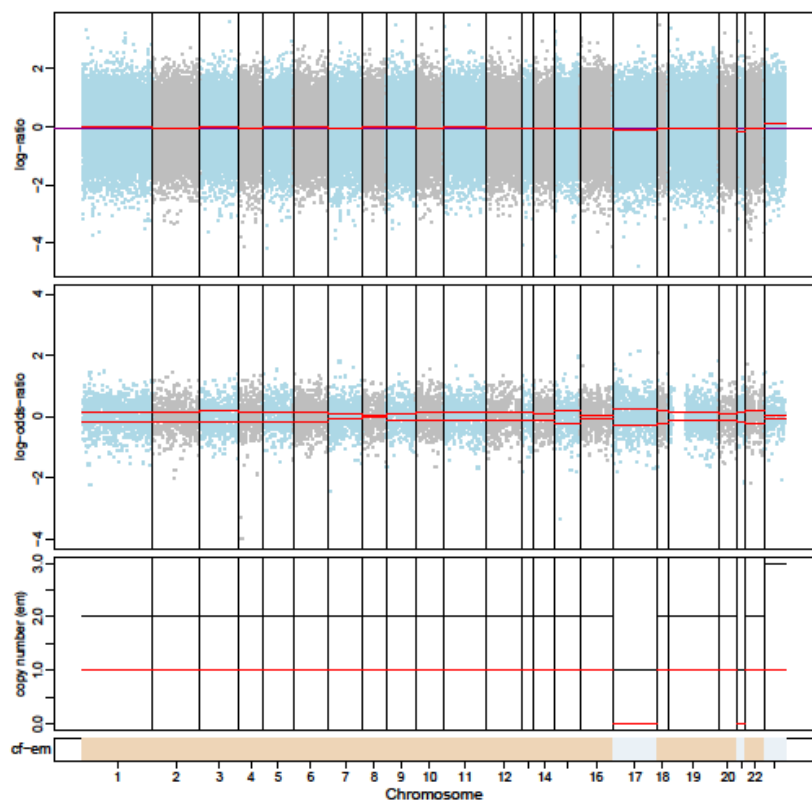
1002-LR2



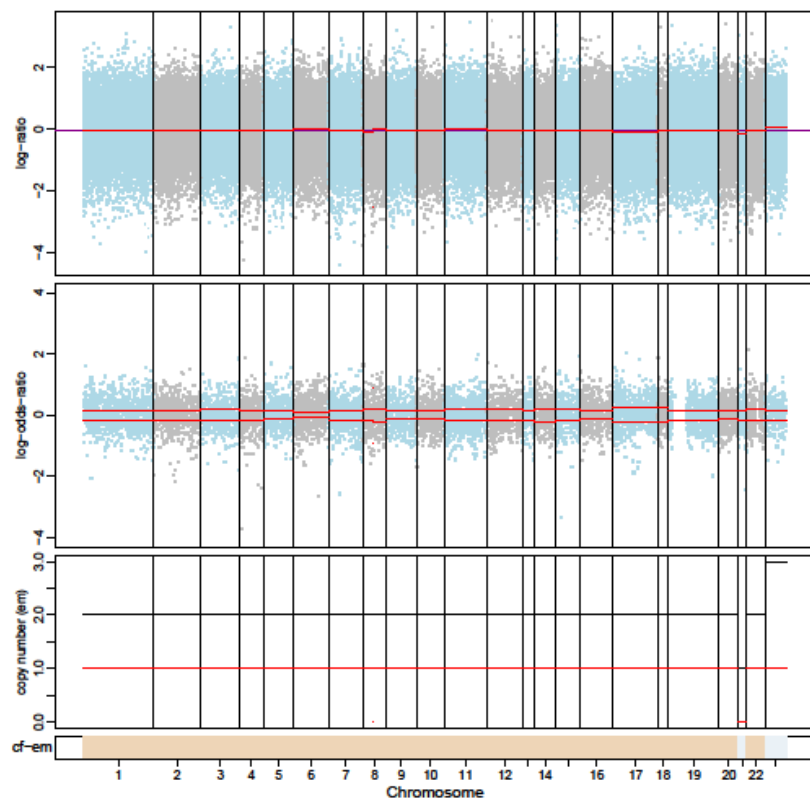
1002-LR3



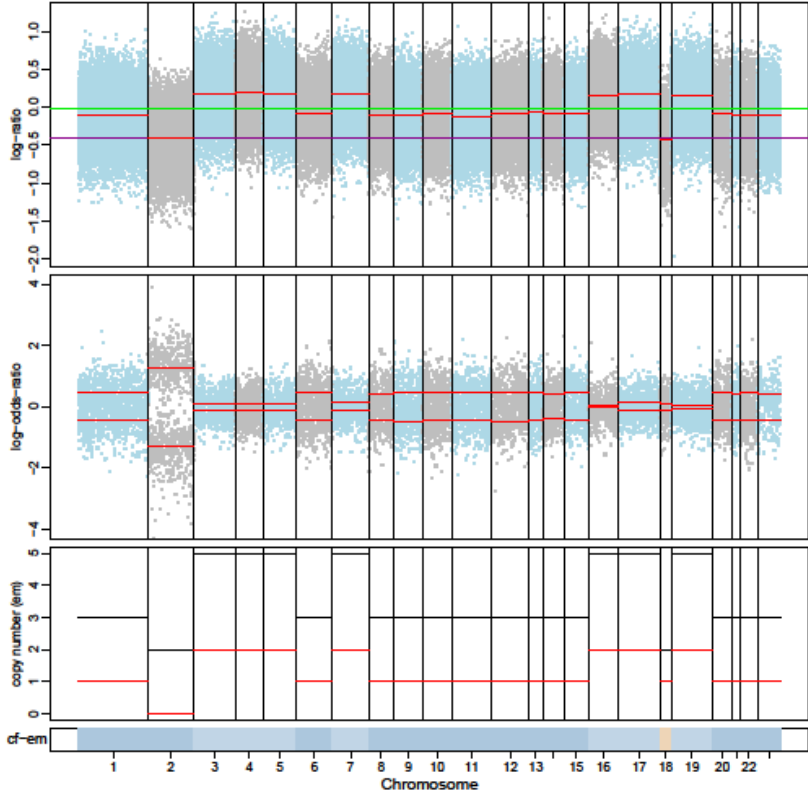
1012-P1



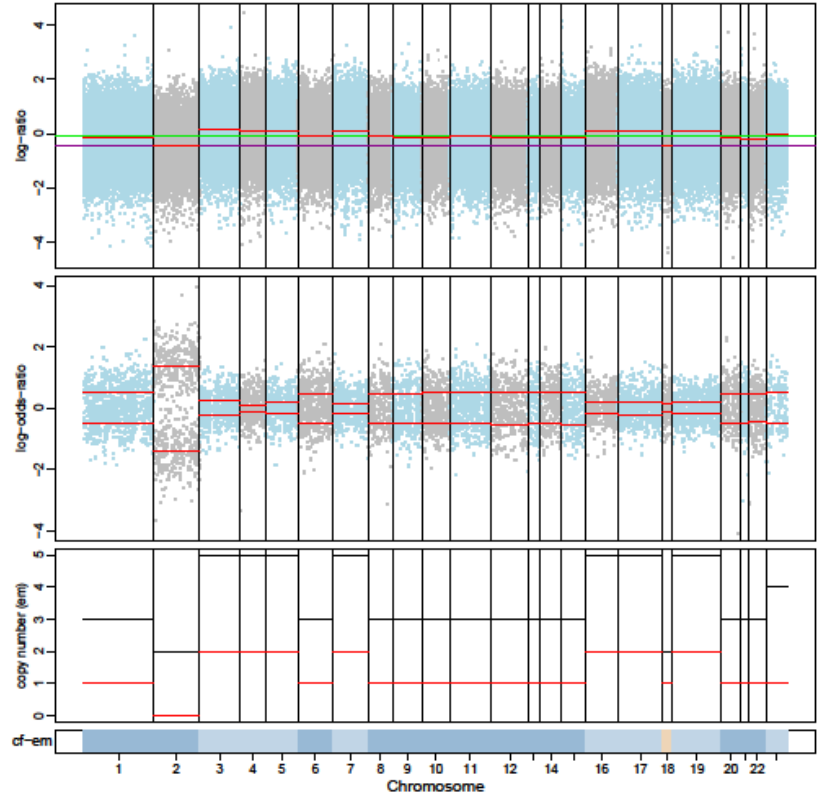
1012-P2



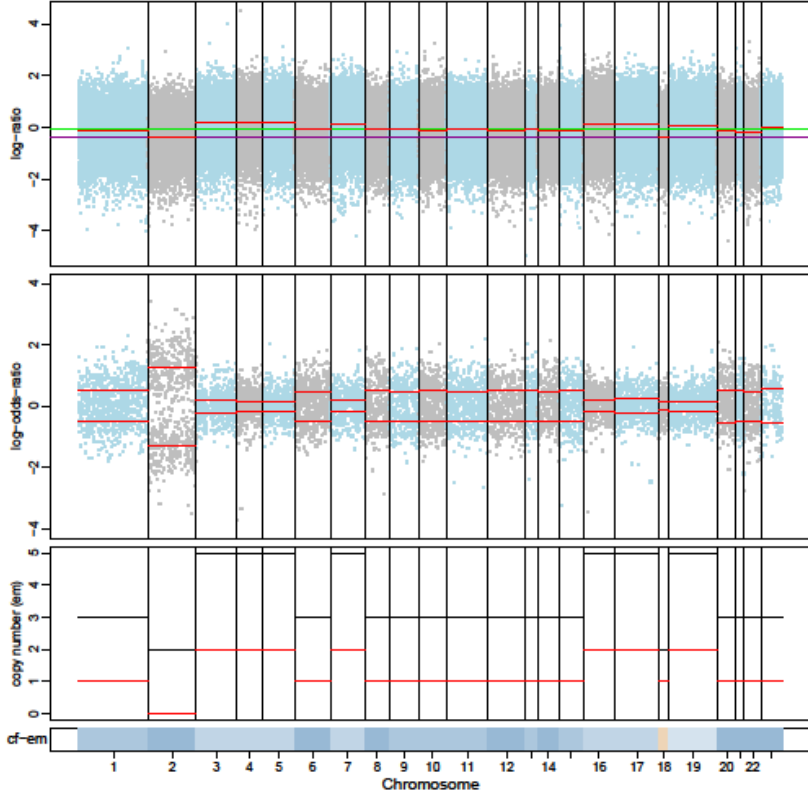
1036-P0



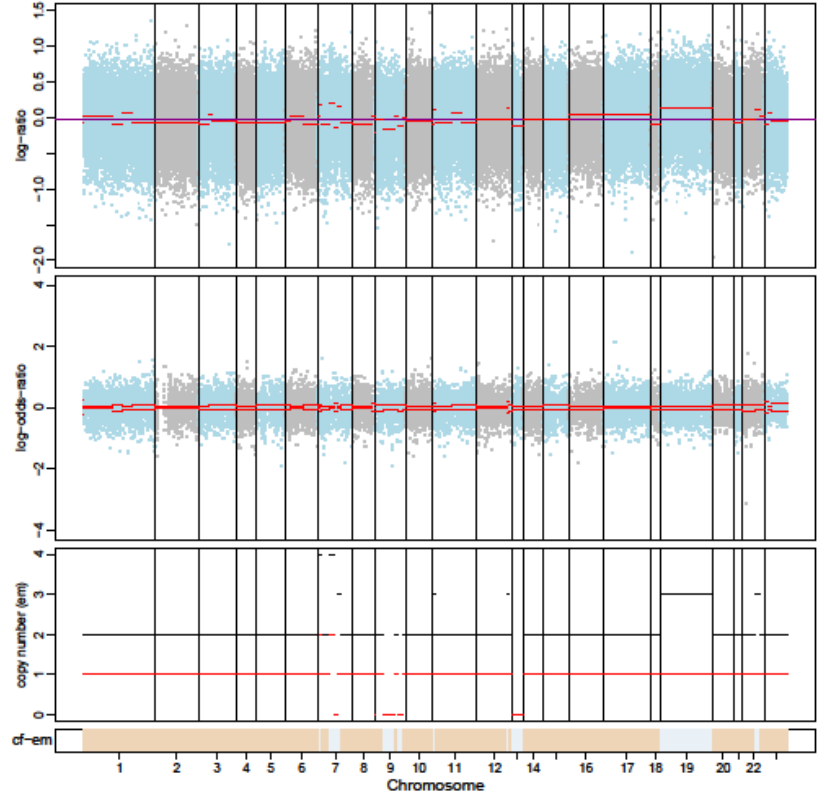
1036-P1



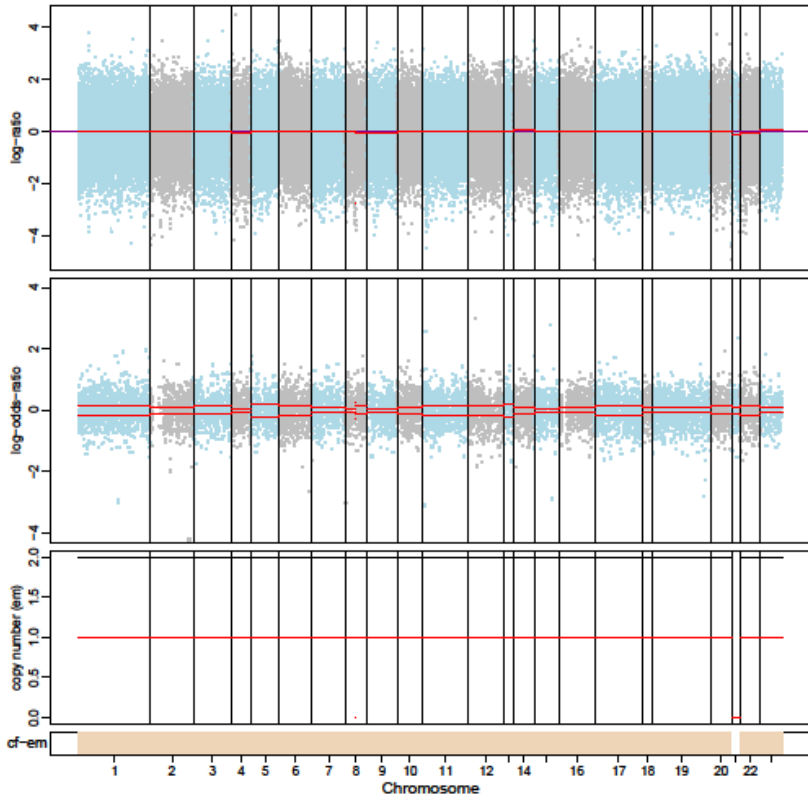
1036-P2



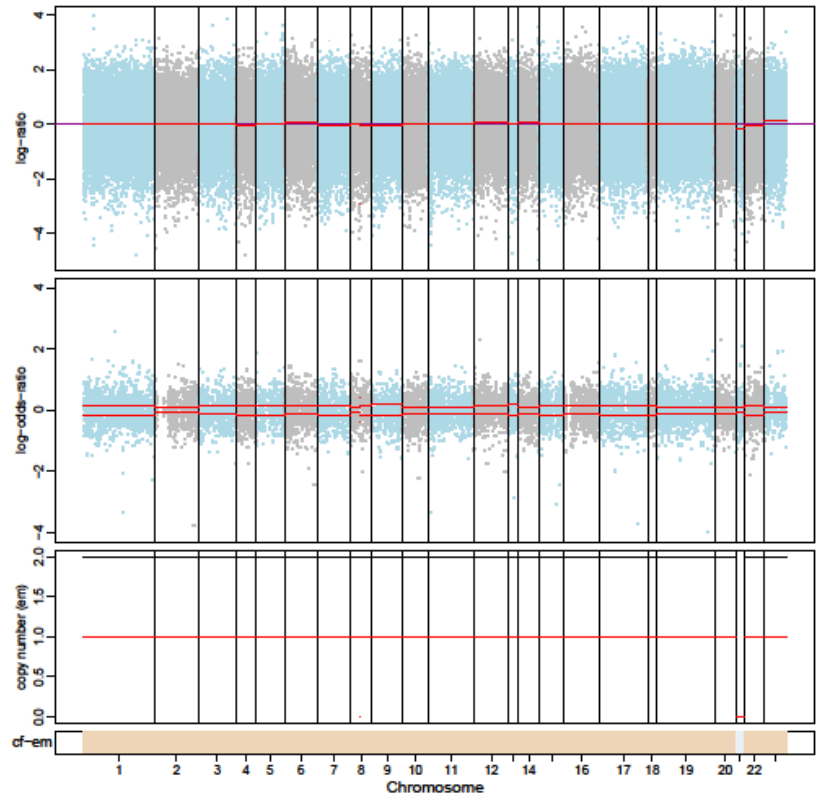
1049-P0



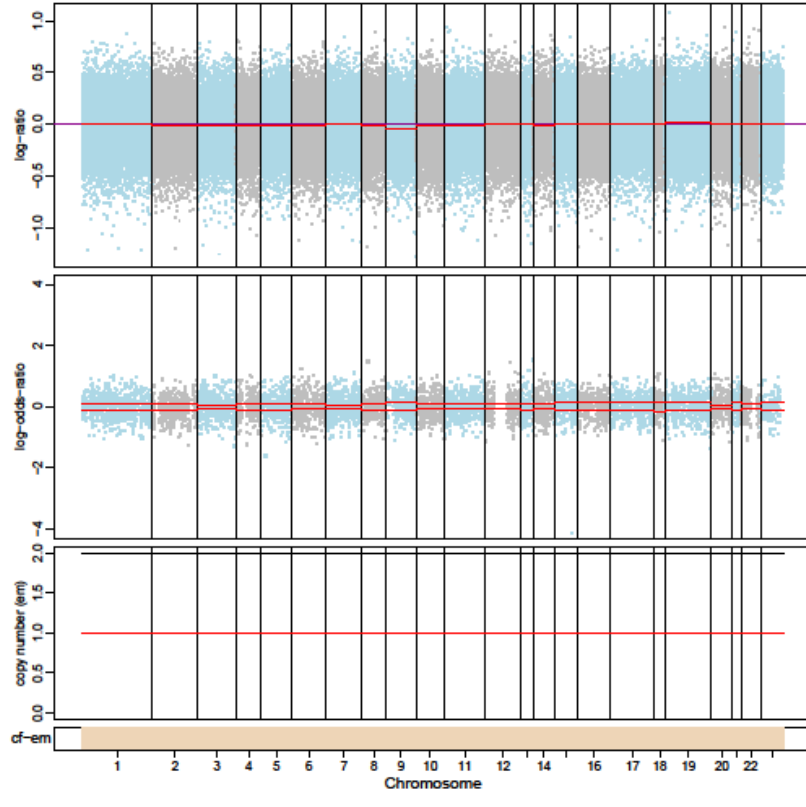
1049-P1



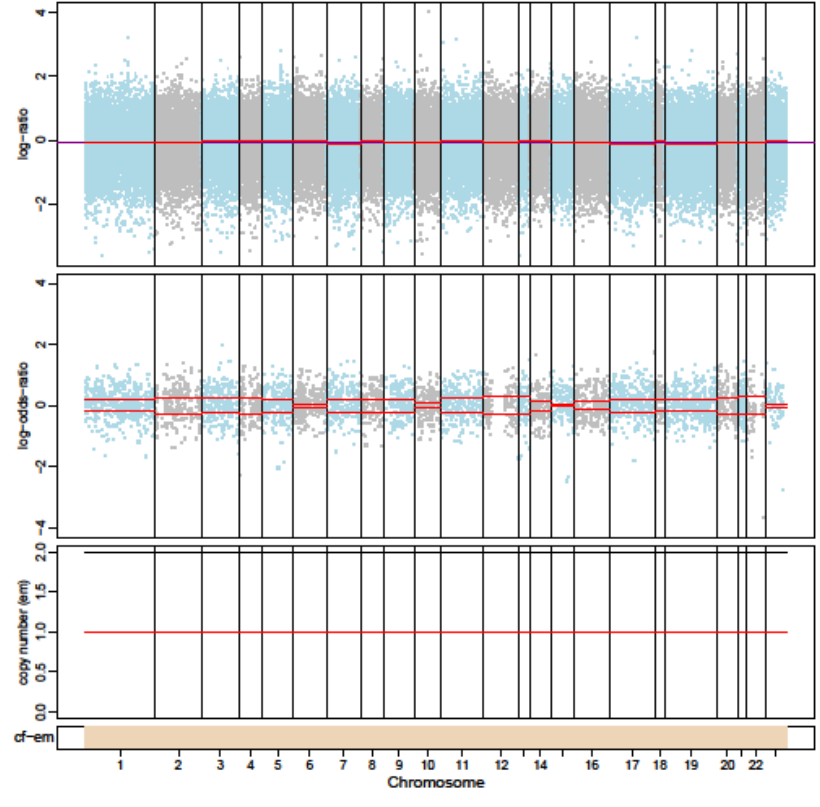
1049-P2



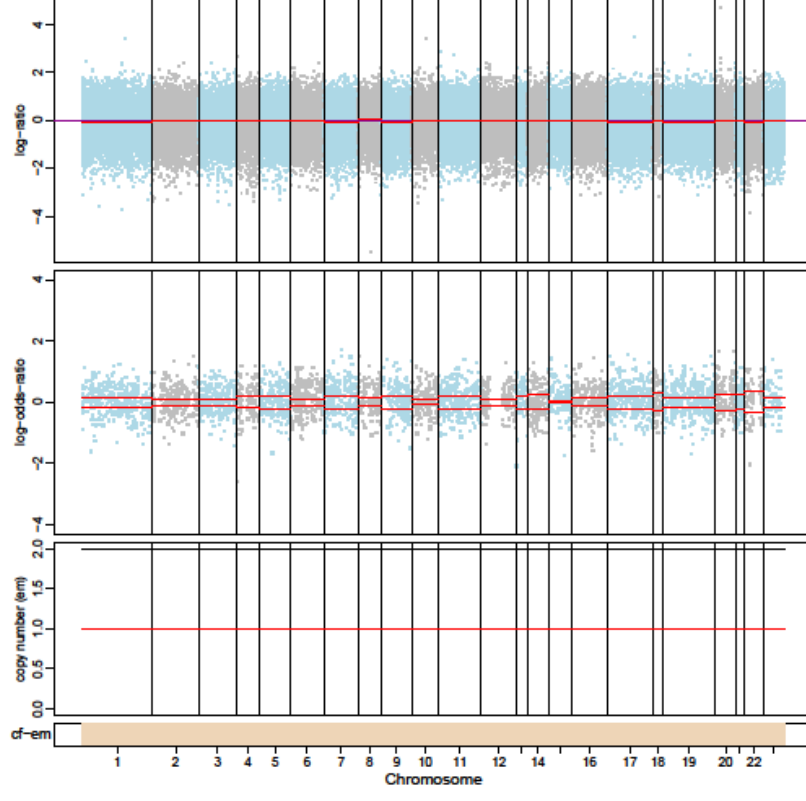
1099-P0



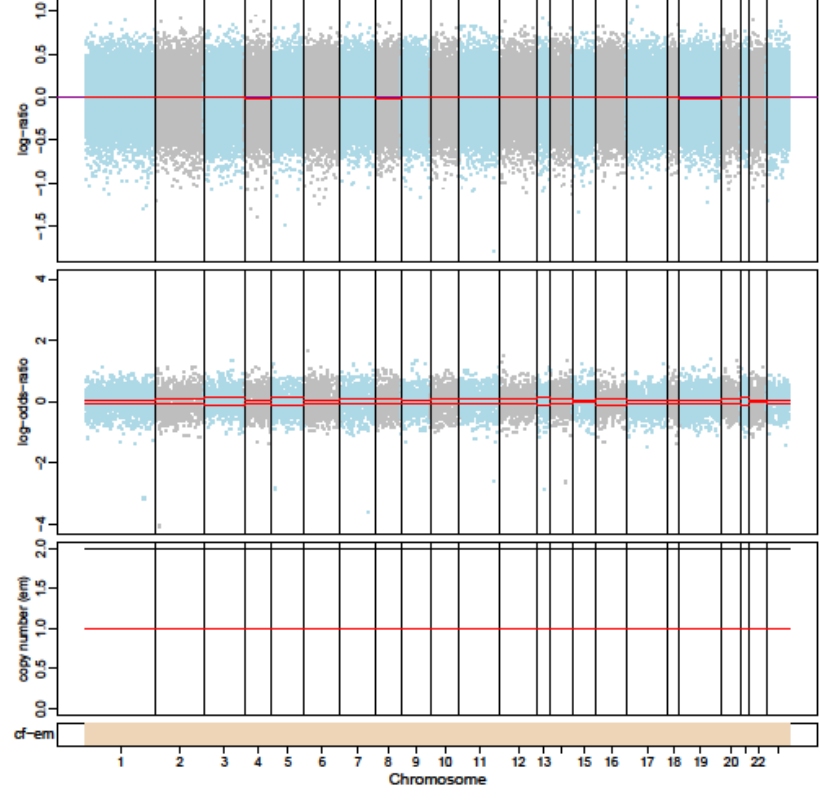
1099-P1



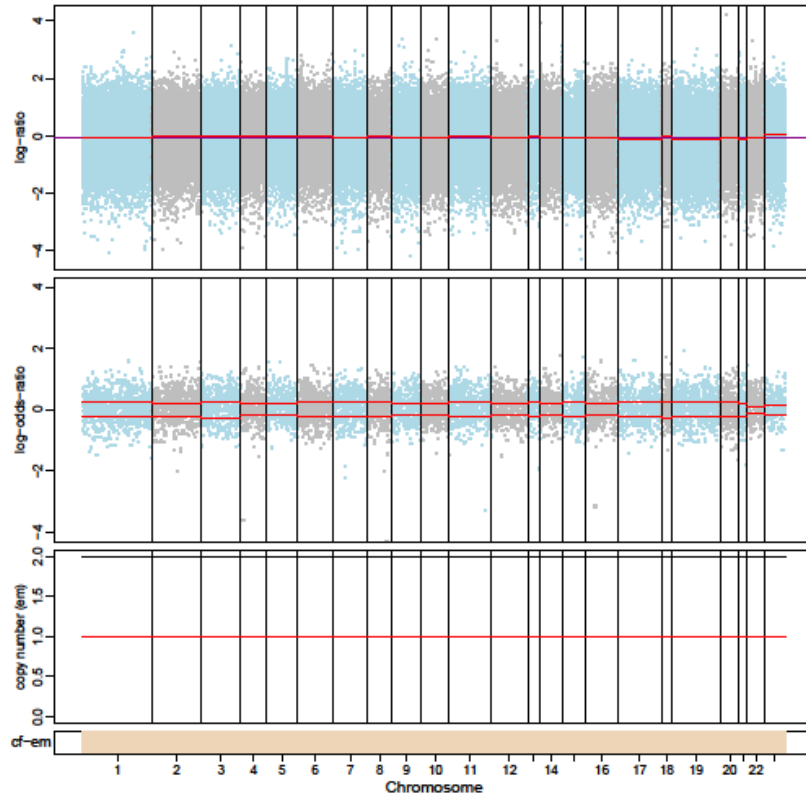
1099-P2



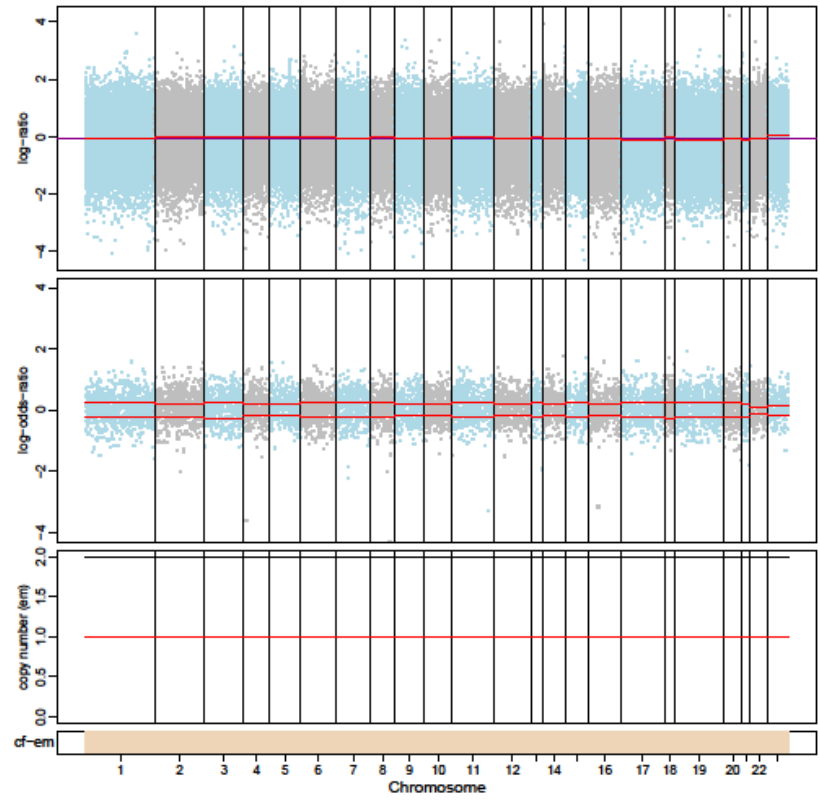
1143-P0



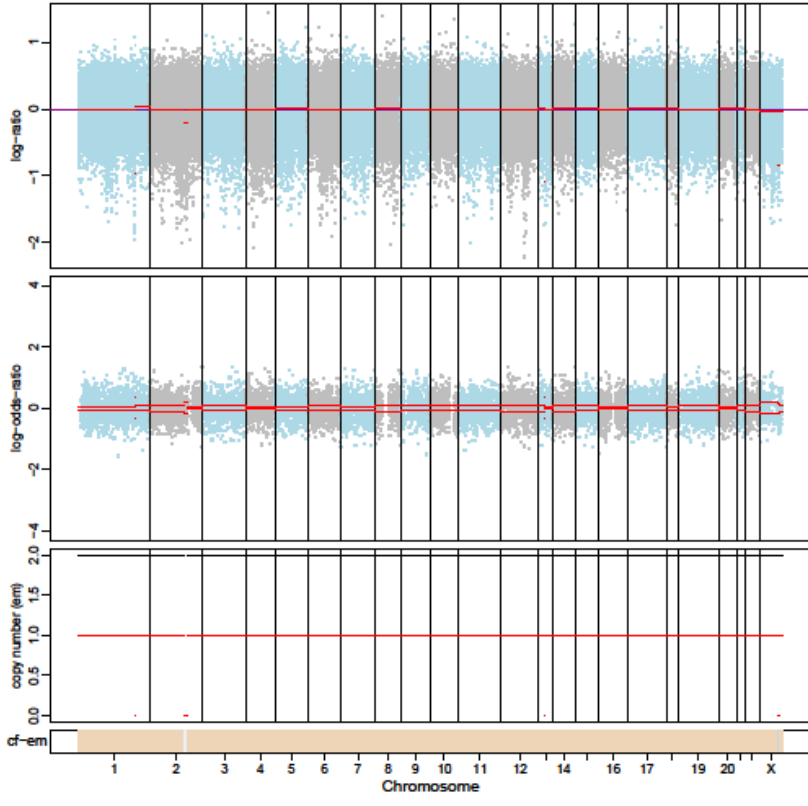
1143-P1



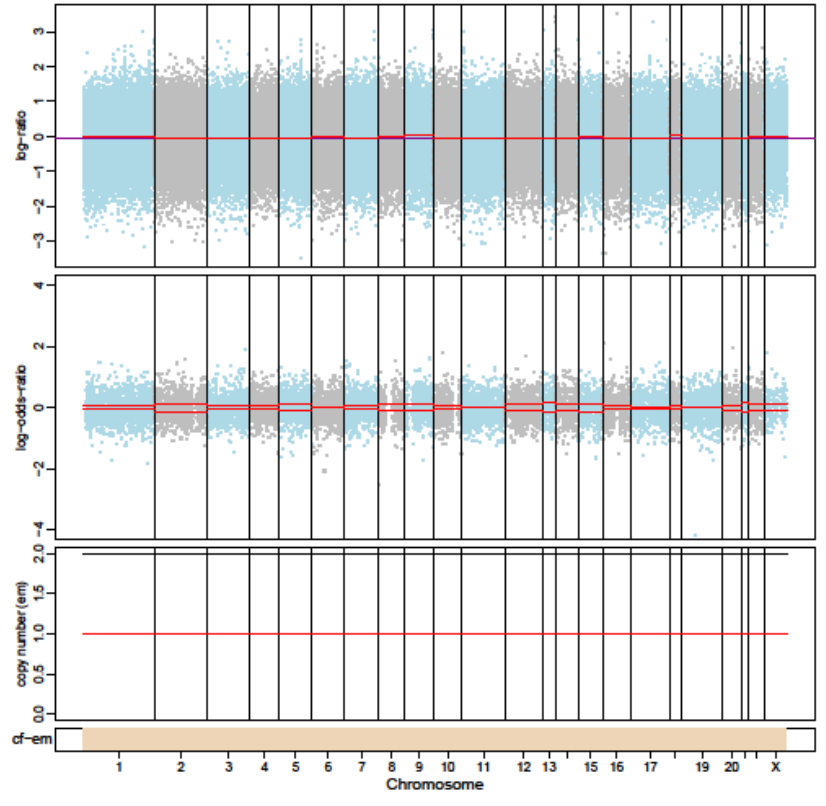
1143-P2



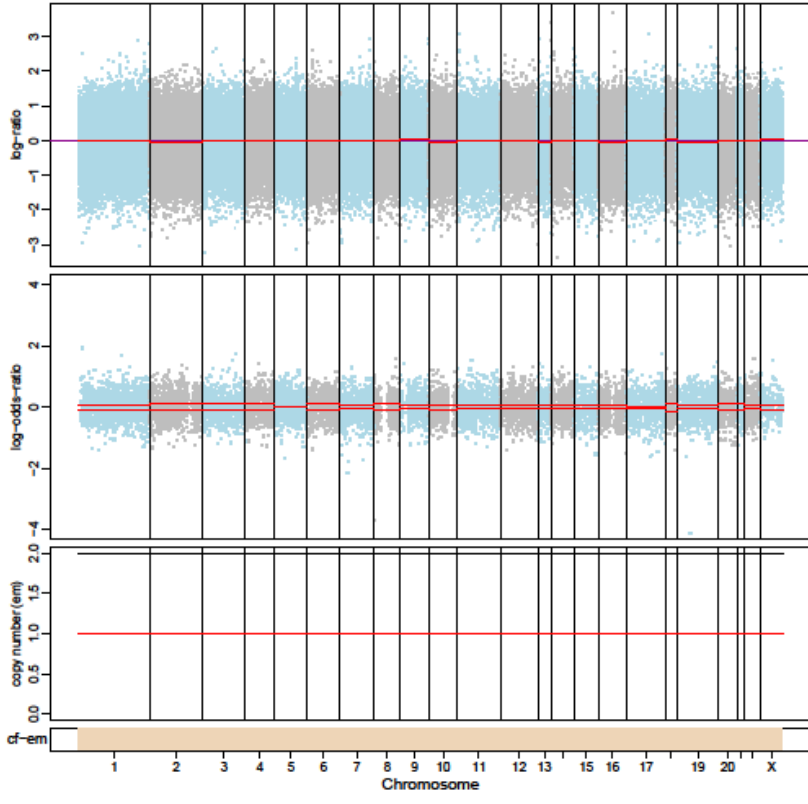
1145-P0



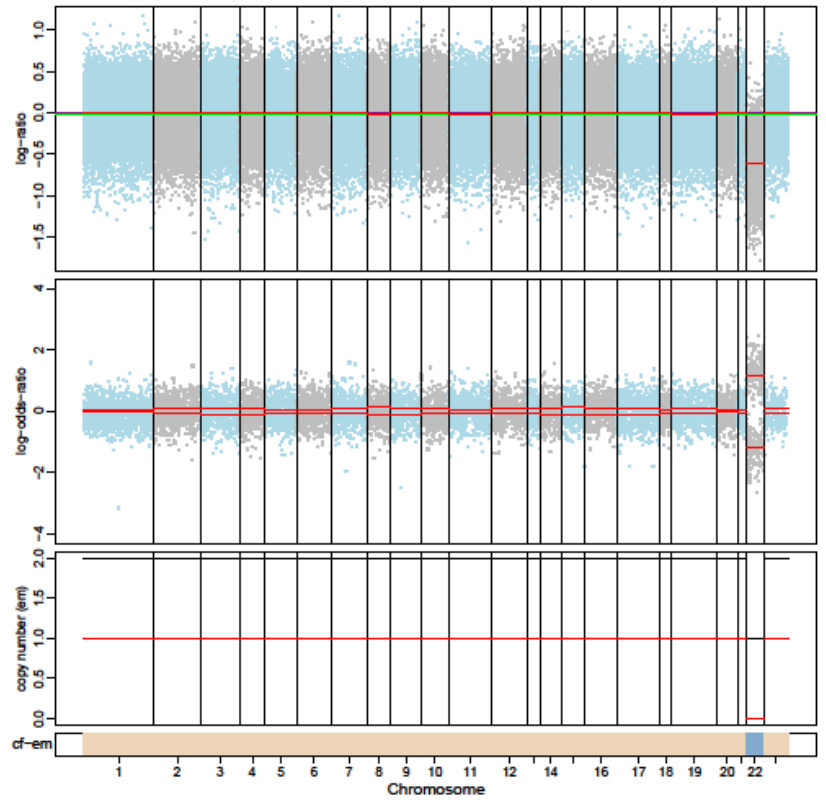
1145-P1



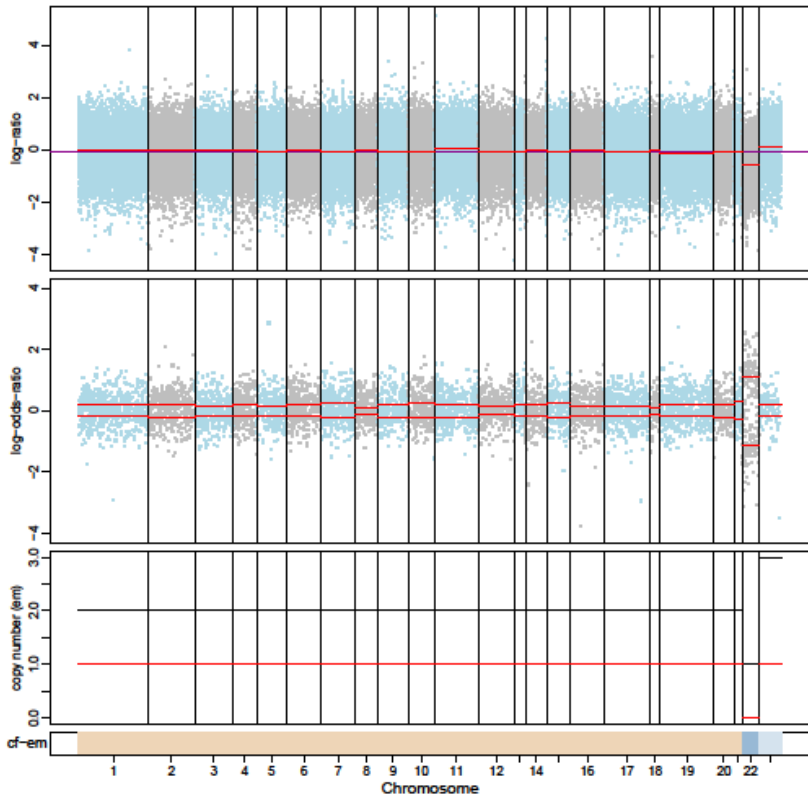
1145-P2



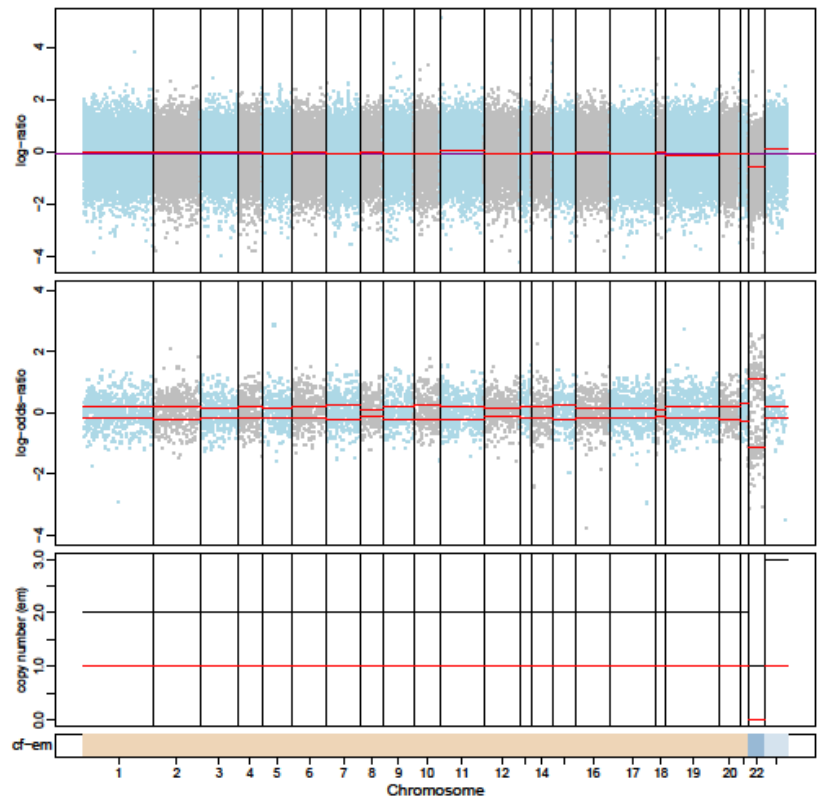
1147-P0



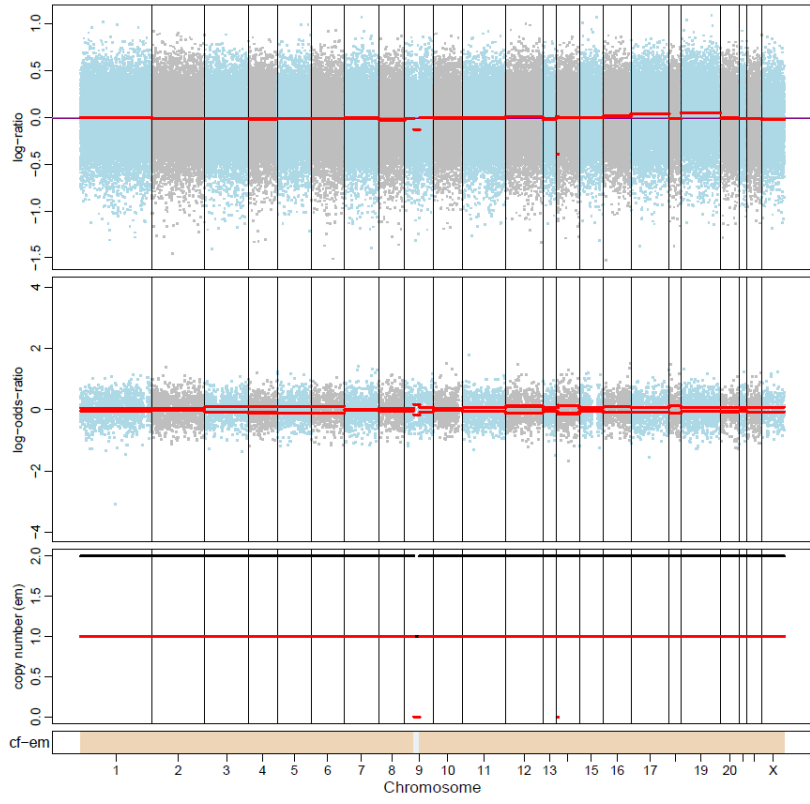
1147-P1



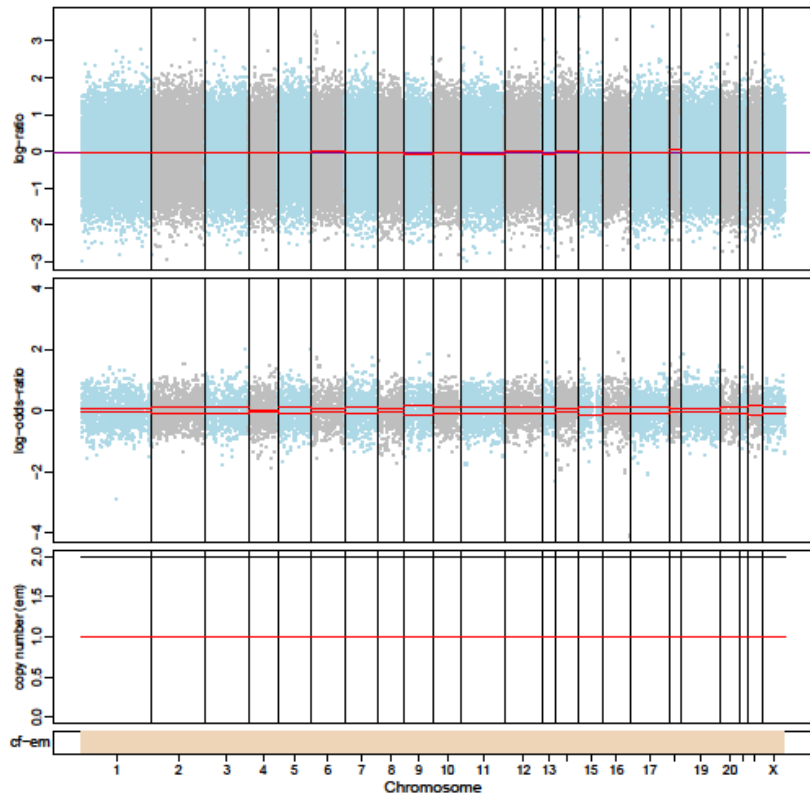
1147-P2



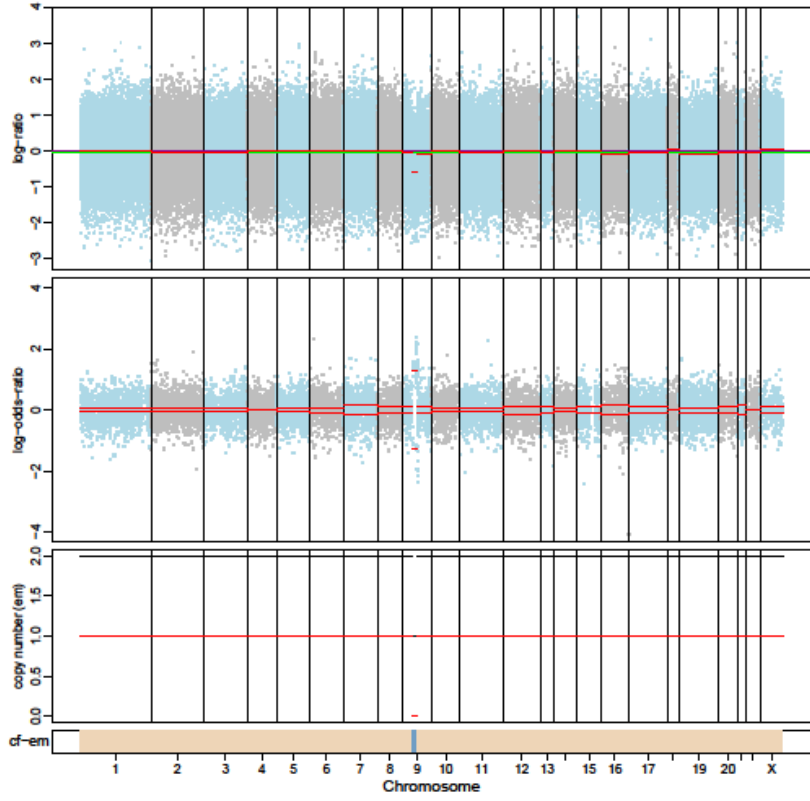
1148-P0



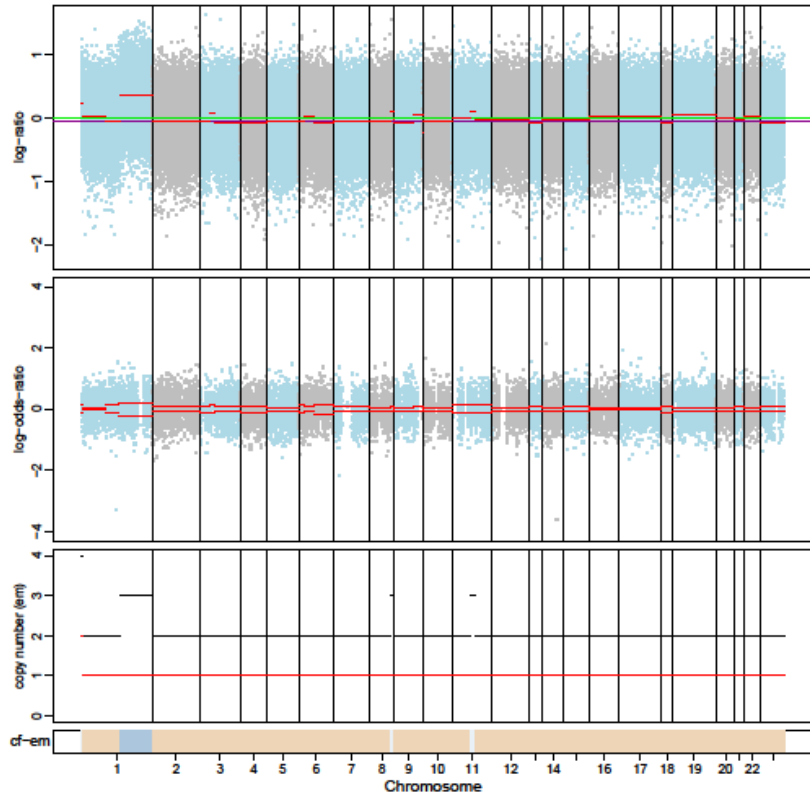
1148-P1



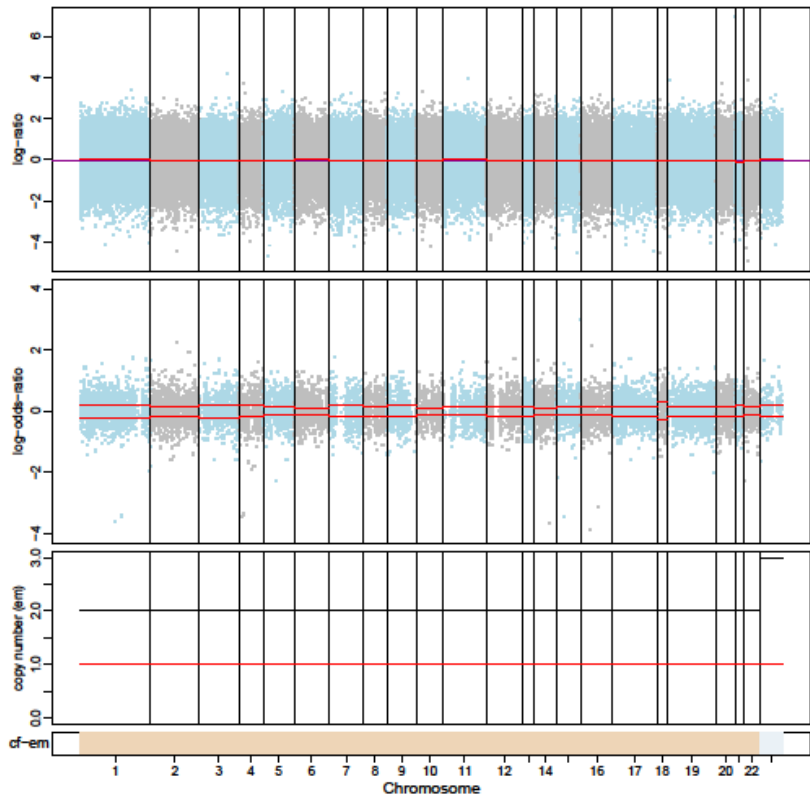
1148-P2



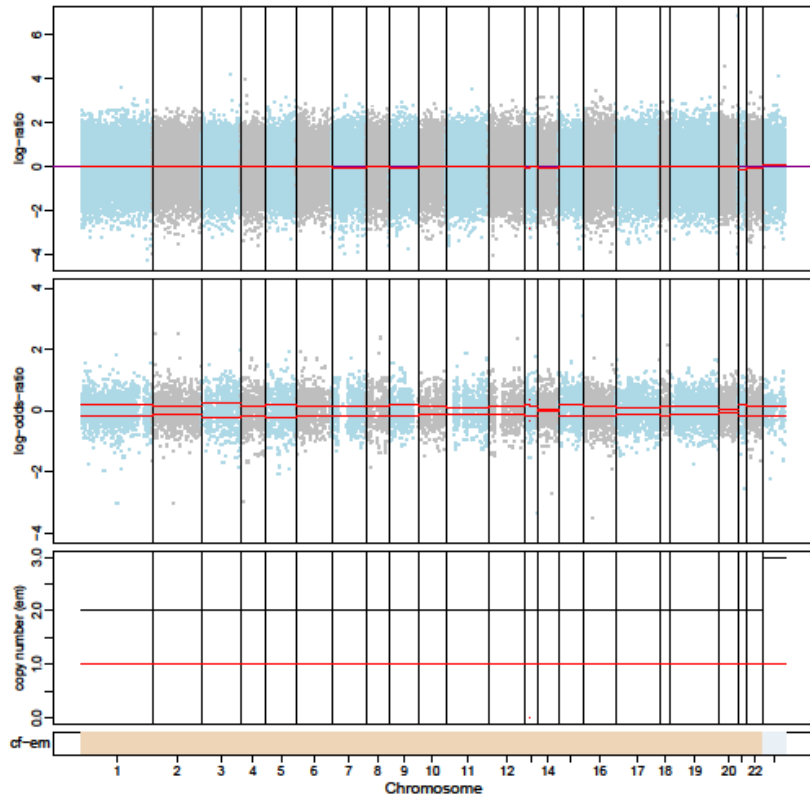
1149-P0



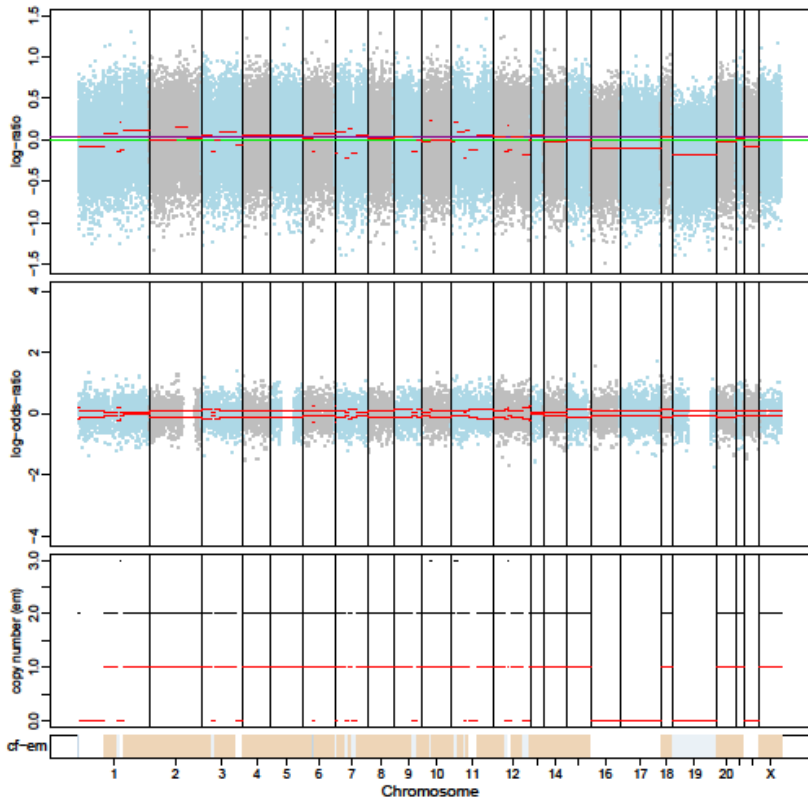
1149-P1



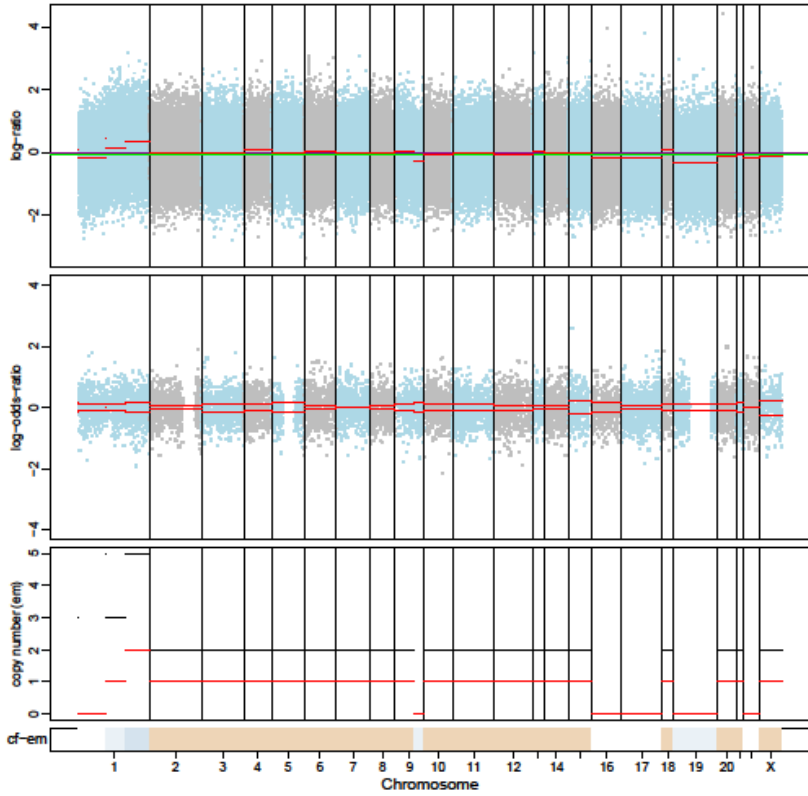
1149-P2



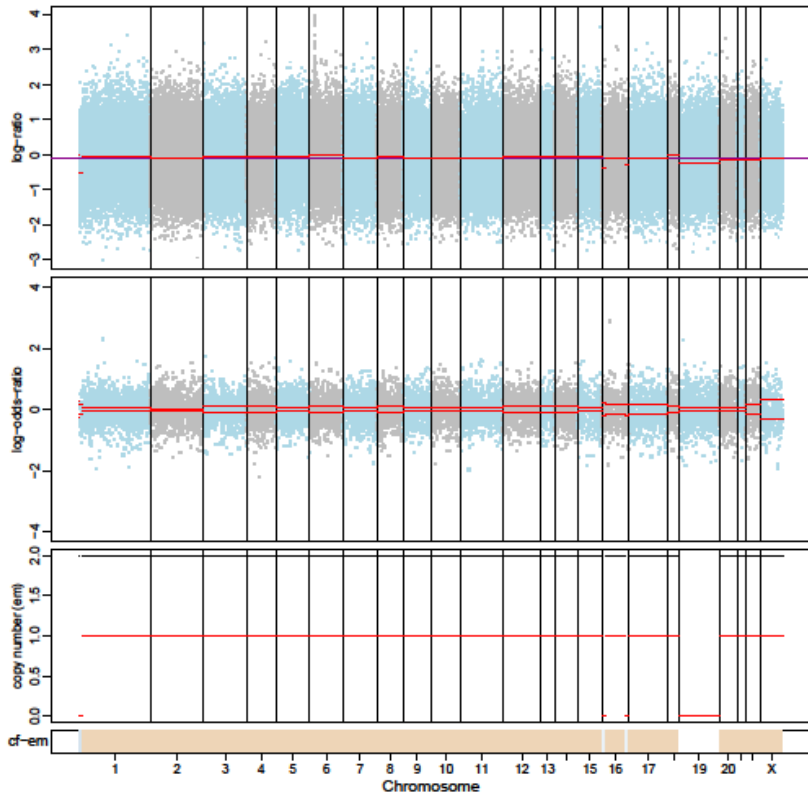
1150-P0



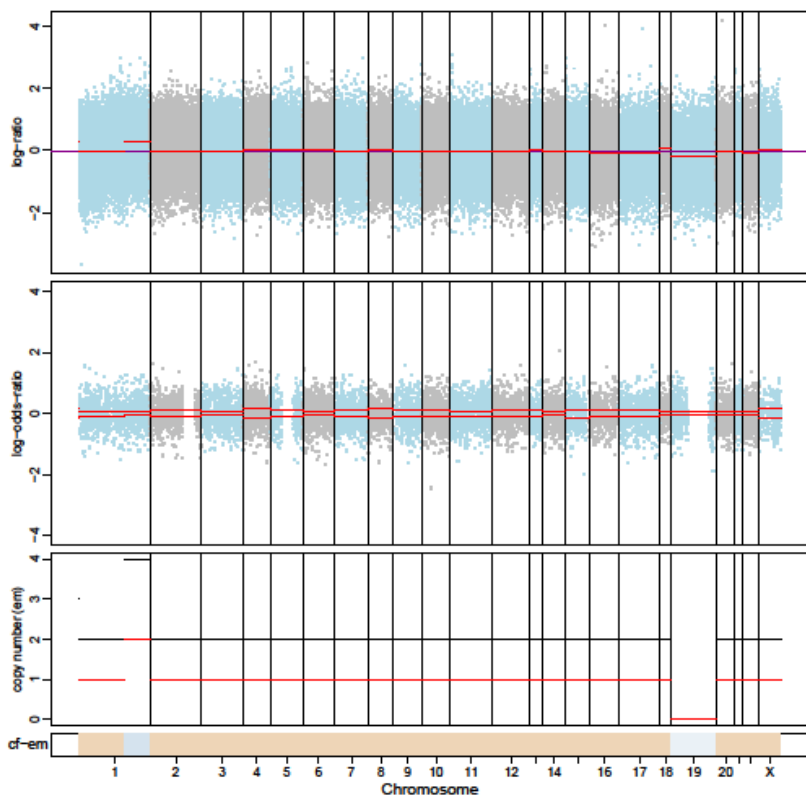
1150-P2



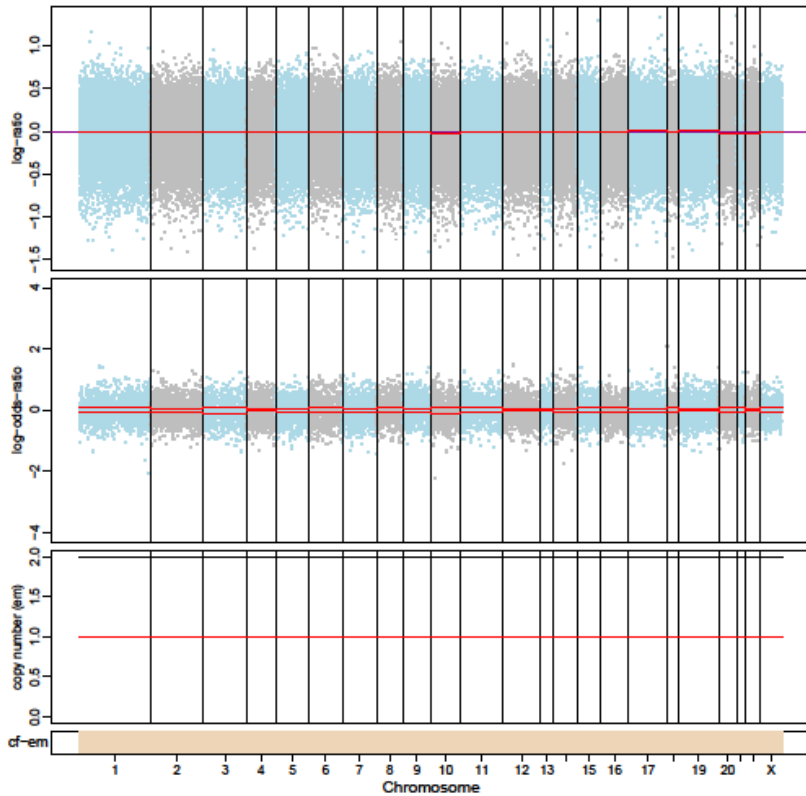
1151-P1



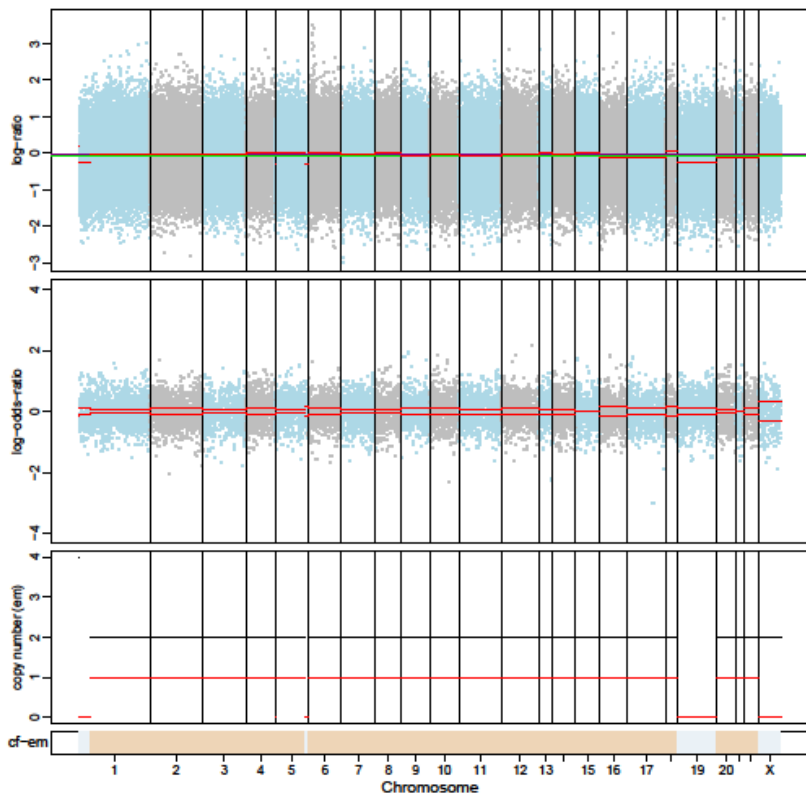
1150-P1



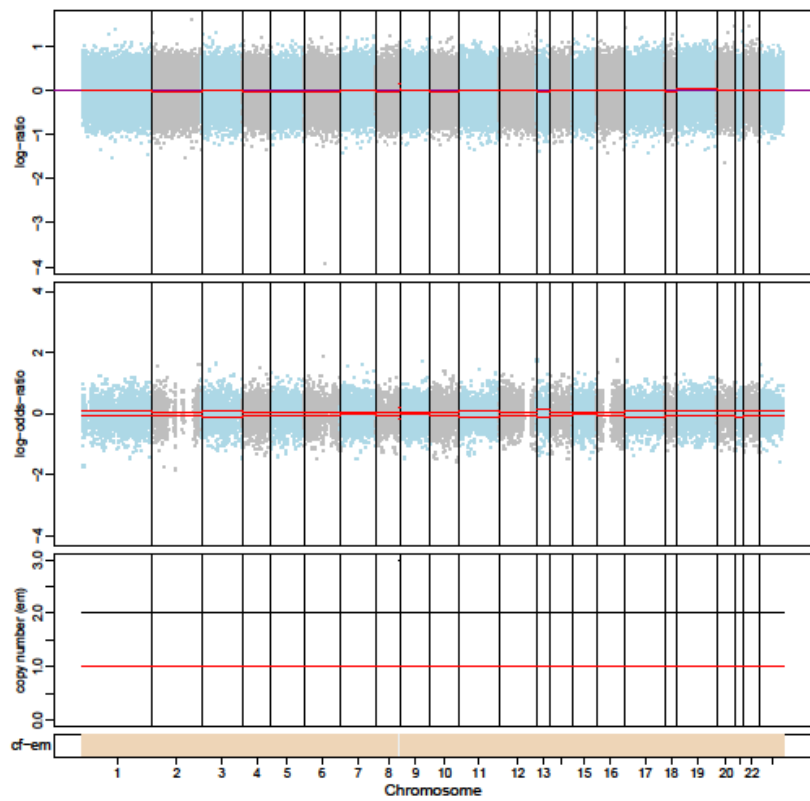
1151-P0



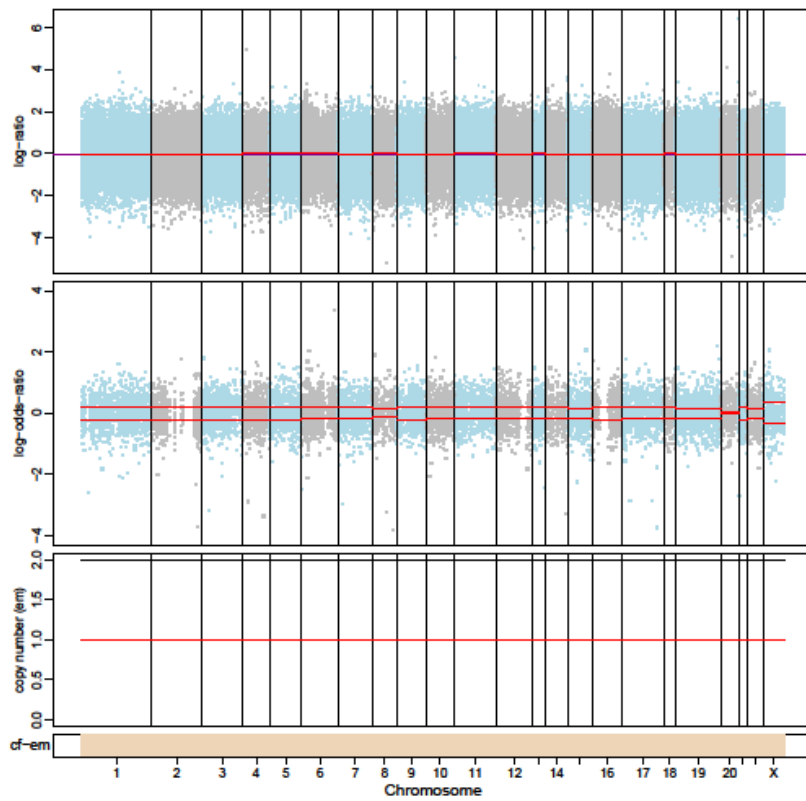
1151-P2



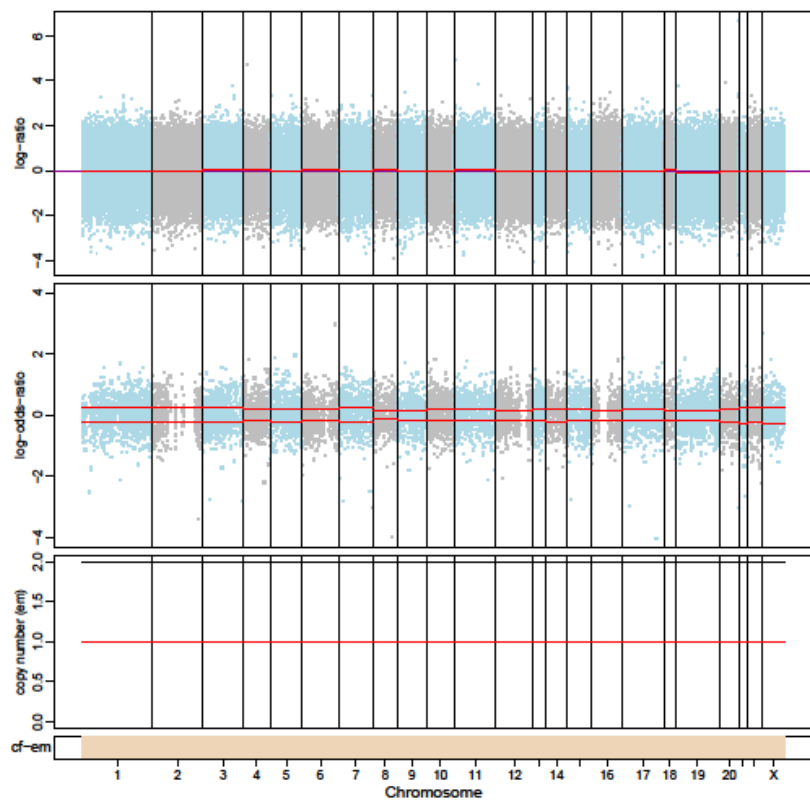
1153-P0



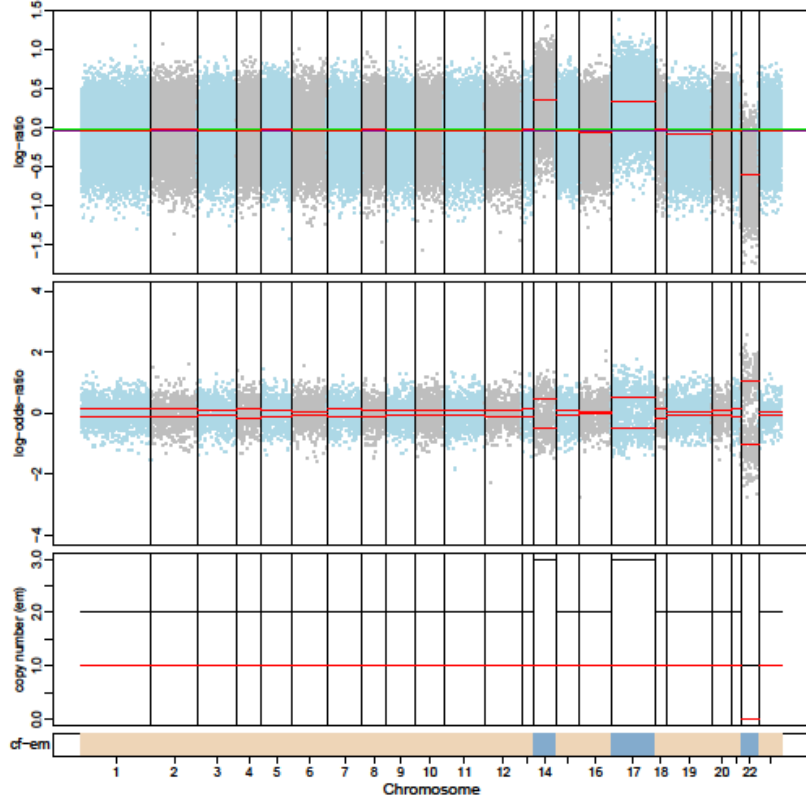
1153-P1



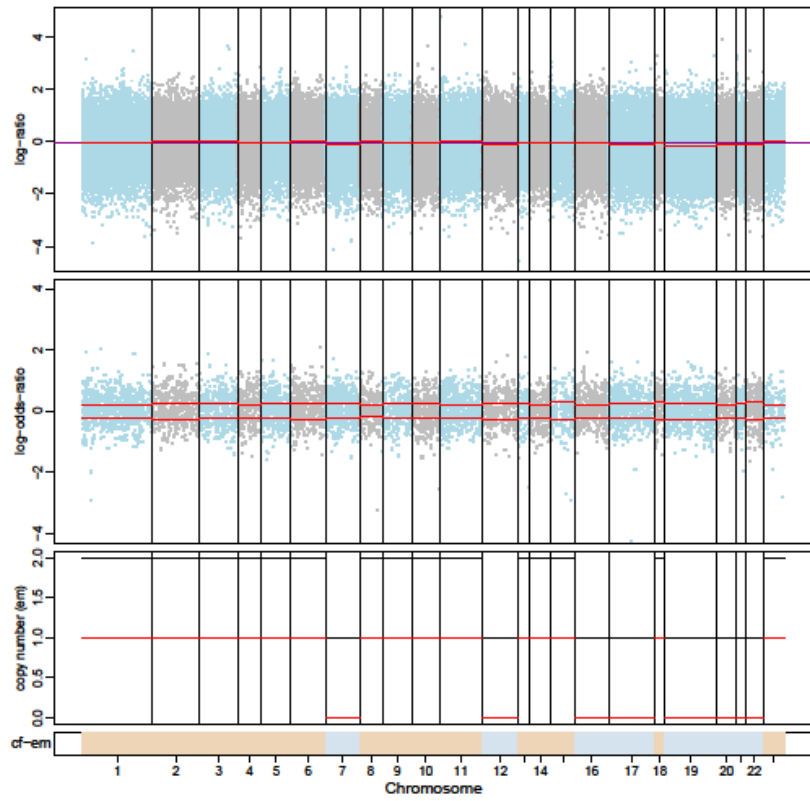
1153-P2



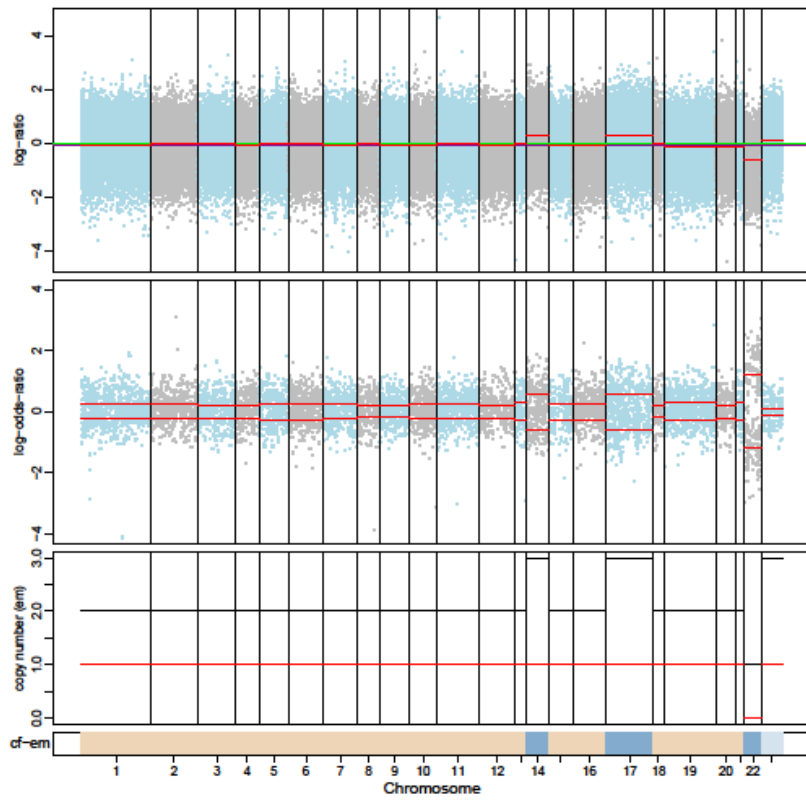
1154-P0



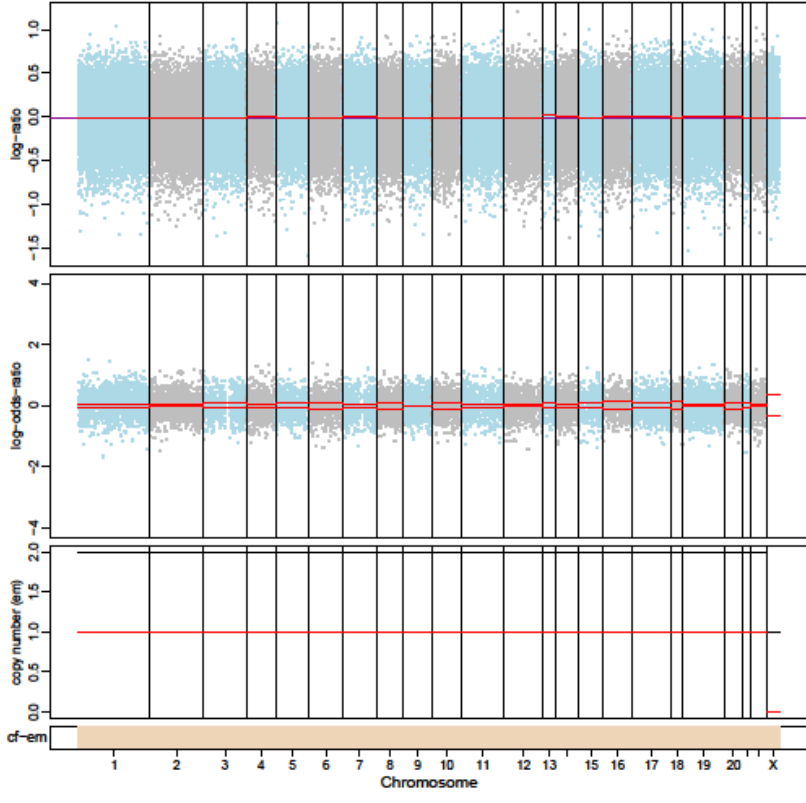
1154-P1



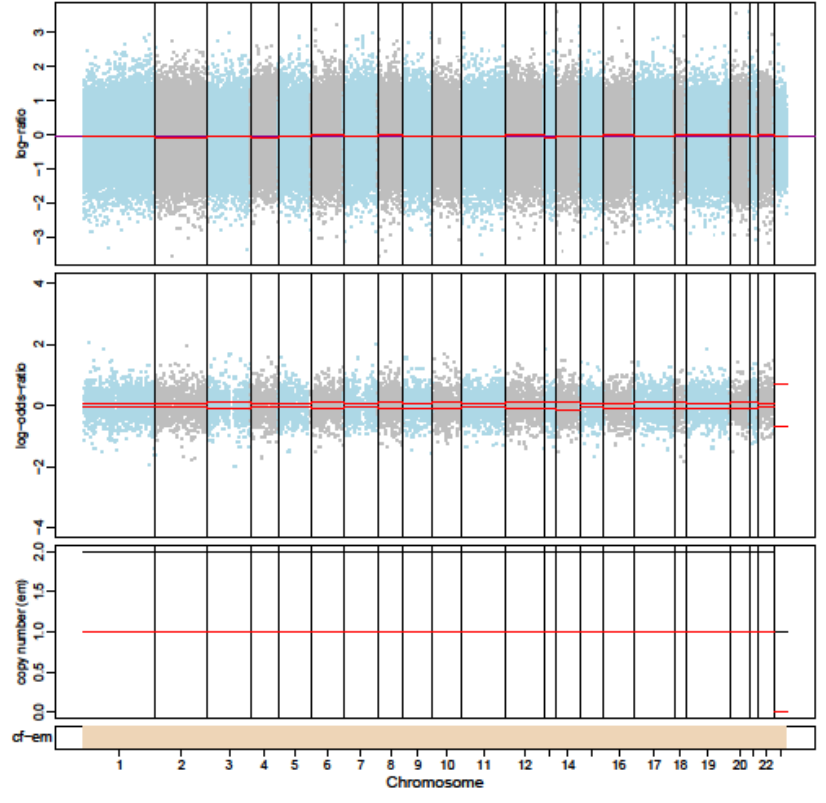
1154-P2



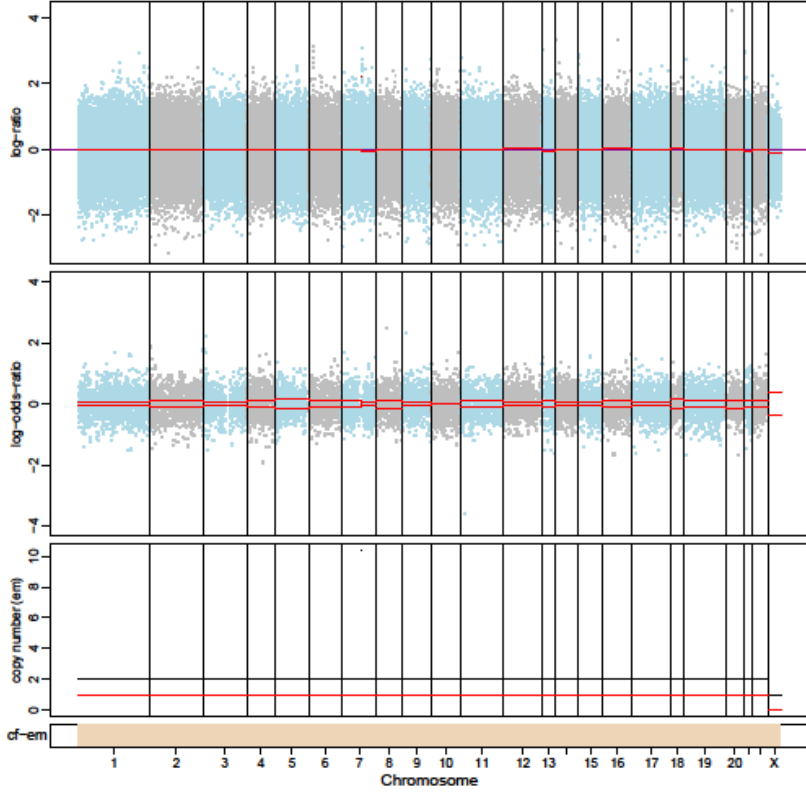
1155-P0



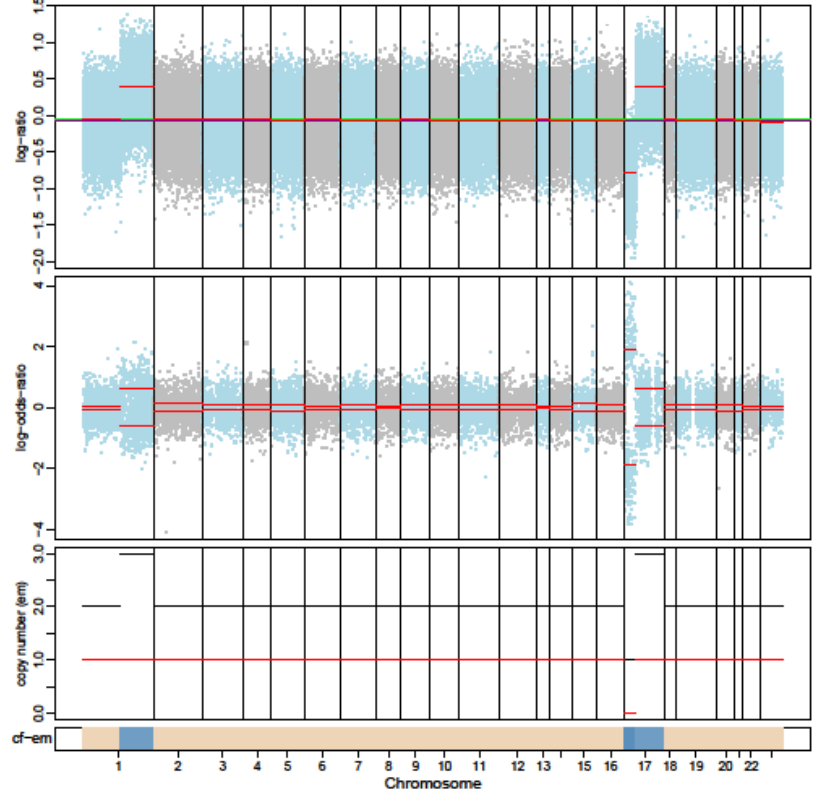
1155-P1



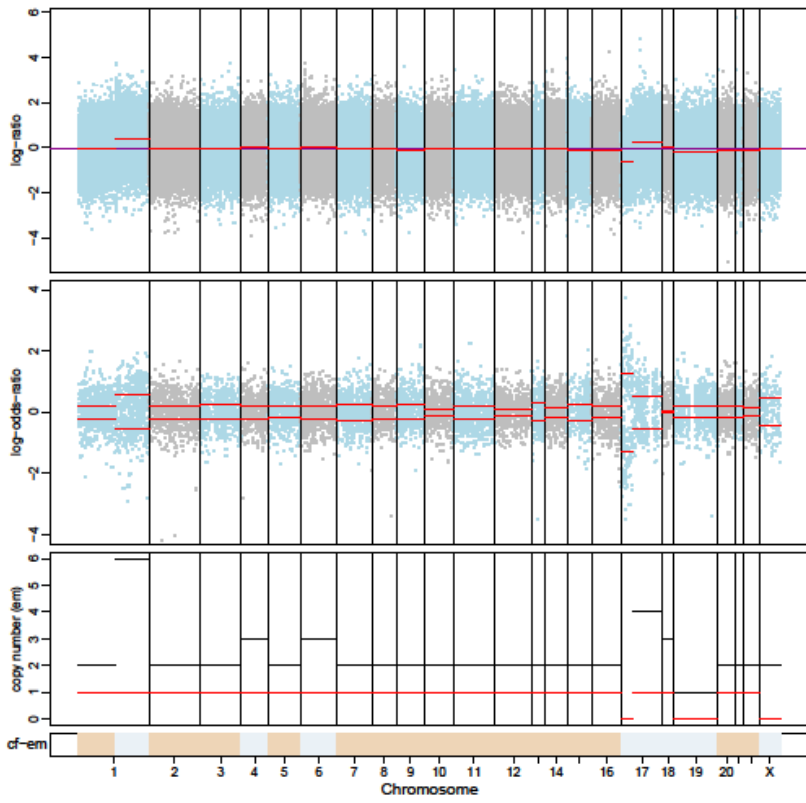
1155-P2



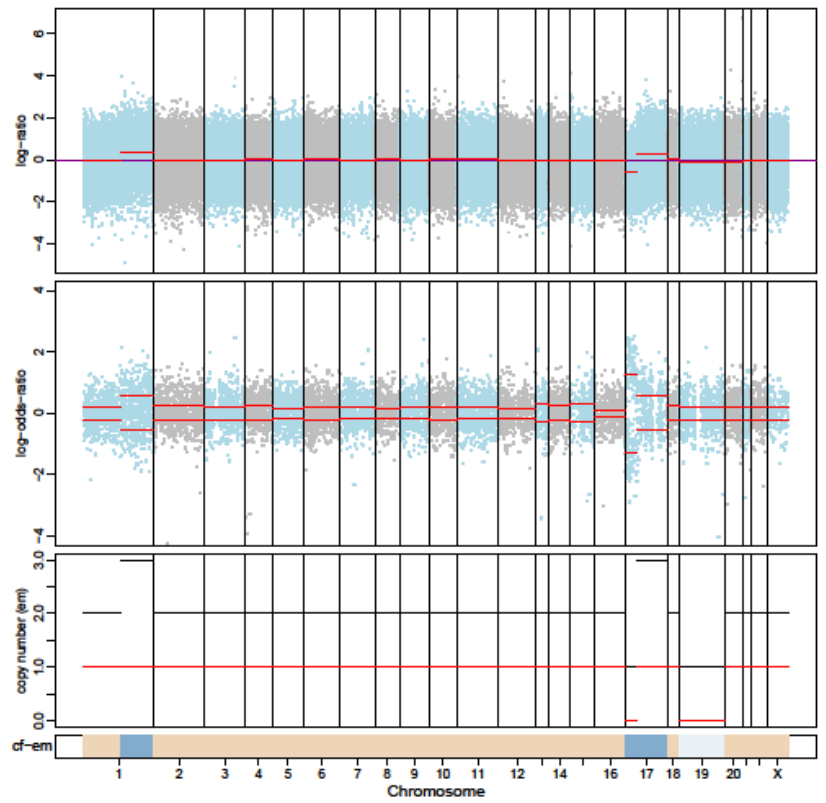
1156-P0



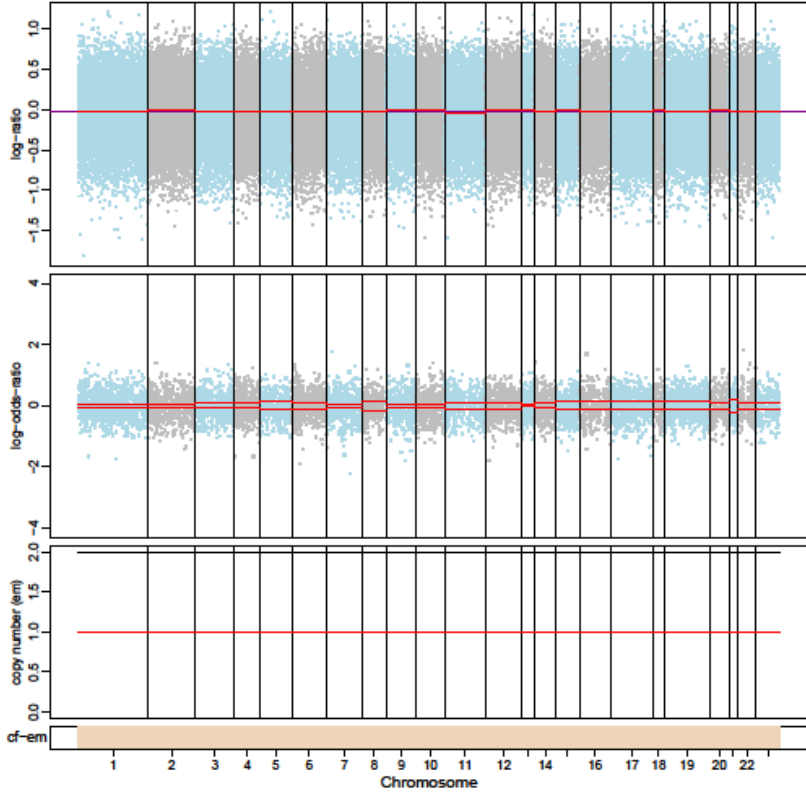
1156-P1



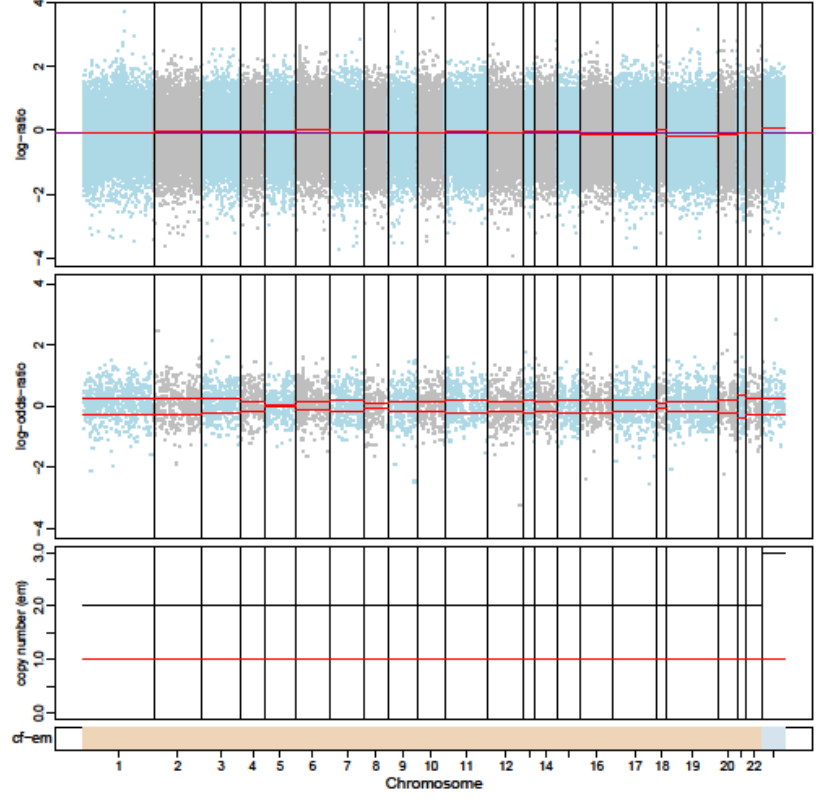
1156-P2



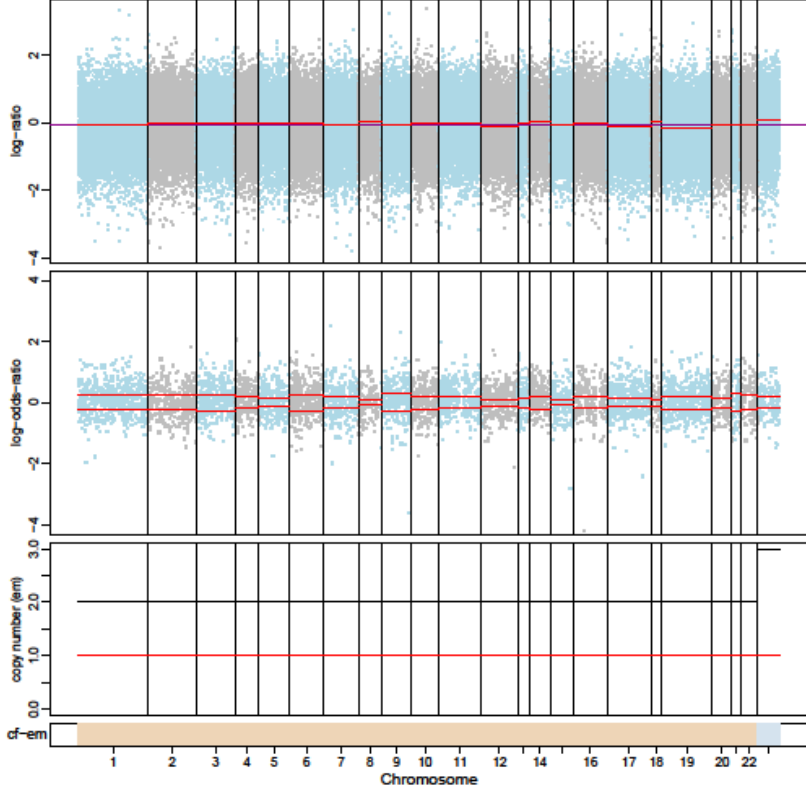
1159-P0



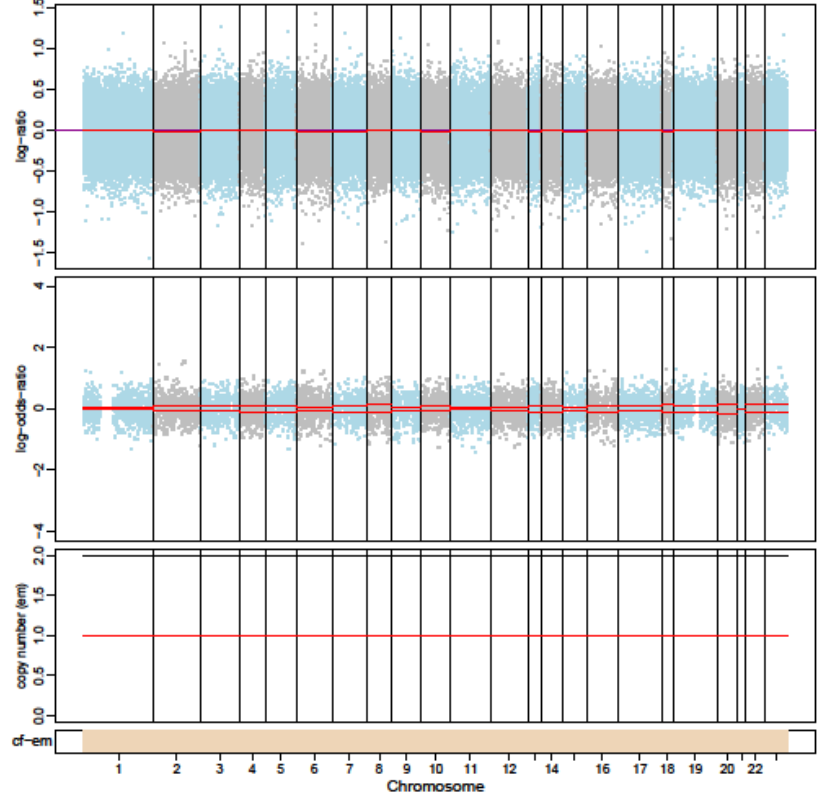
1159-P1



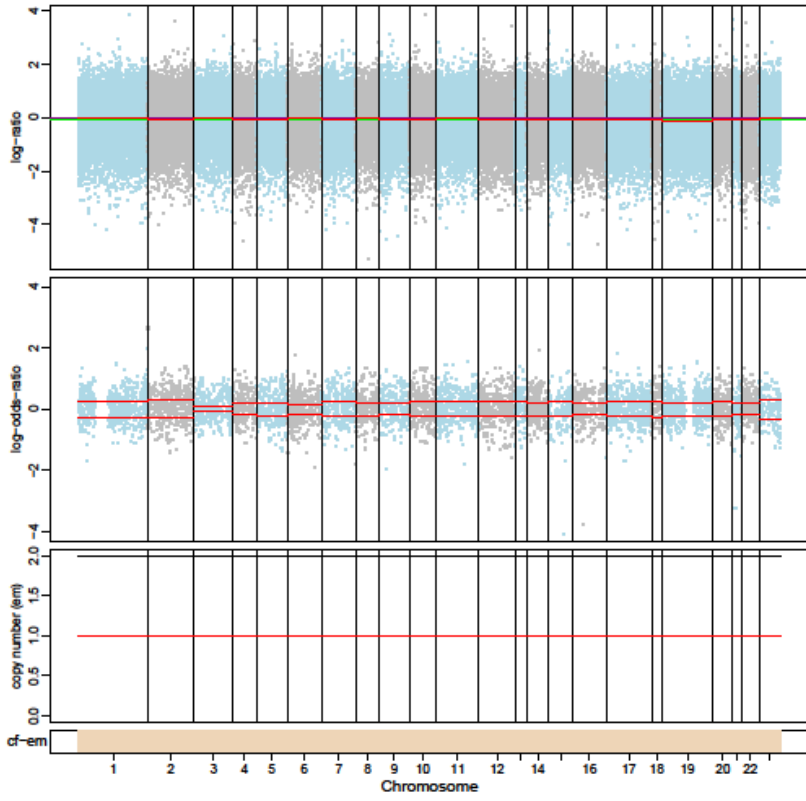
1159-P2



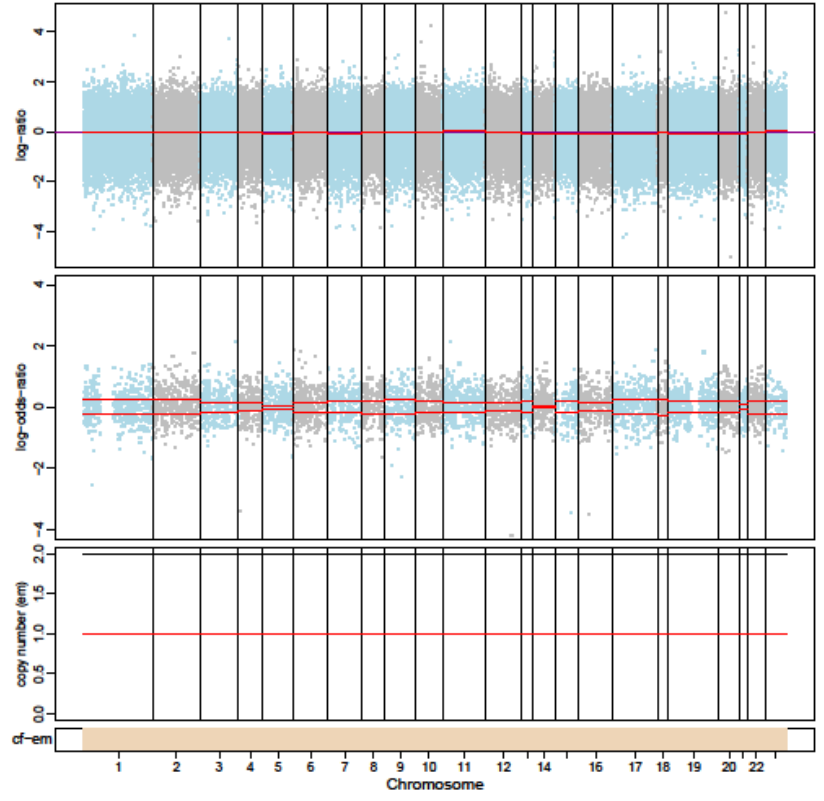
1161-P0



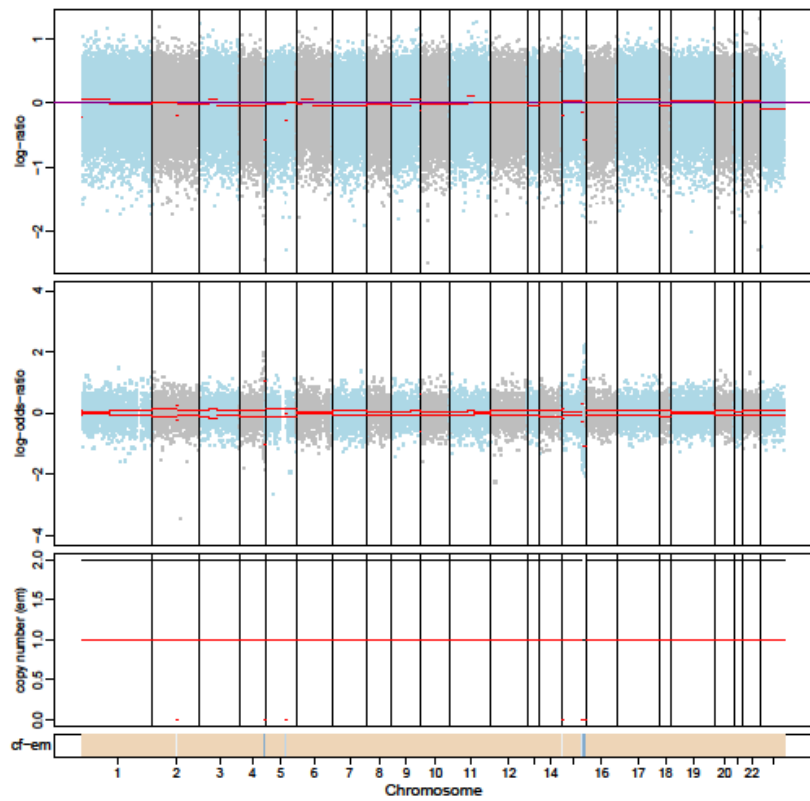
1161-P1



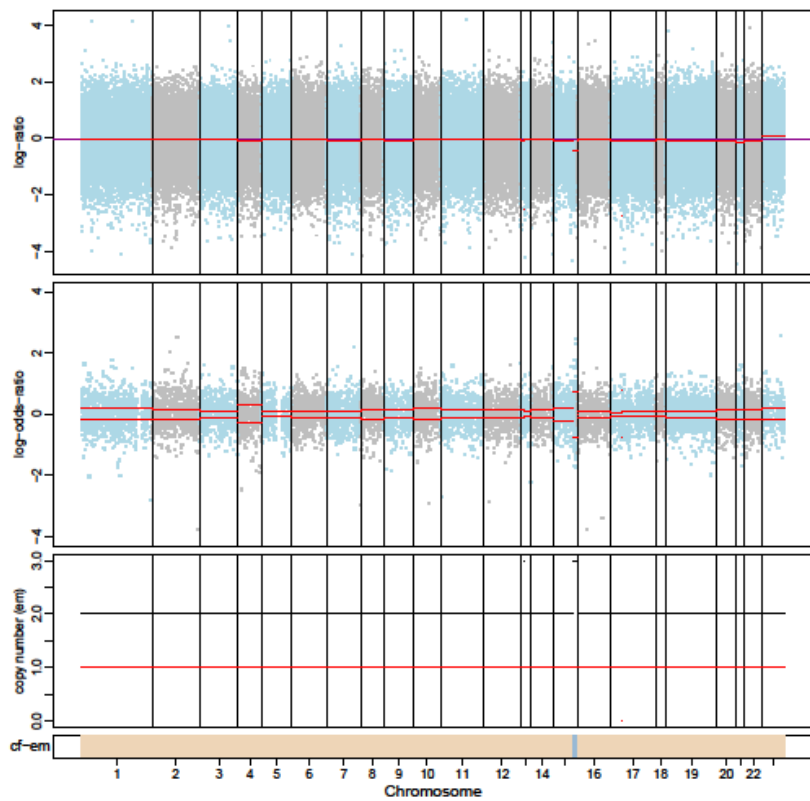
1161-P2



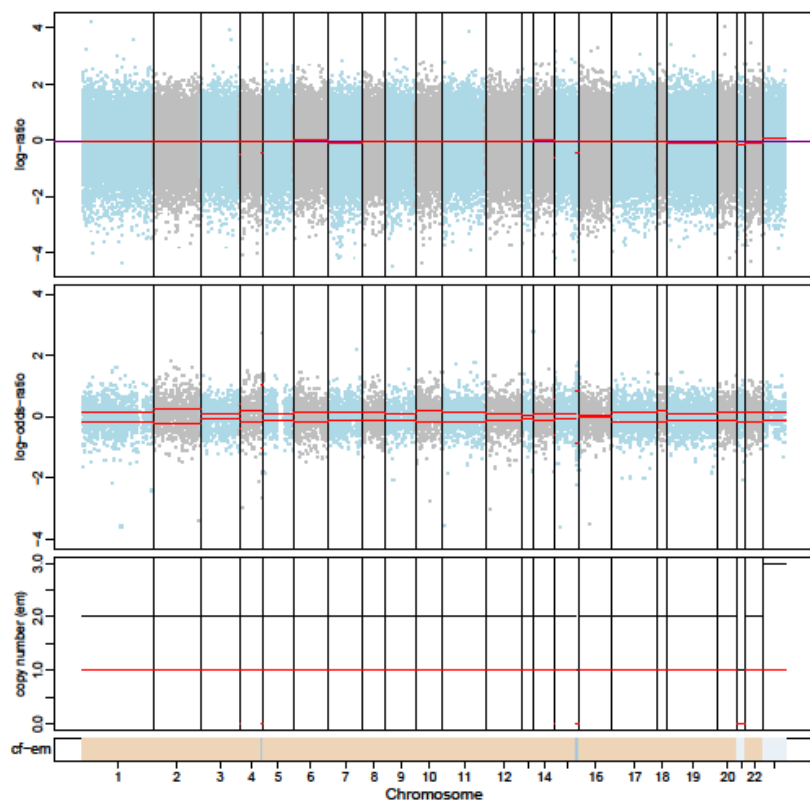
1164-P0



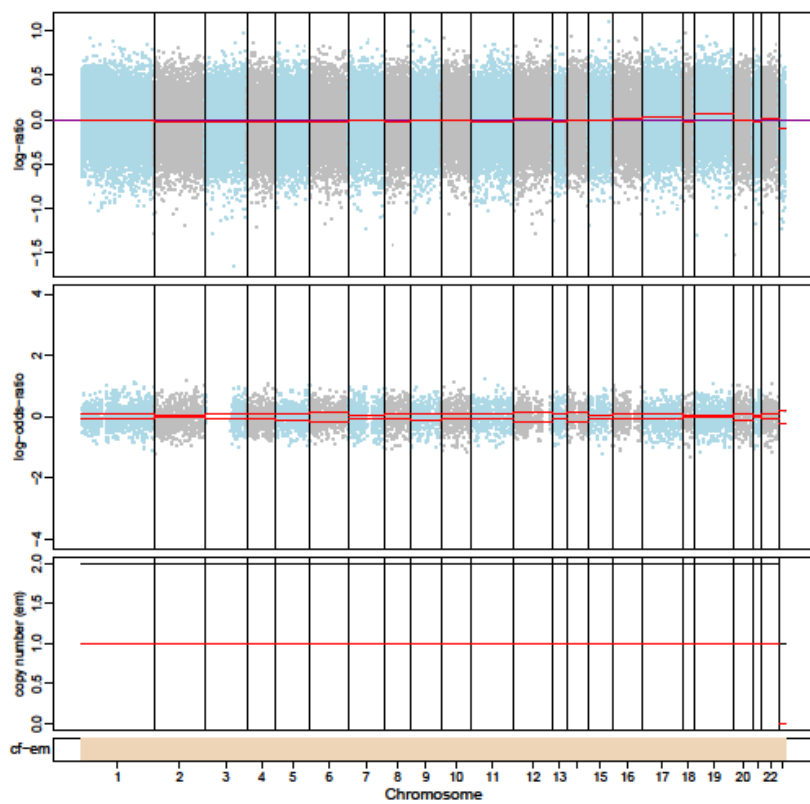
1164-P1



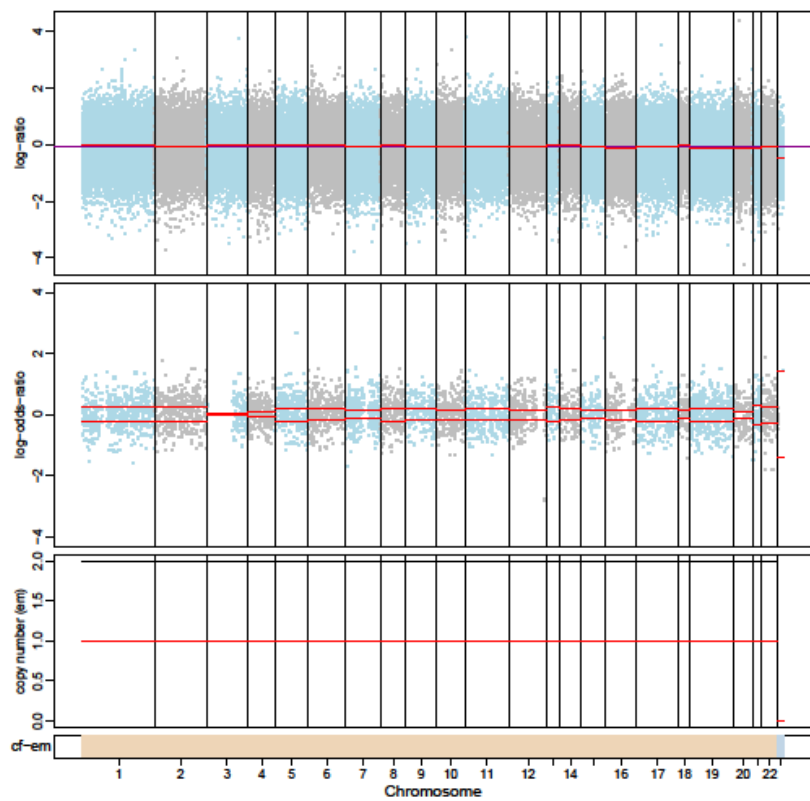
1164-P2



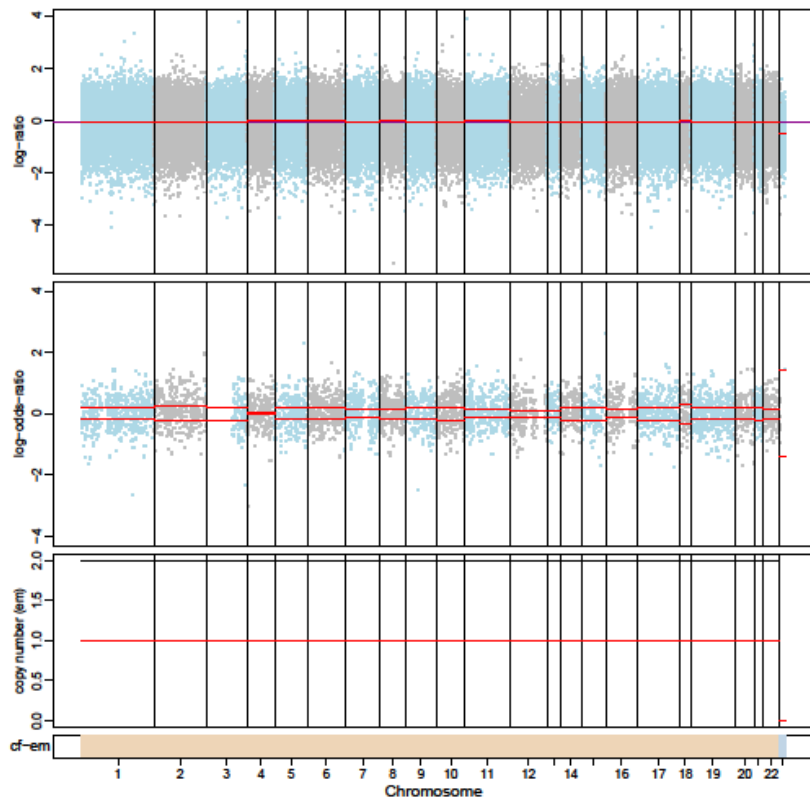
1165-P0



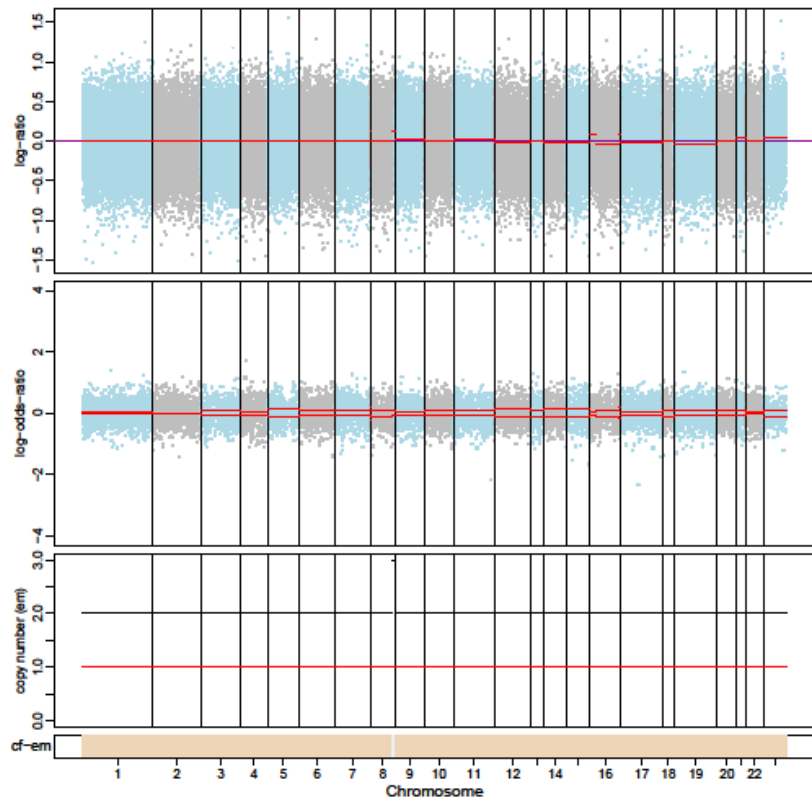
1165-P1



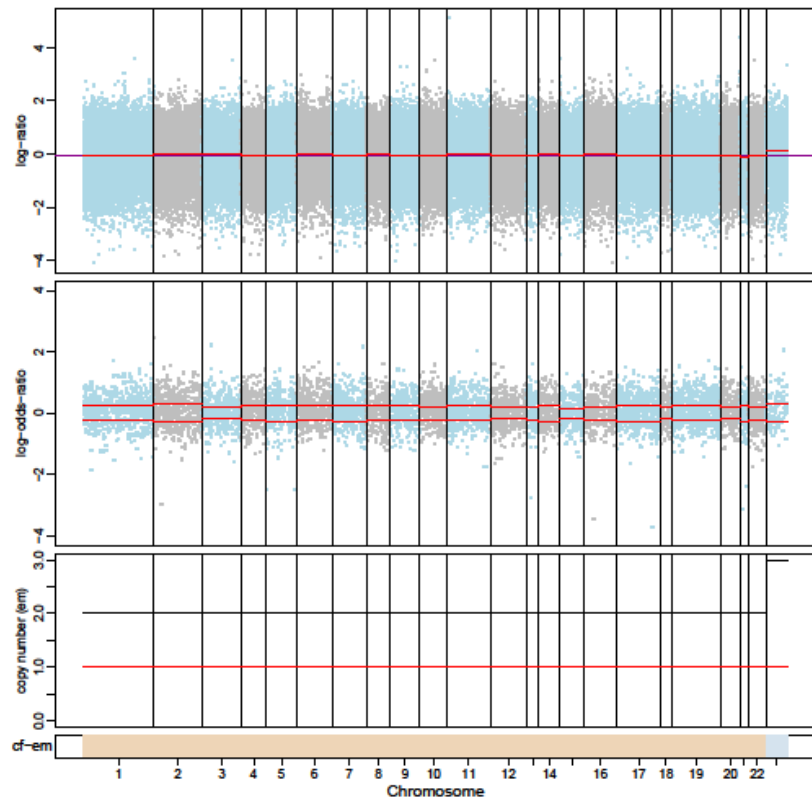
1165-P2



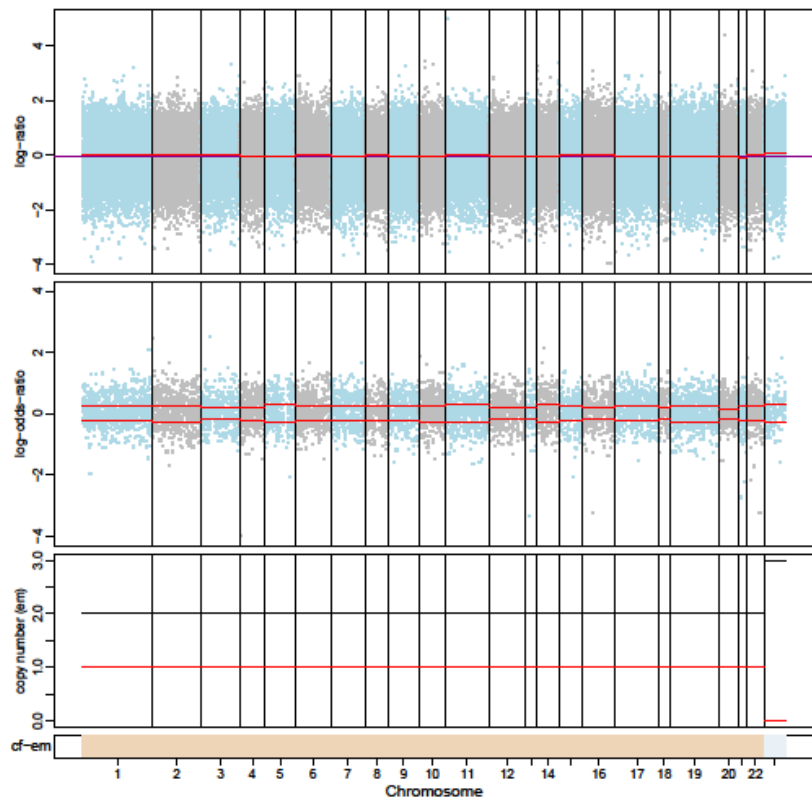
1167-P0



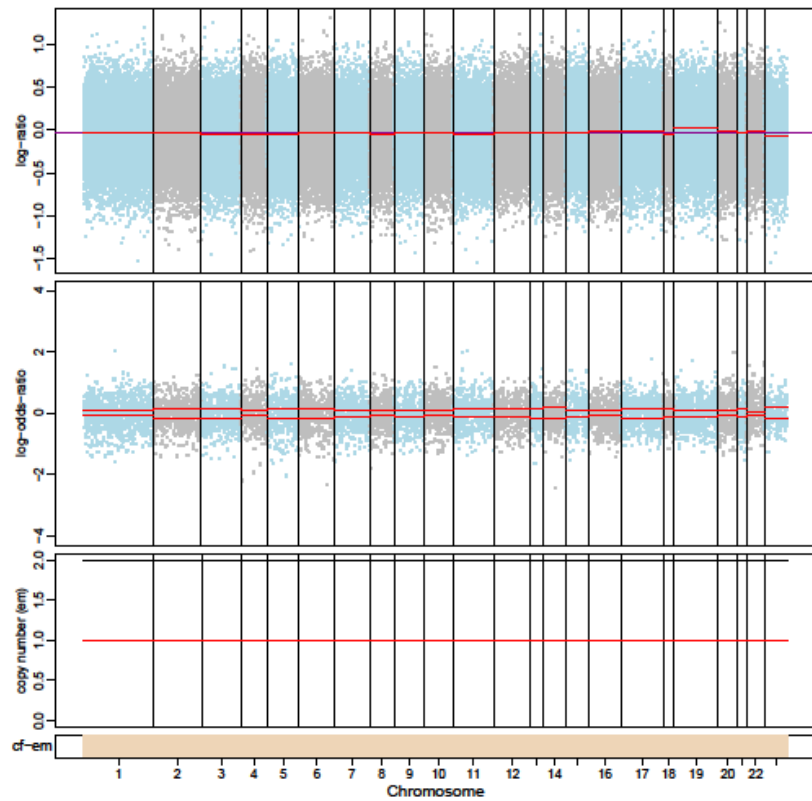
1167-P1



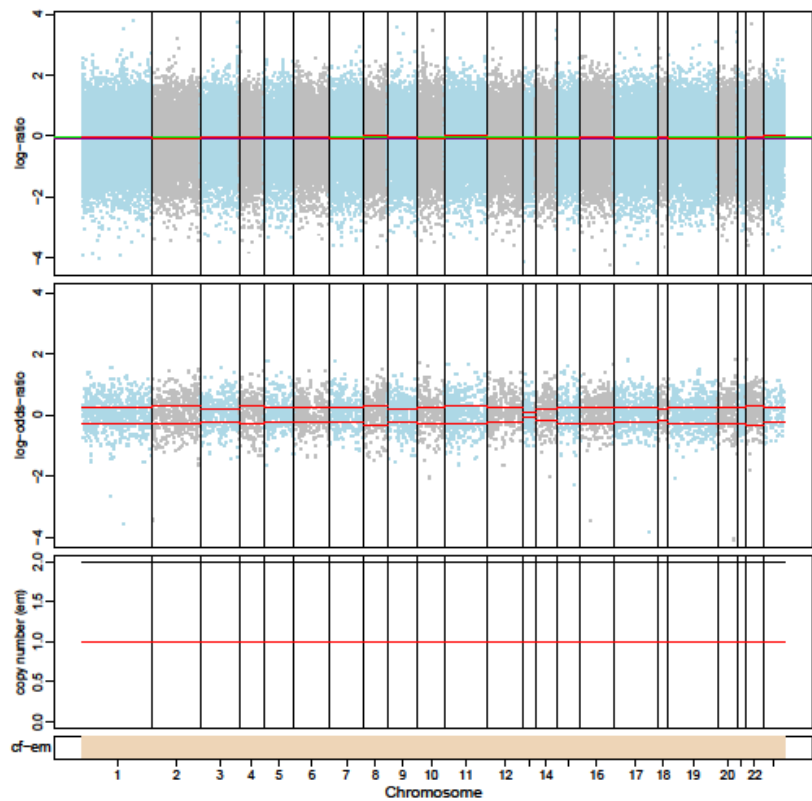
1167-P2



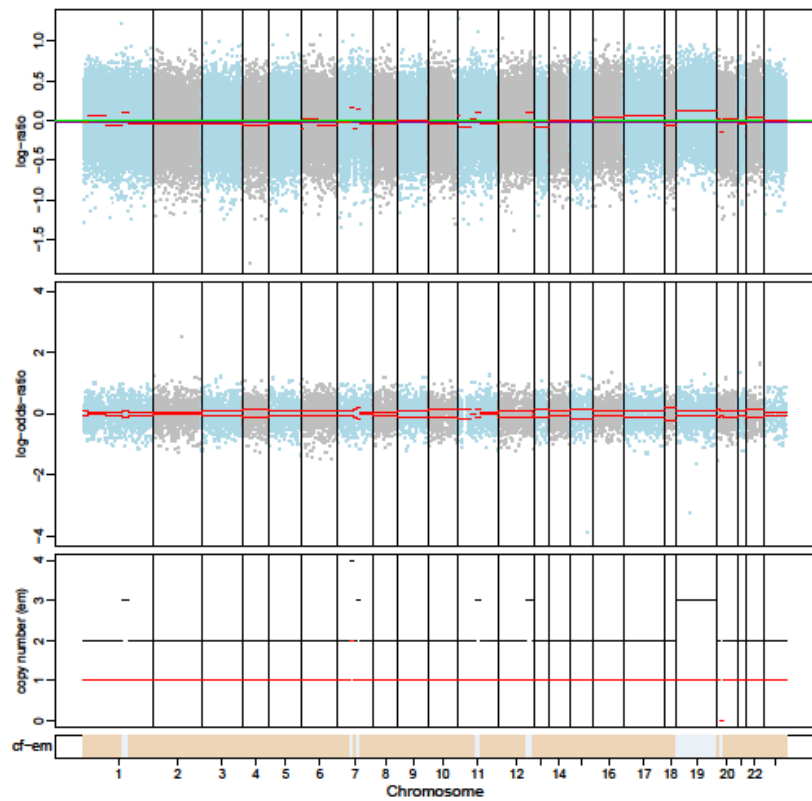
1168-P0



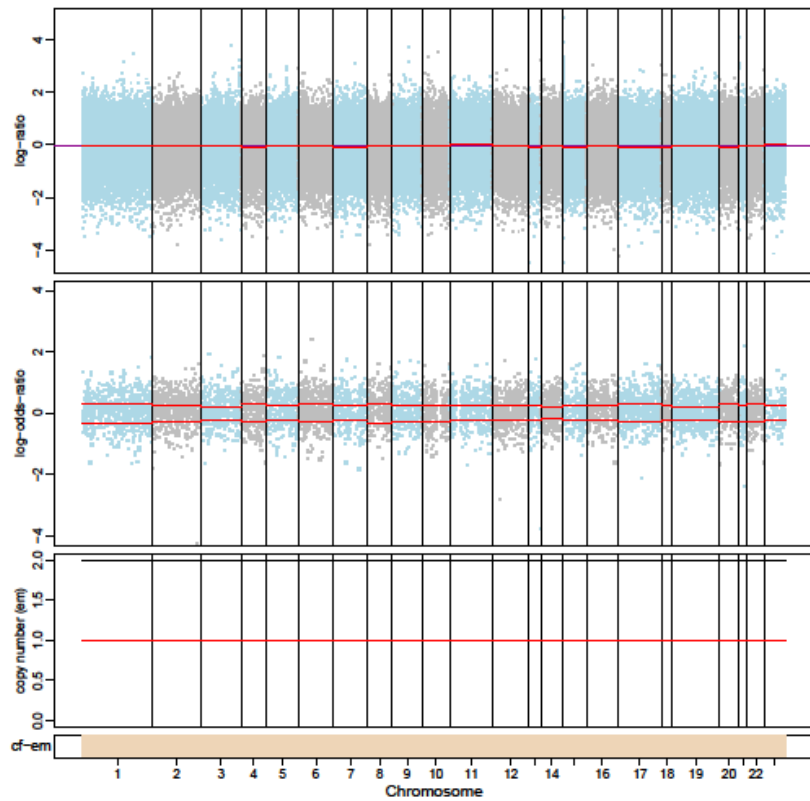
1168-P1



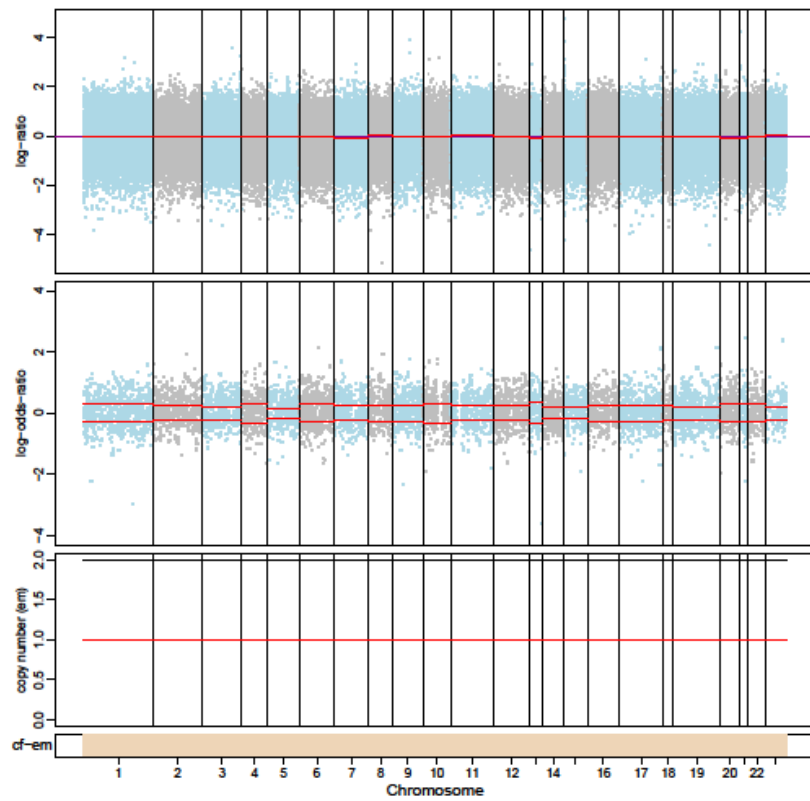
1170-P0



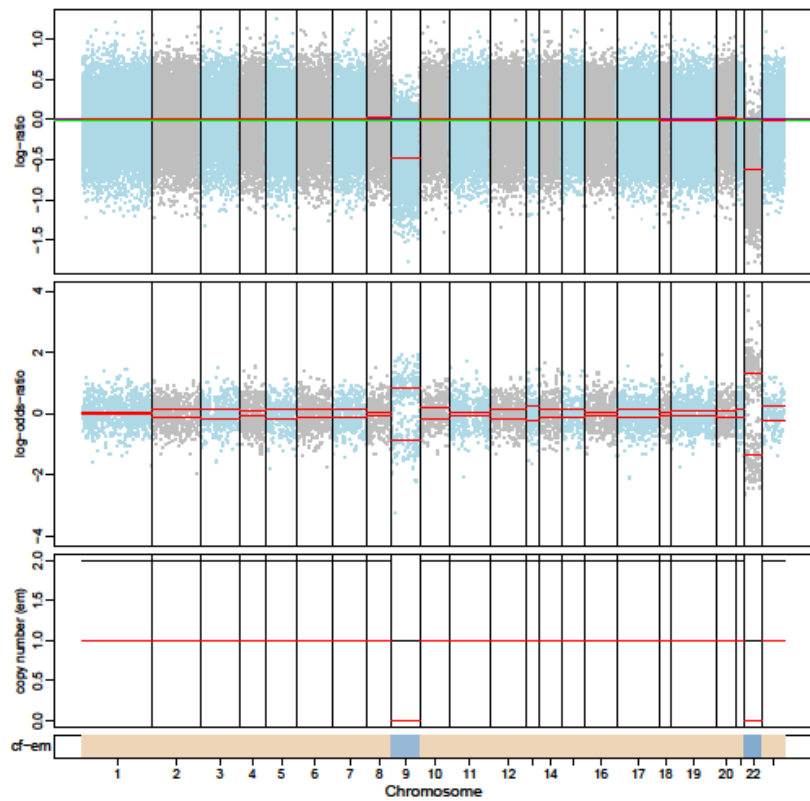
1170-P1



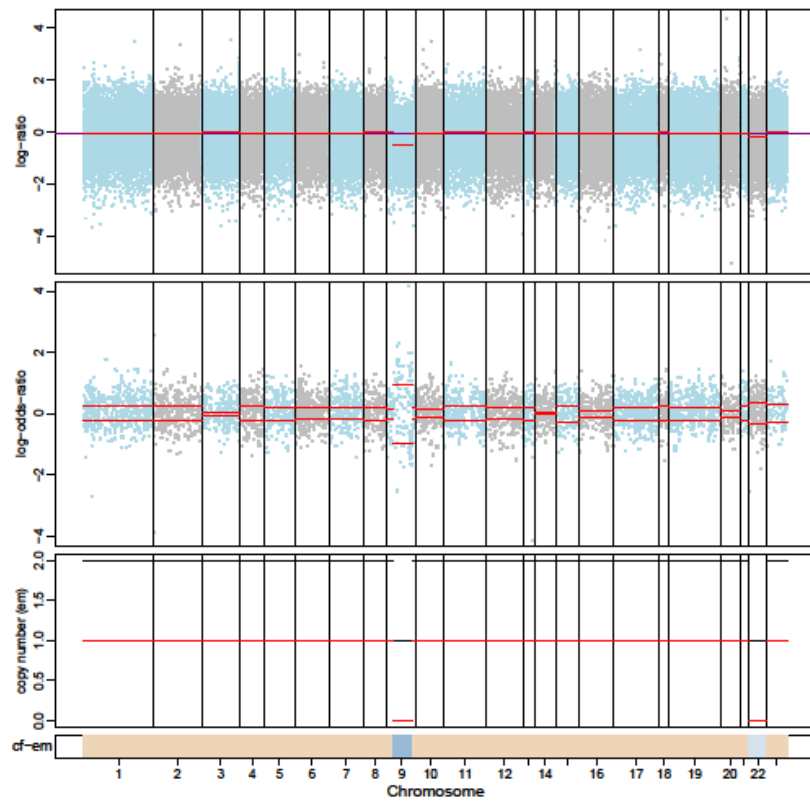
1170-P2



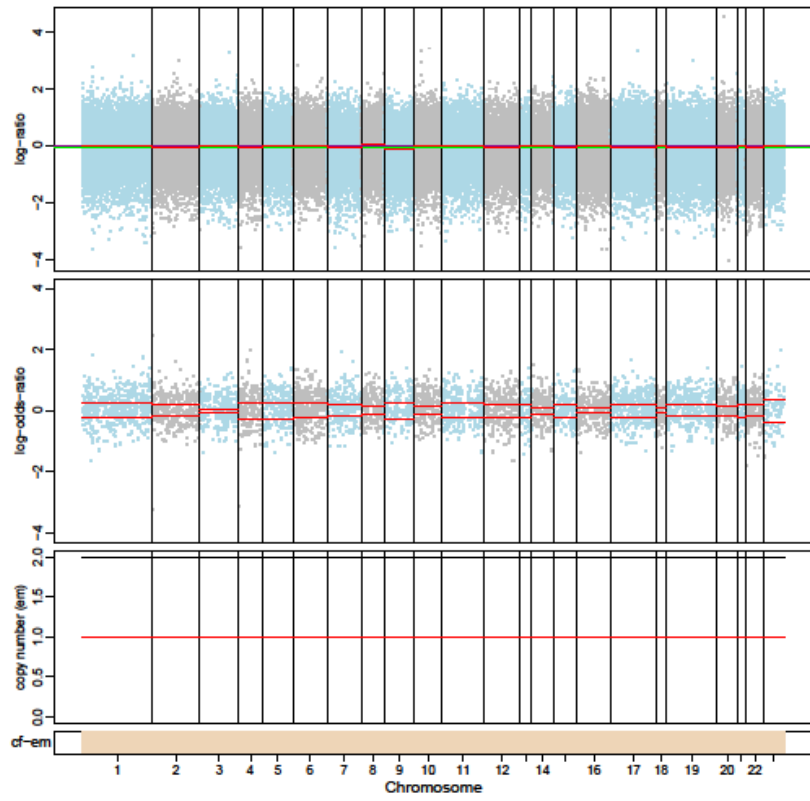
1171-P0



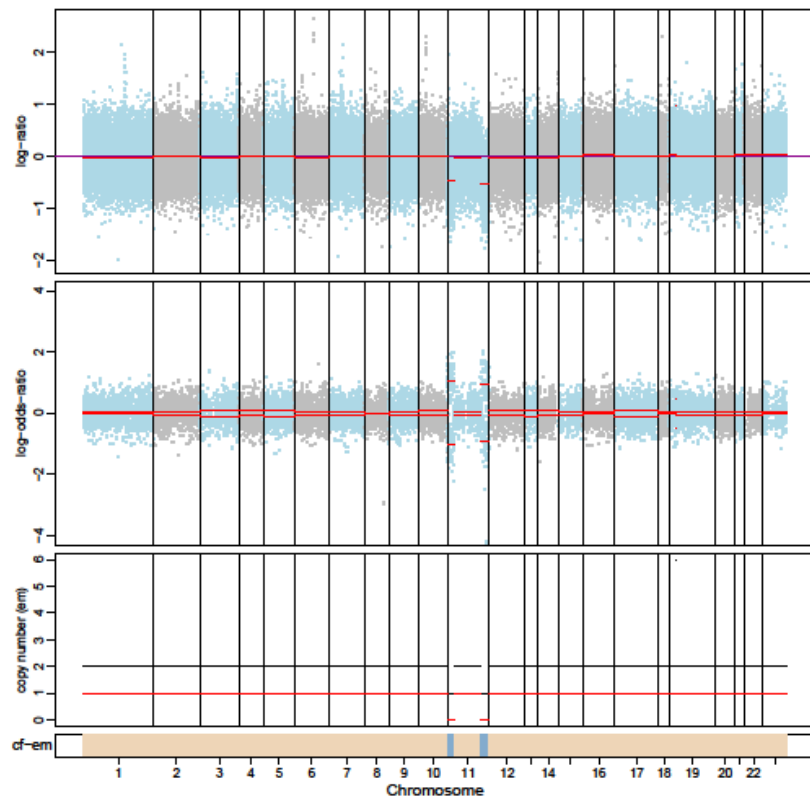
1171-P1



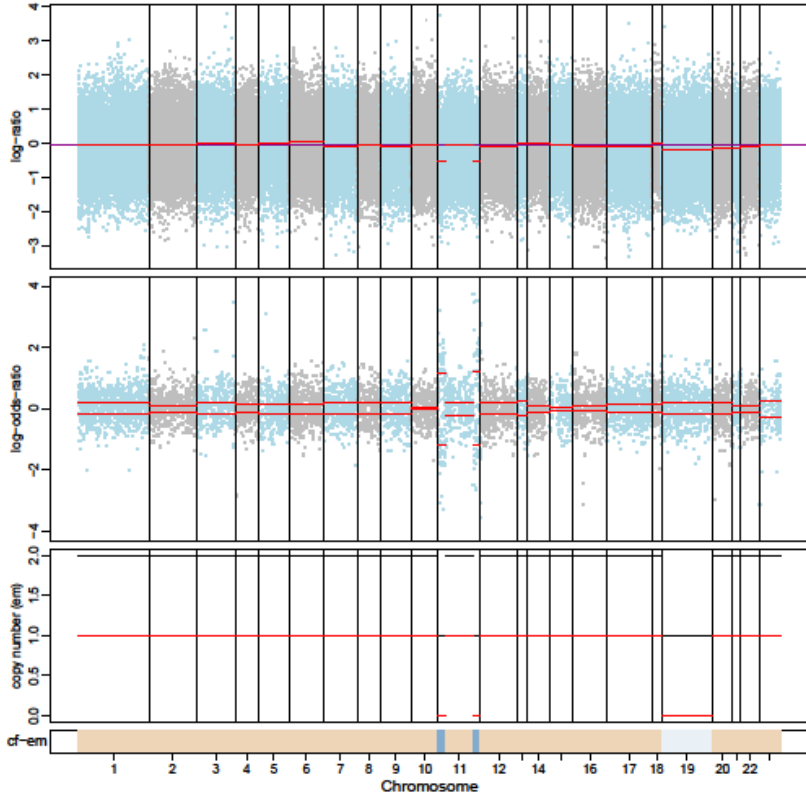
1171-P2



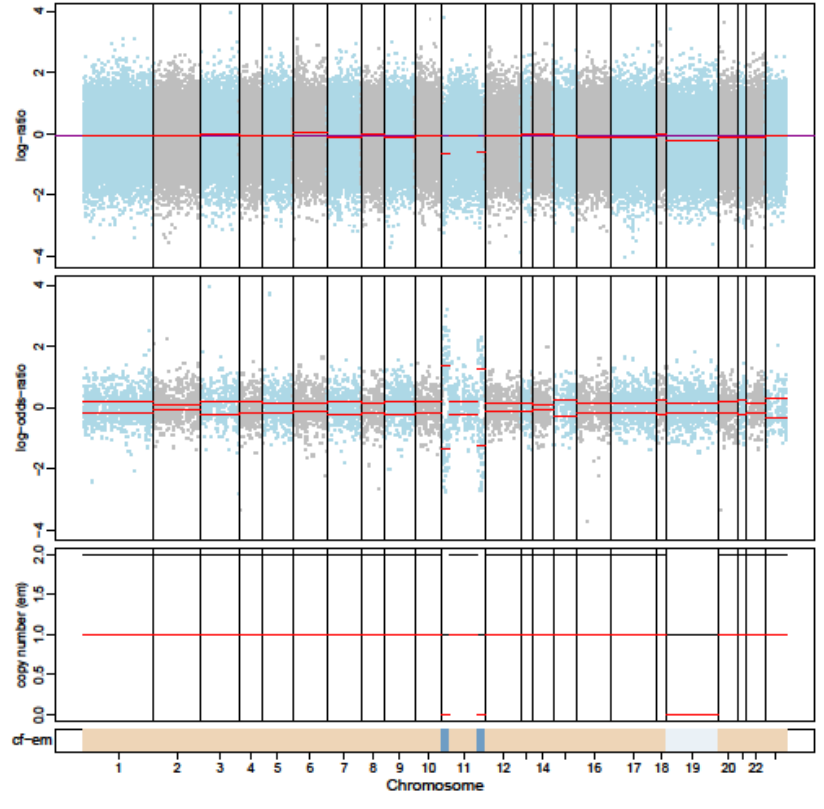
1174-P0



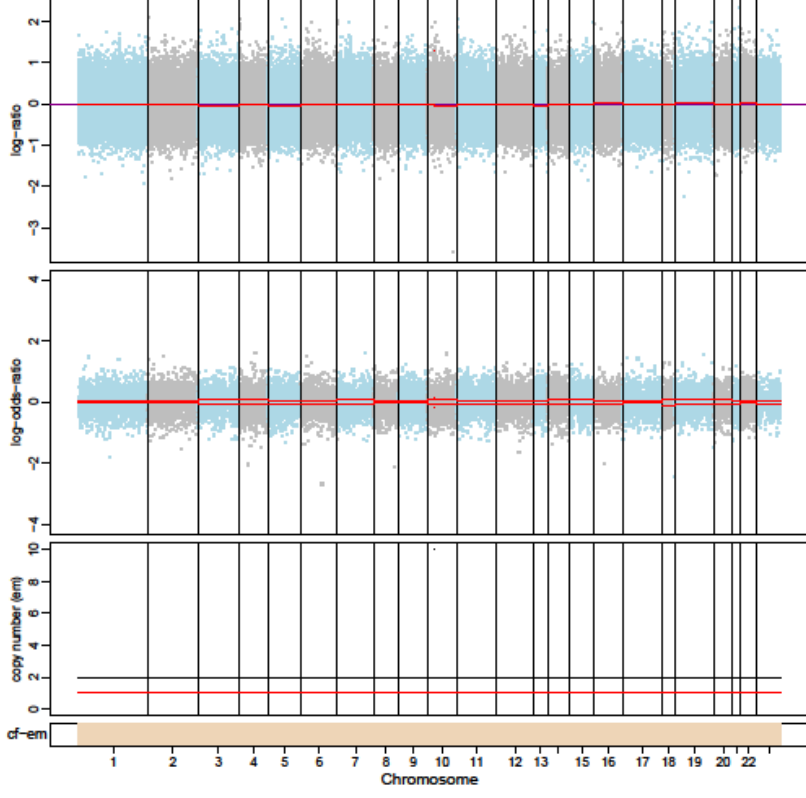
1174-P1



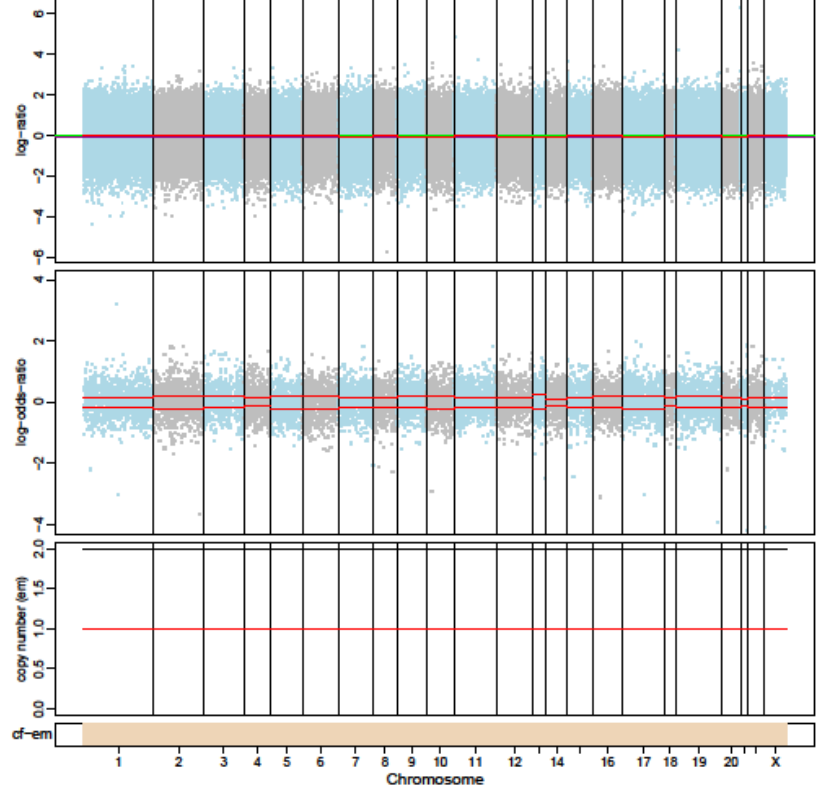
1174-P2



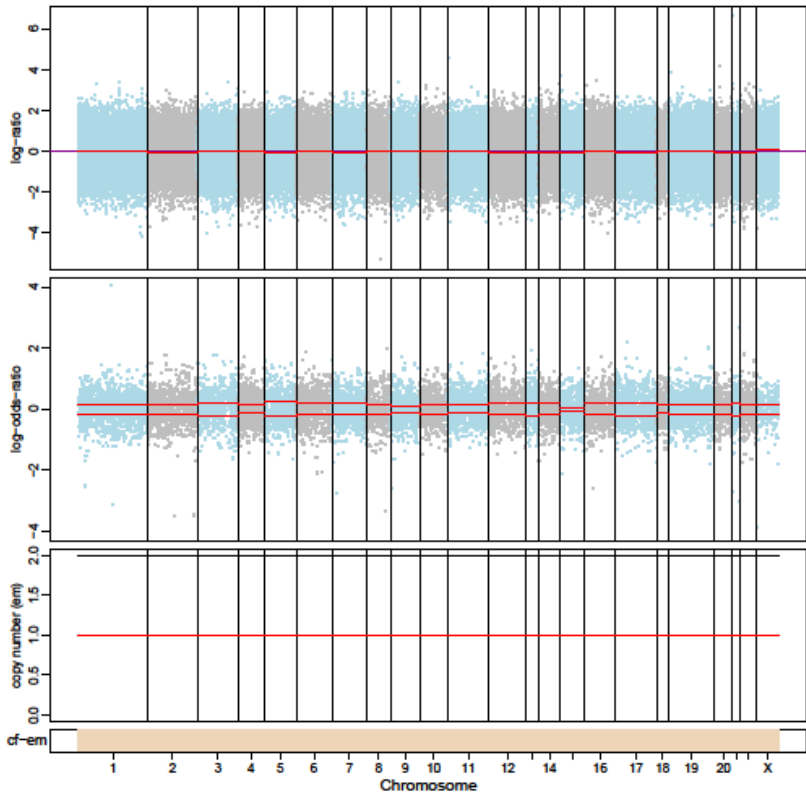
1176-P0



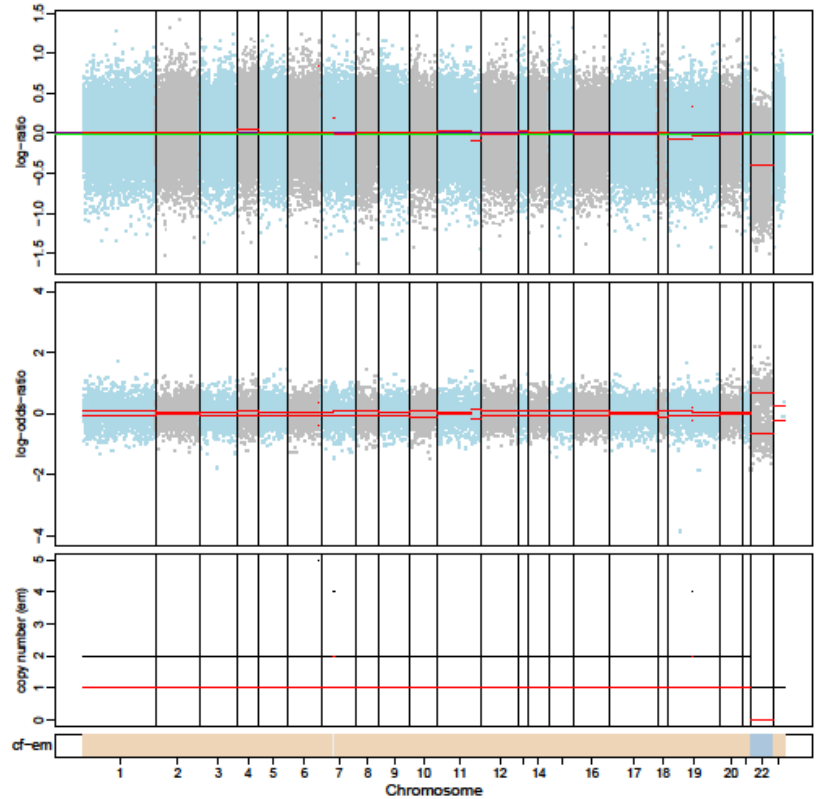
1176-P1



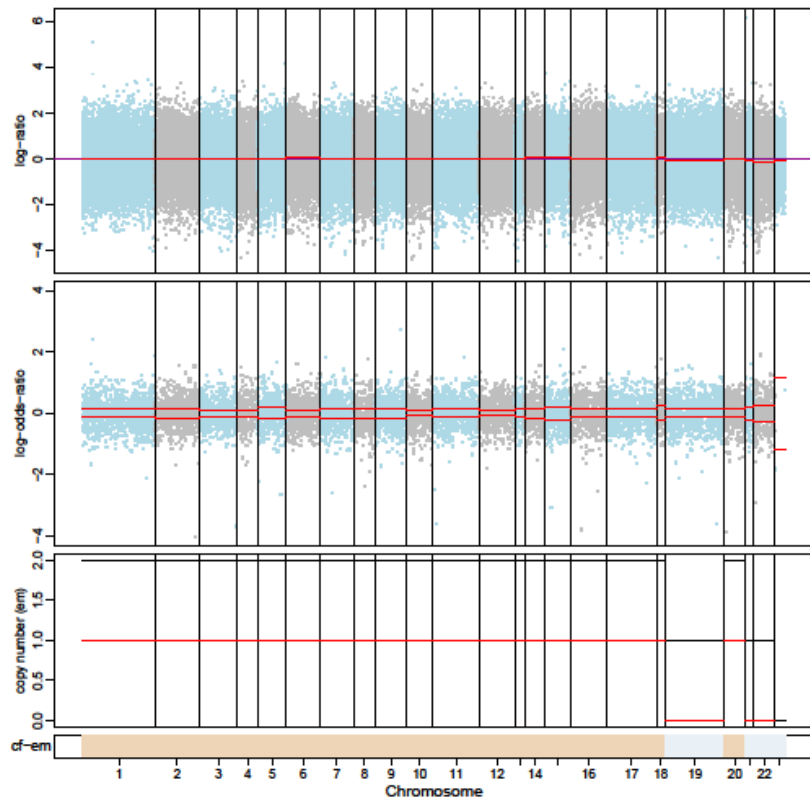
1176-P2



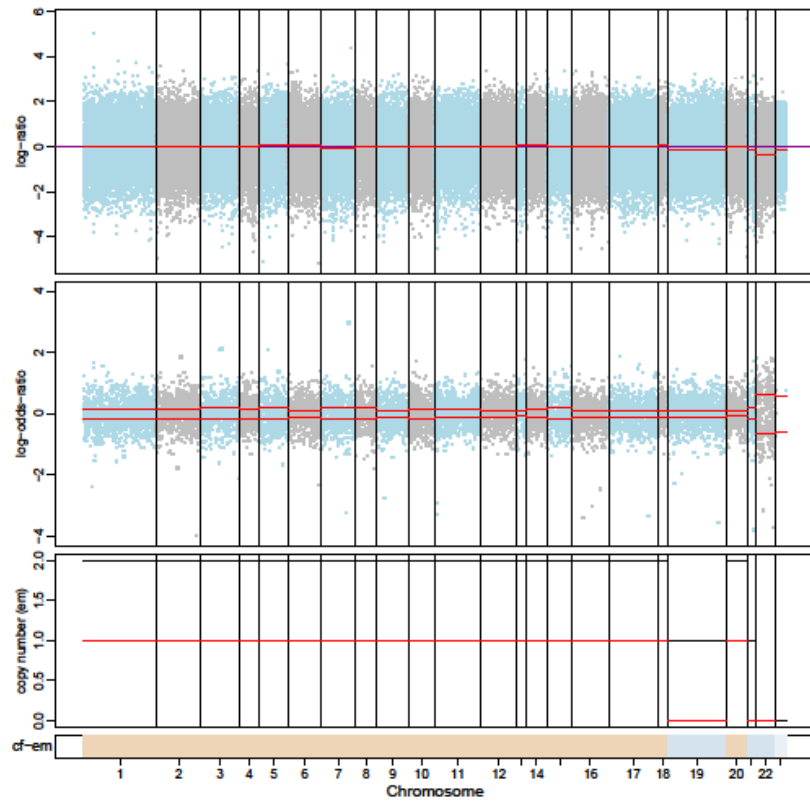
1180-P0



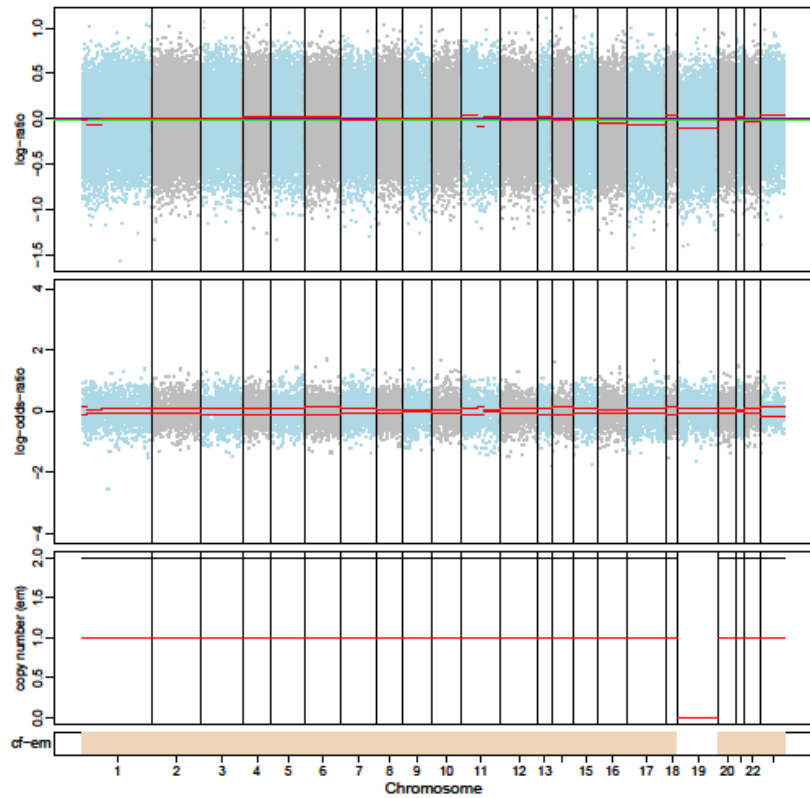
1180-P1



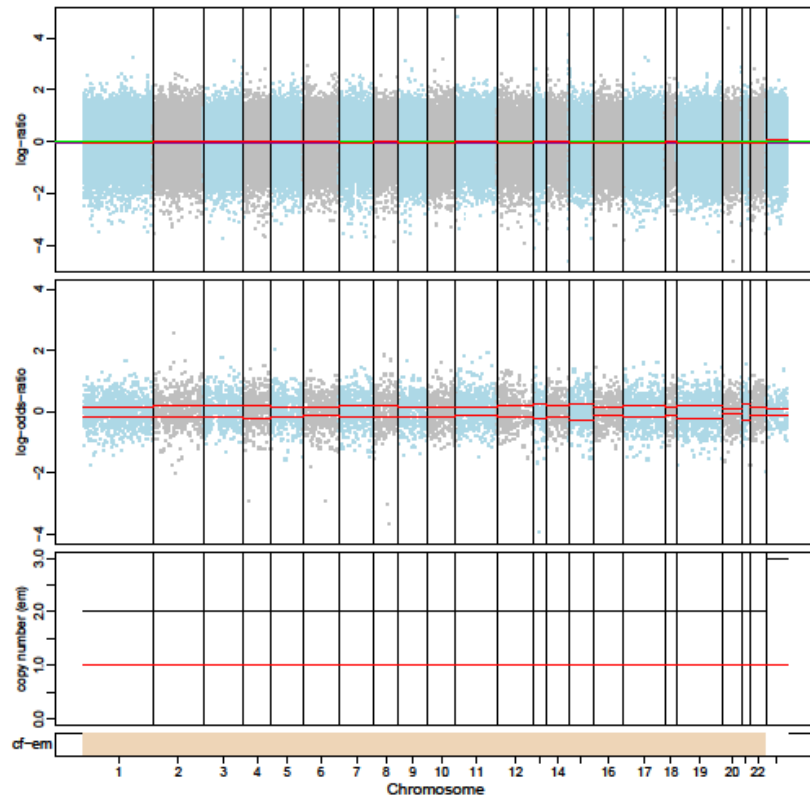
1180-P2



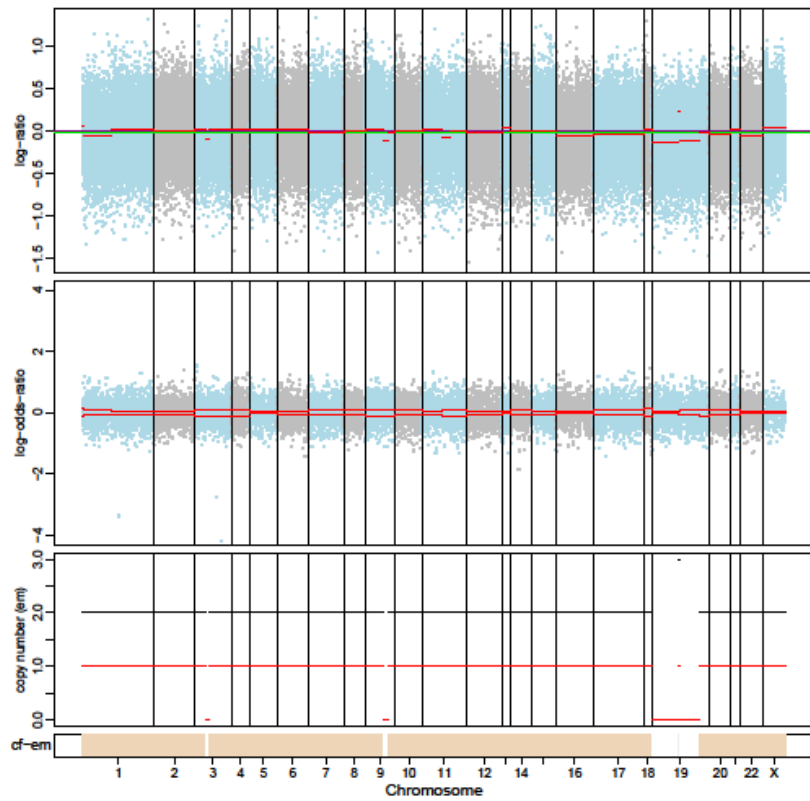
986-P0



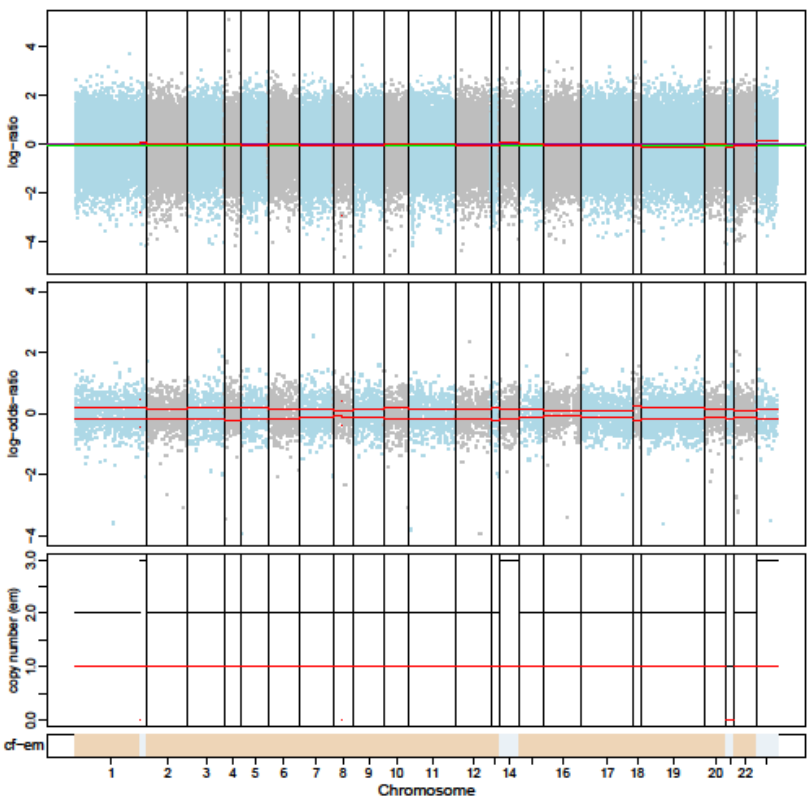
986-P1



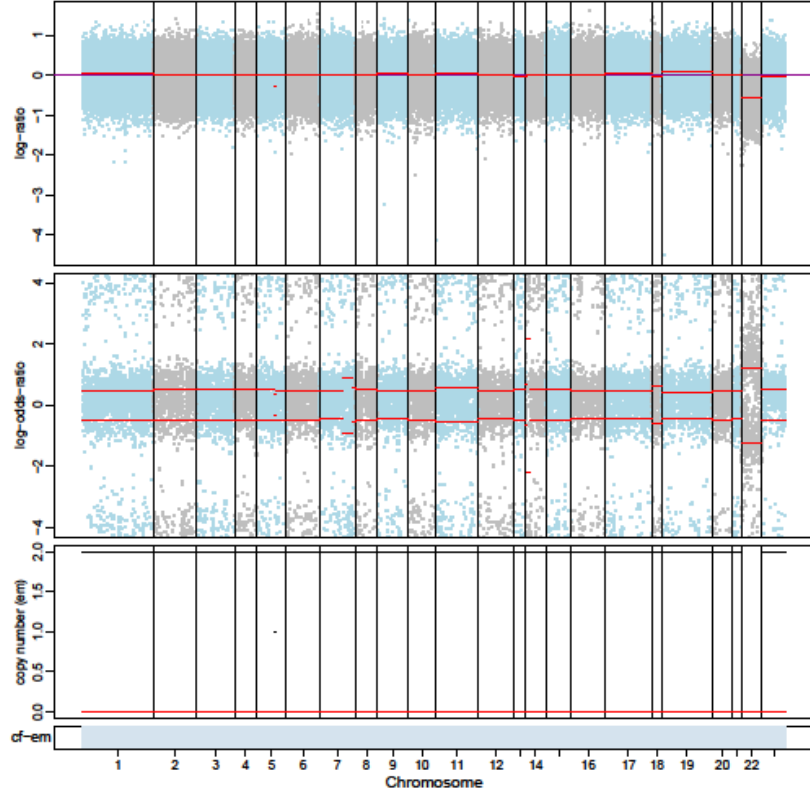
1181-P0



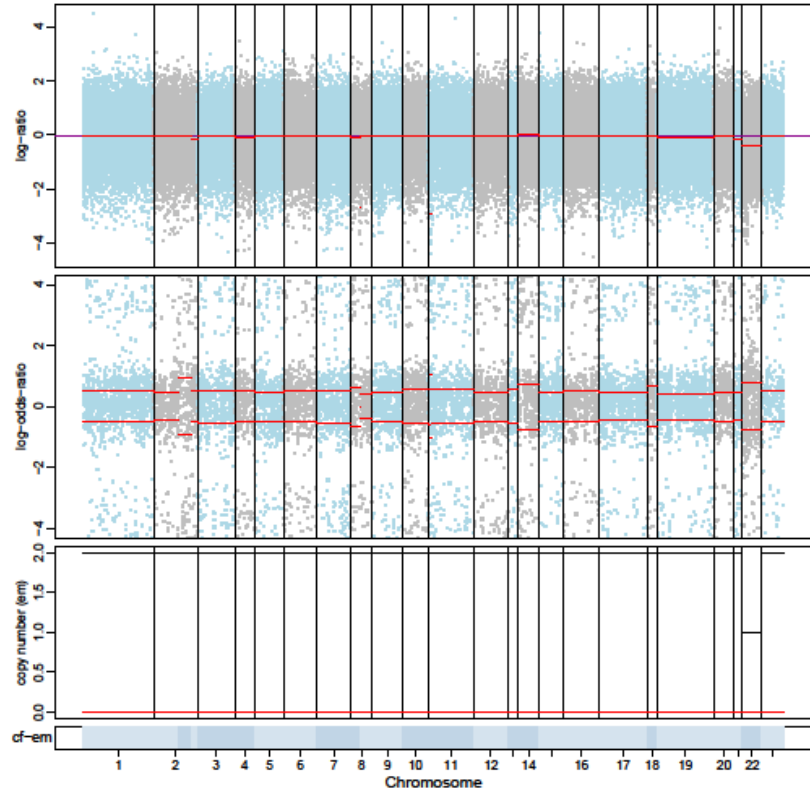
1181-P1



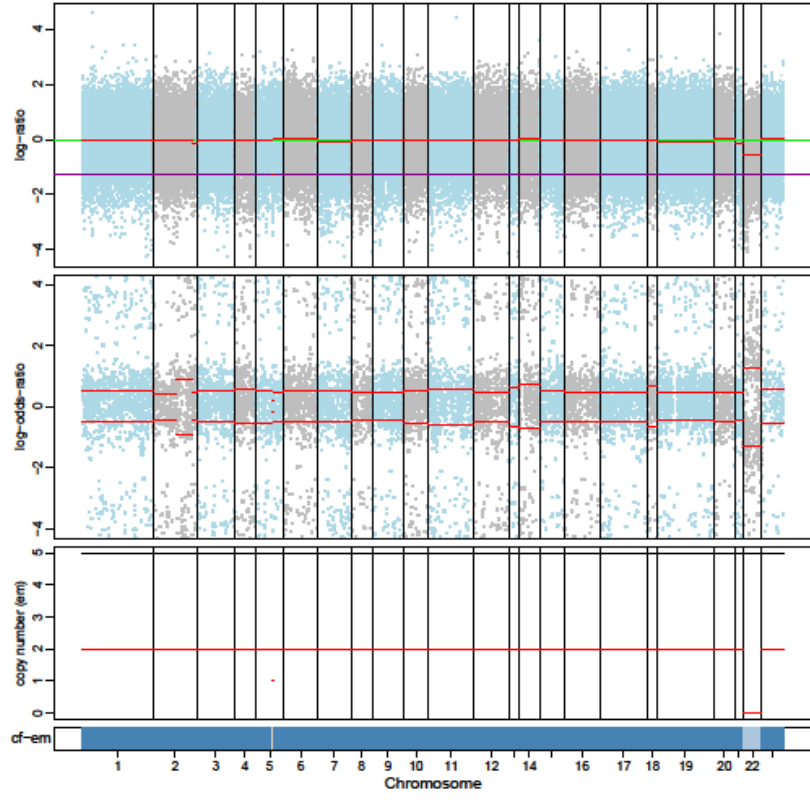
1183-P0



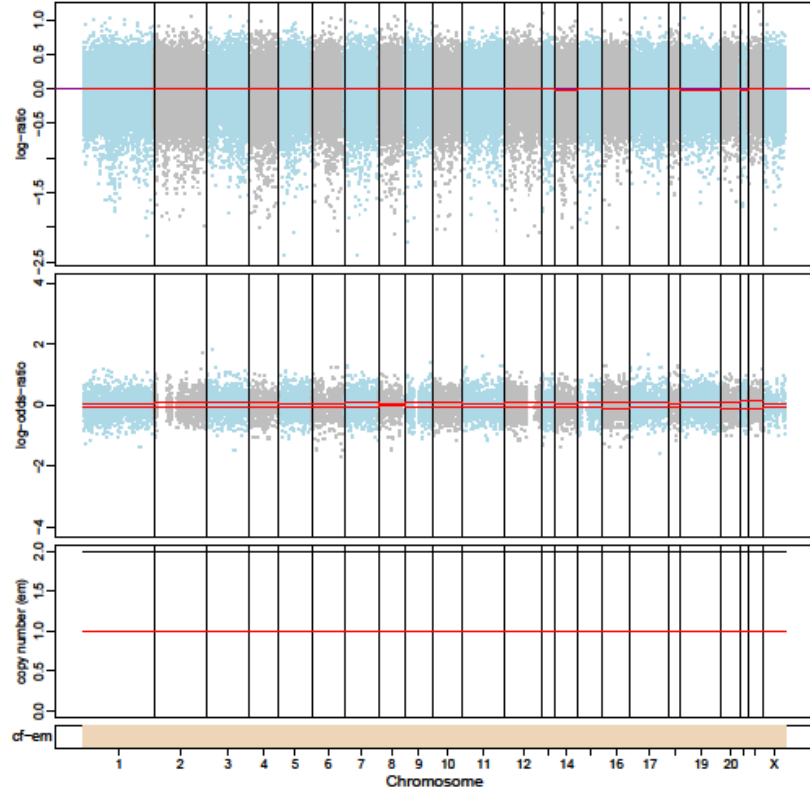
1183-P1



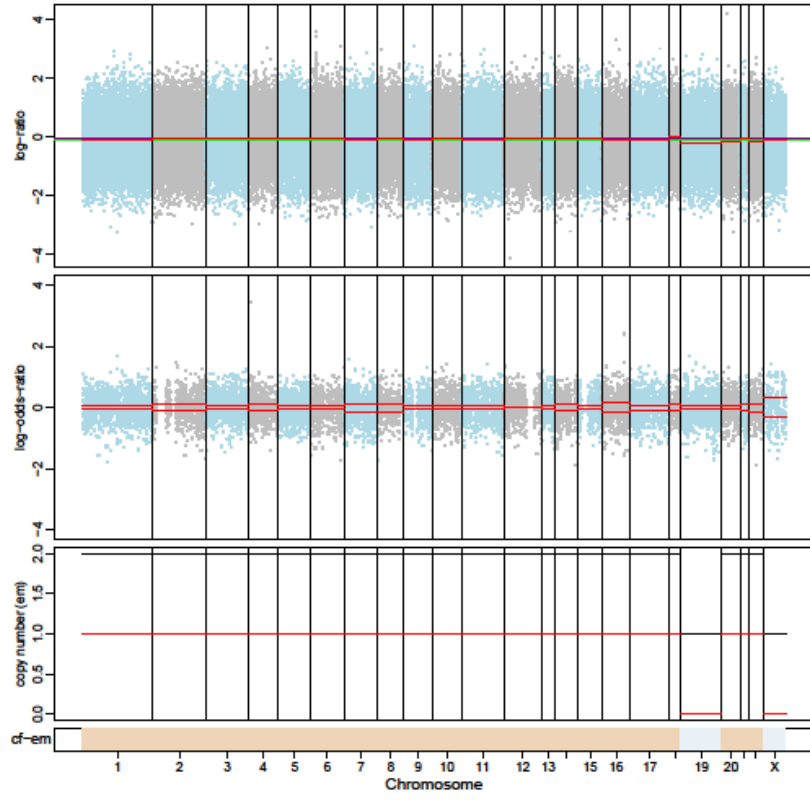
1183-P2



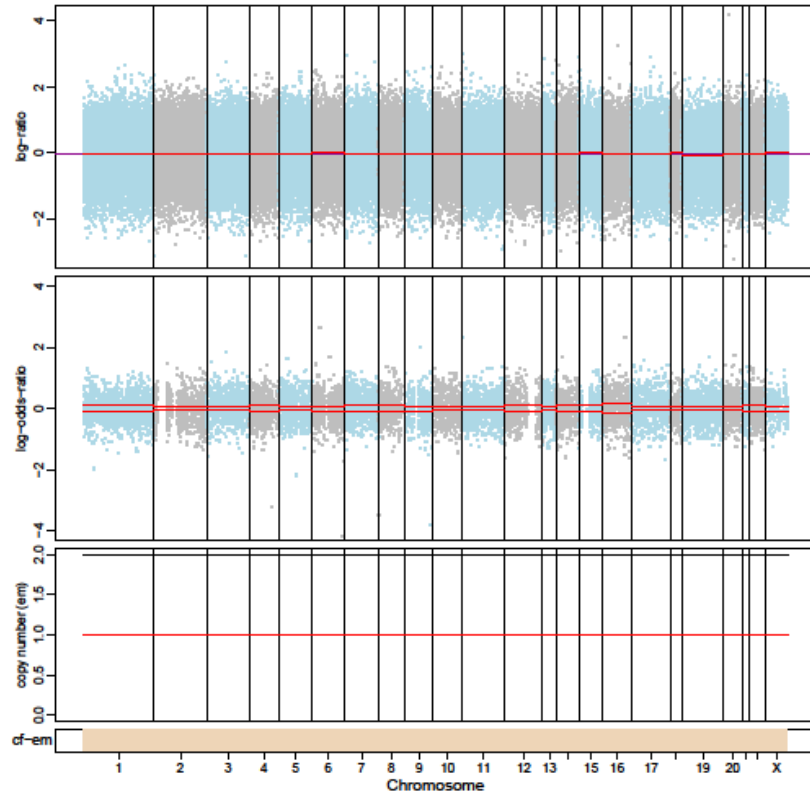
1184-P0



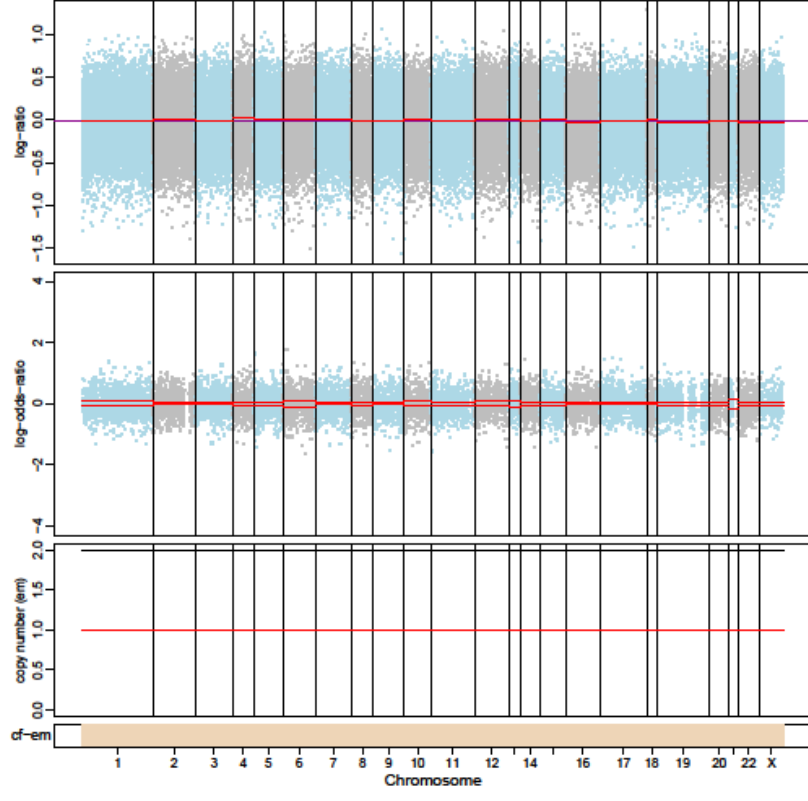
1184-P1



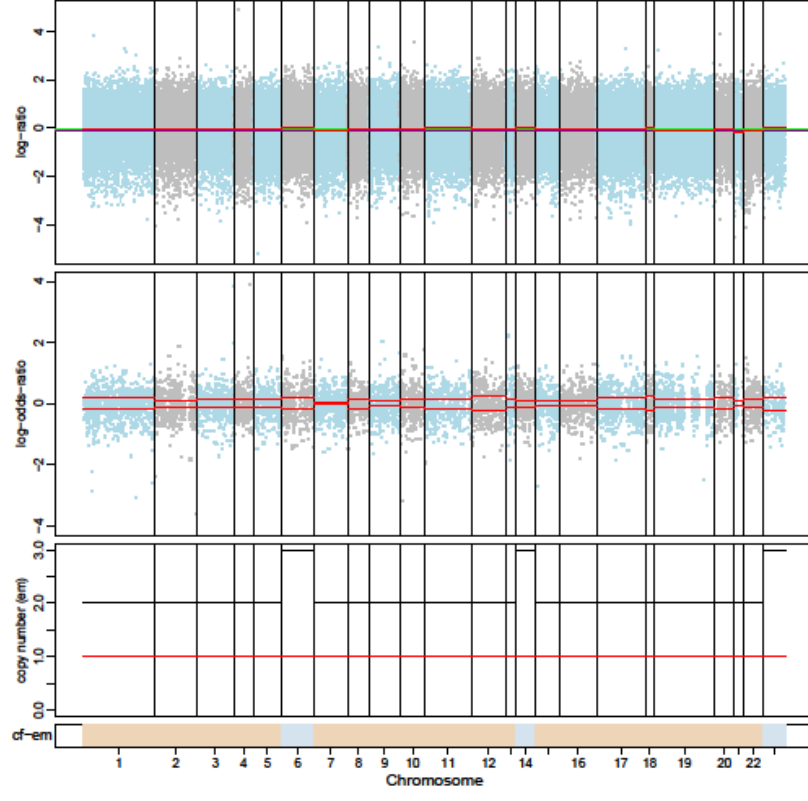
1184-P2



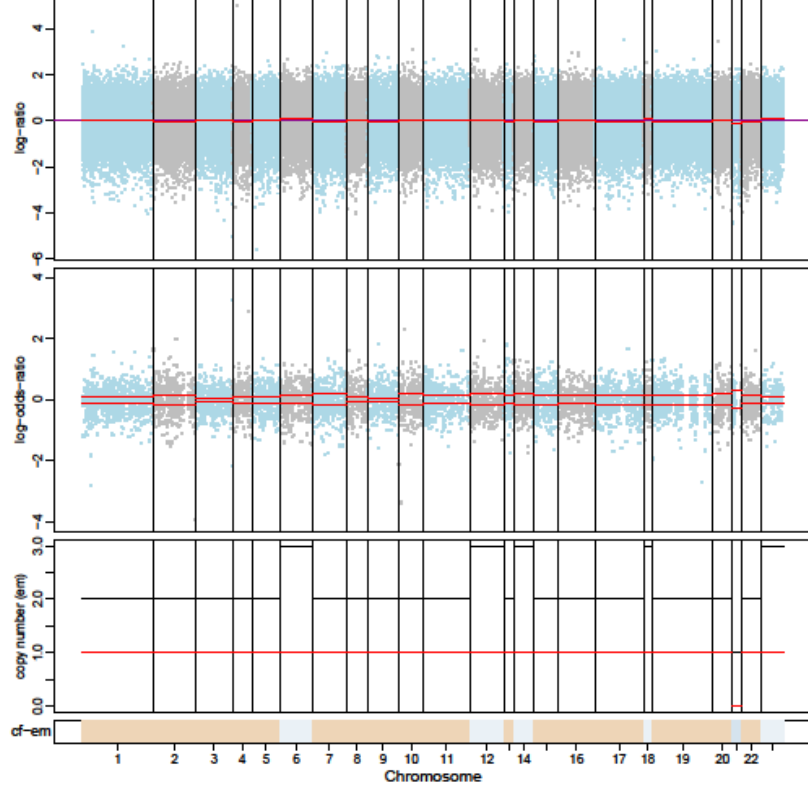
1188-P0



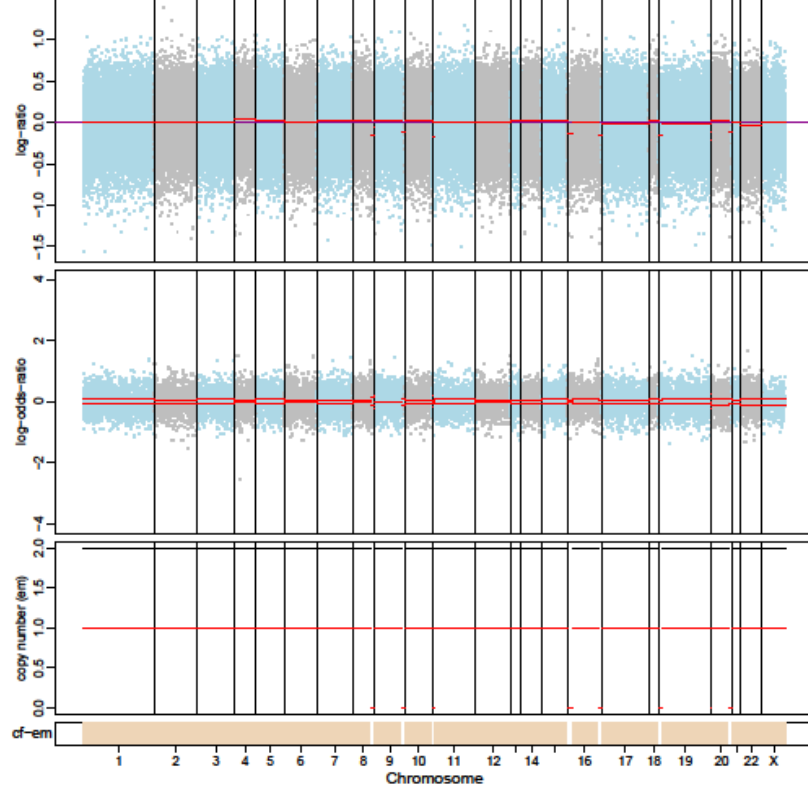
1188-P1



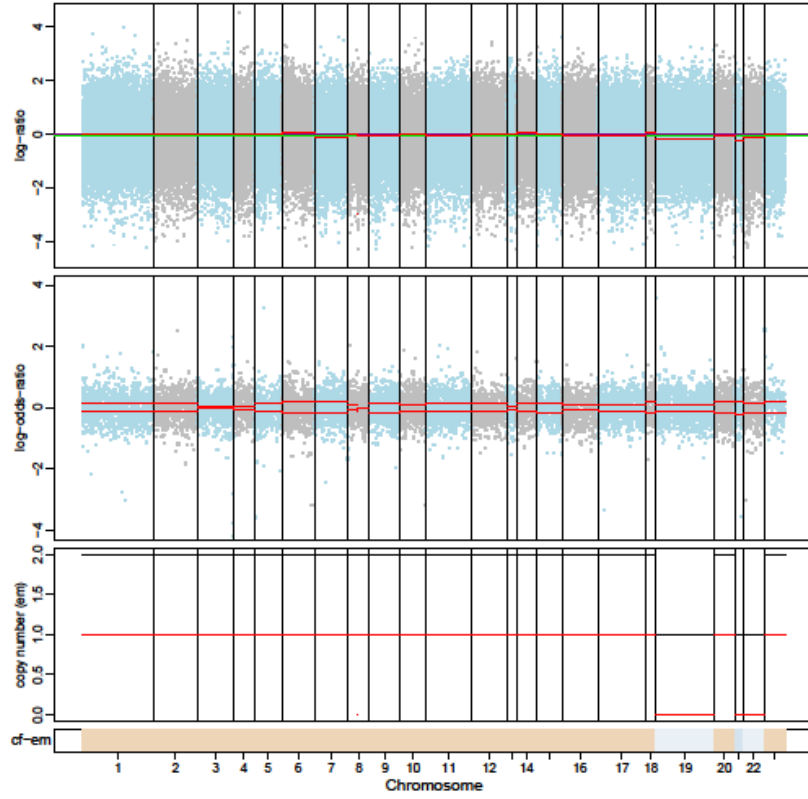
1188-P2



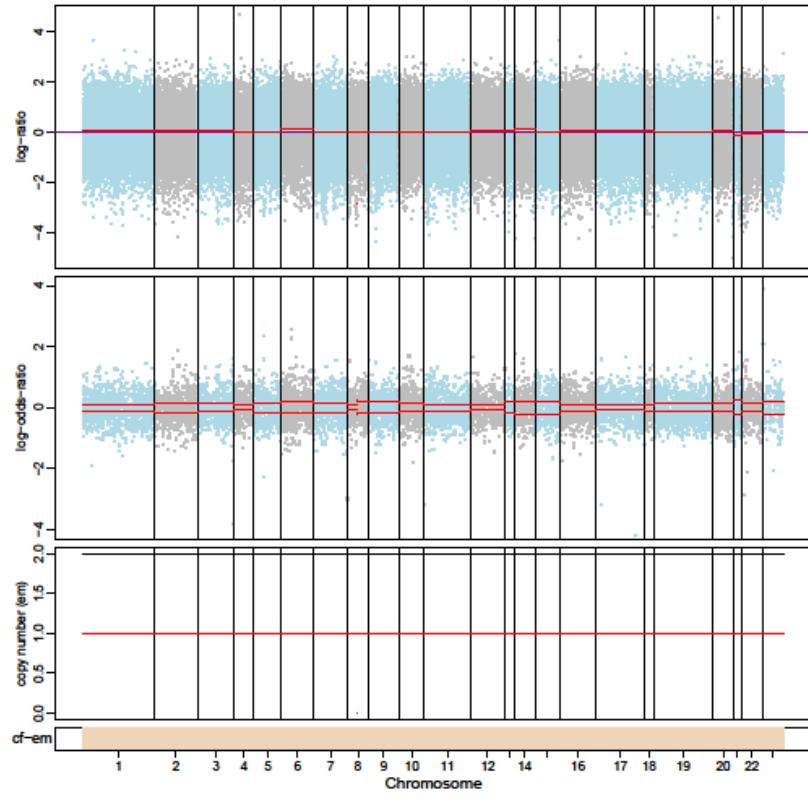
1189-P0



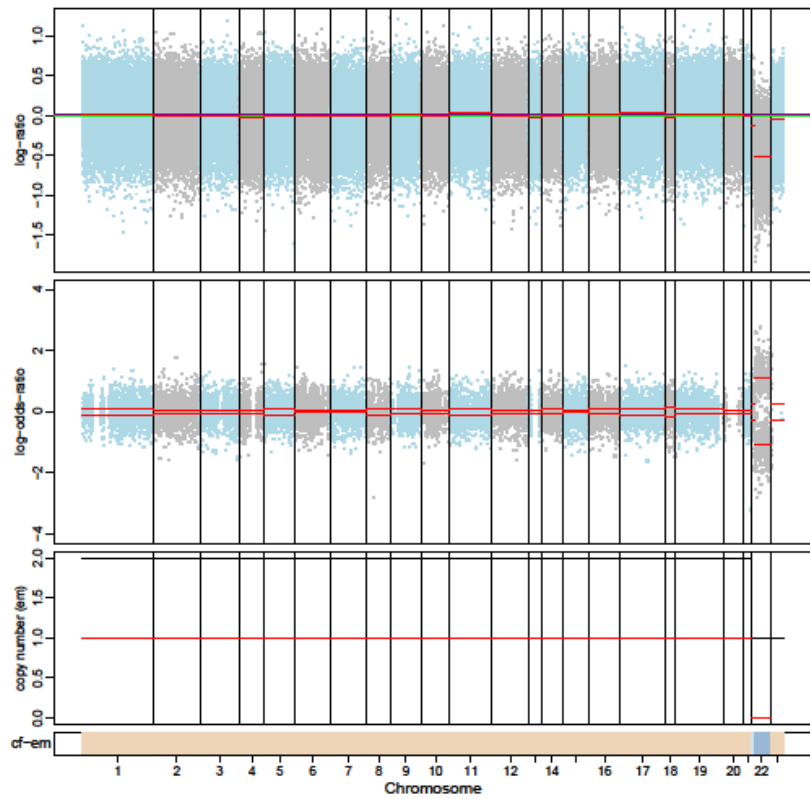
1189-P1



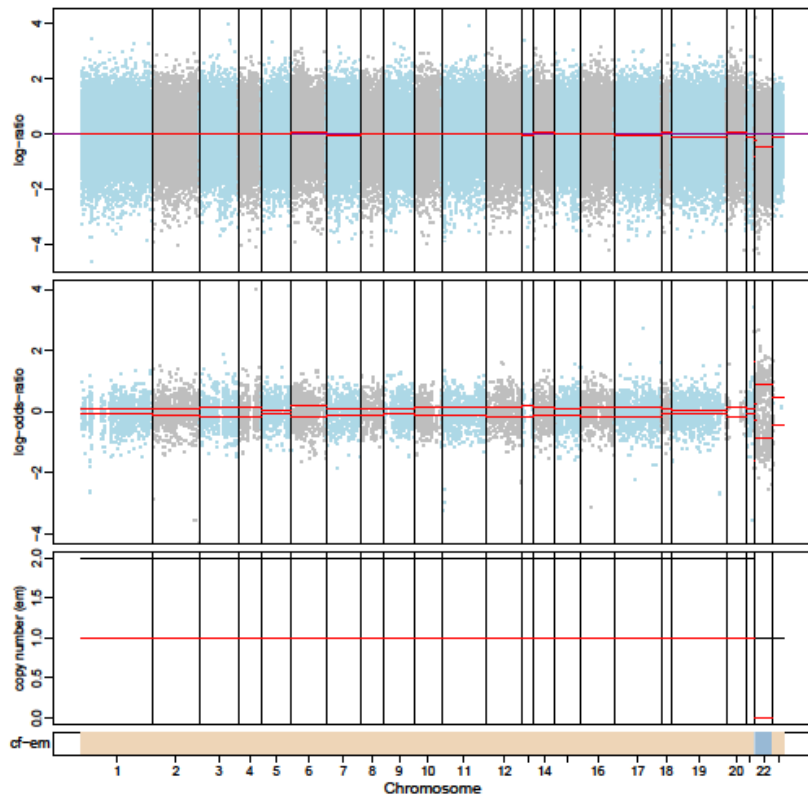
1189-P2



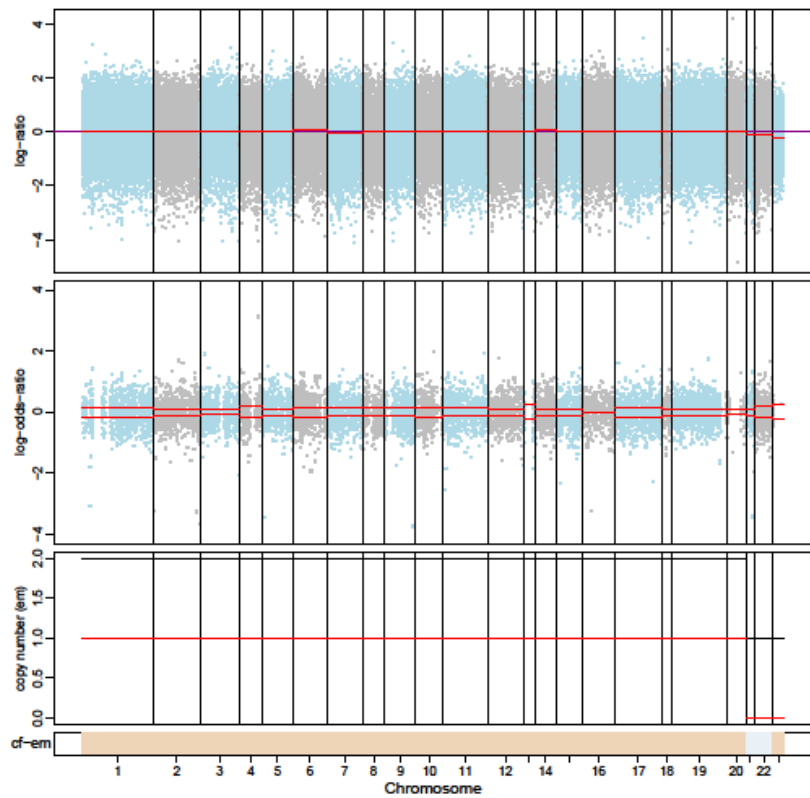
1191-P0



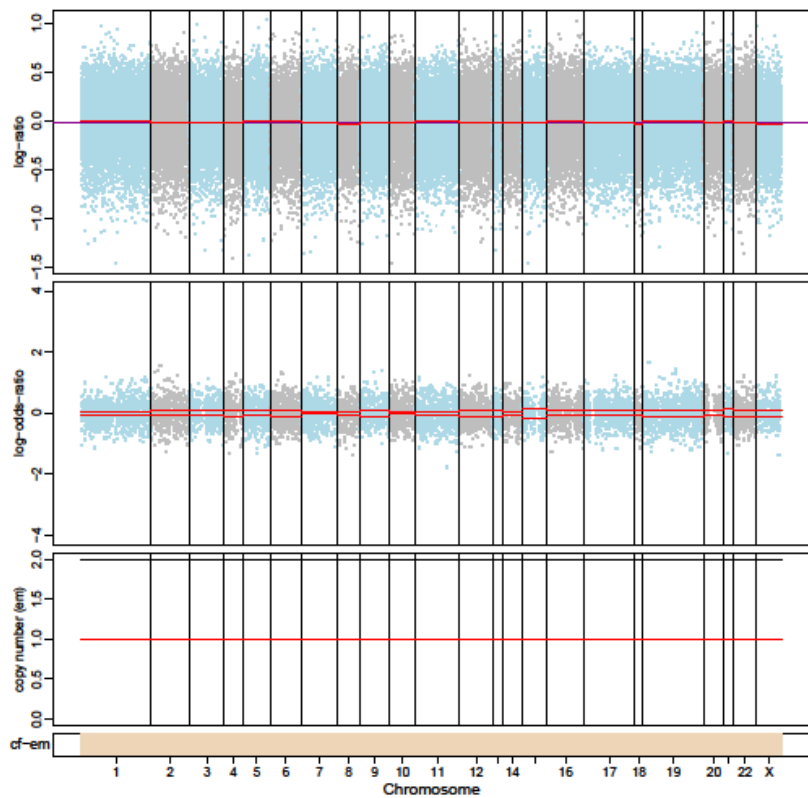
1191-P1



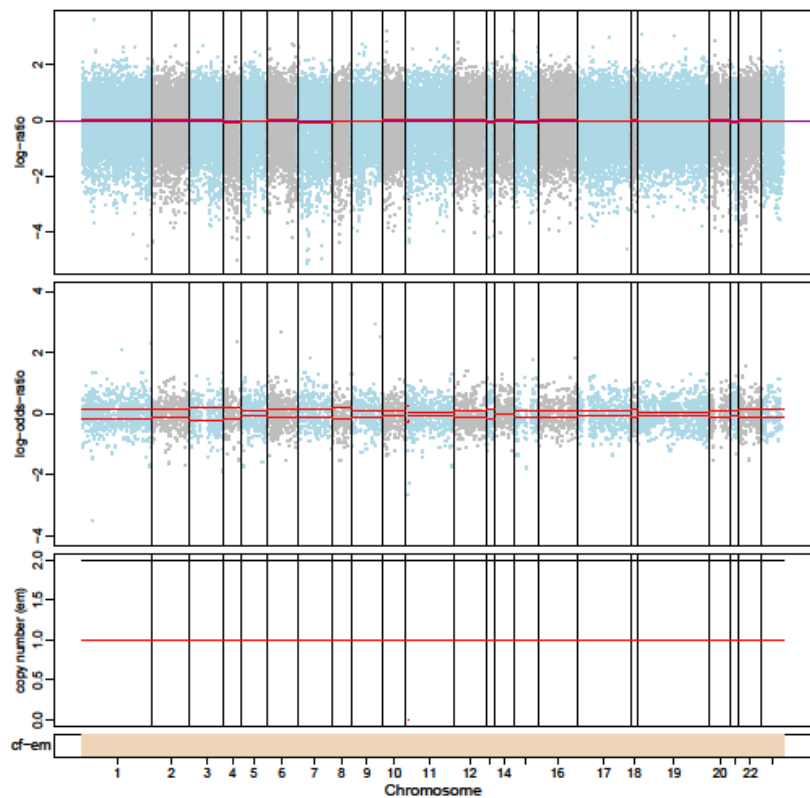
1191-P2



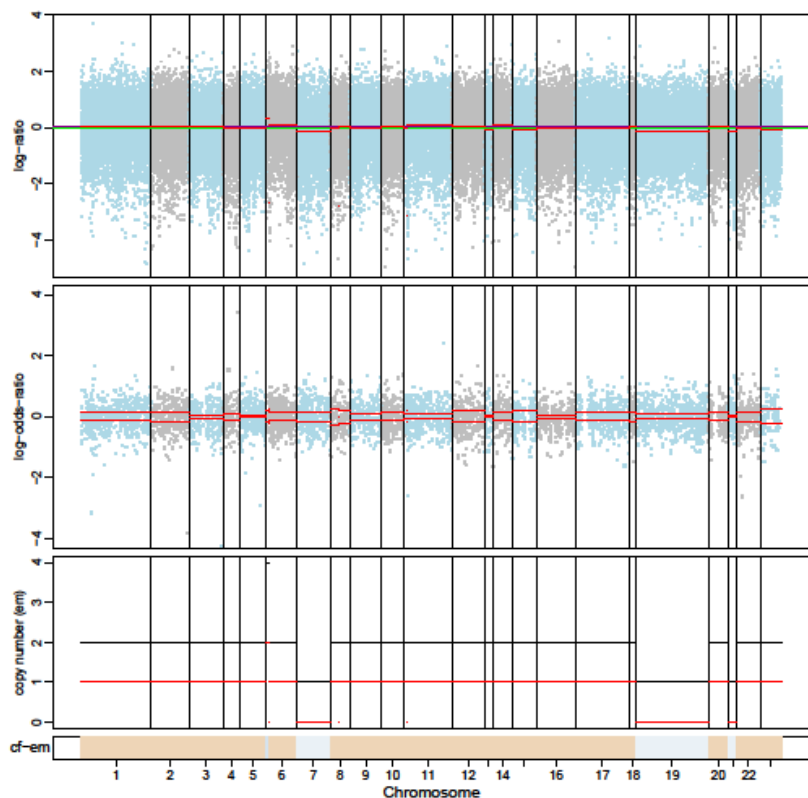
1195-P0



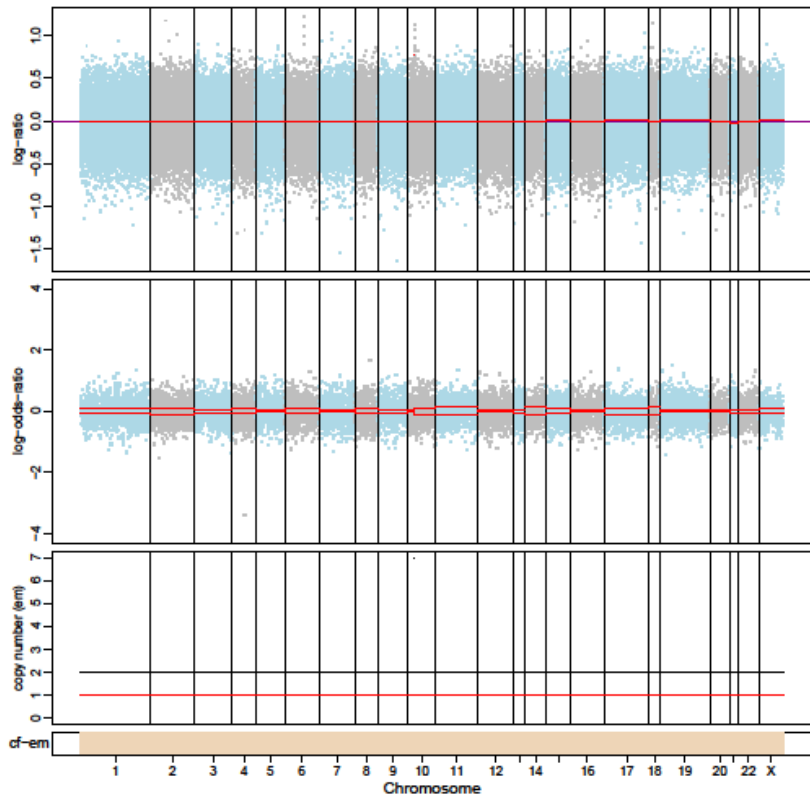
1195-P1



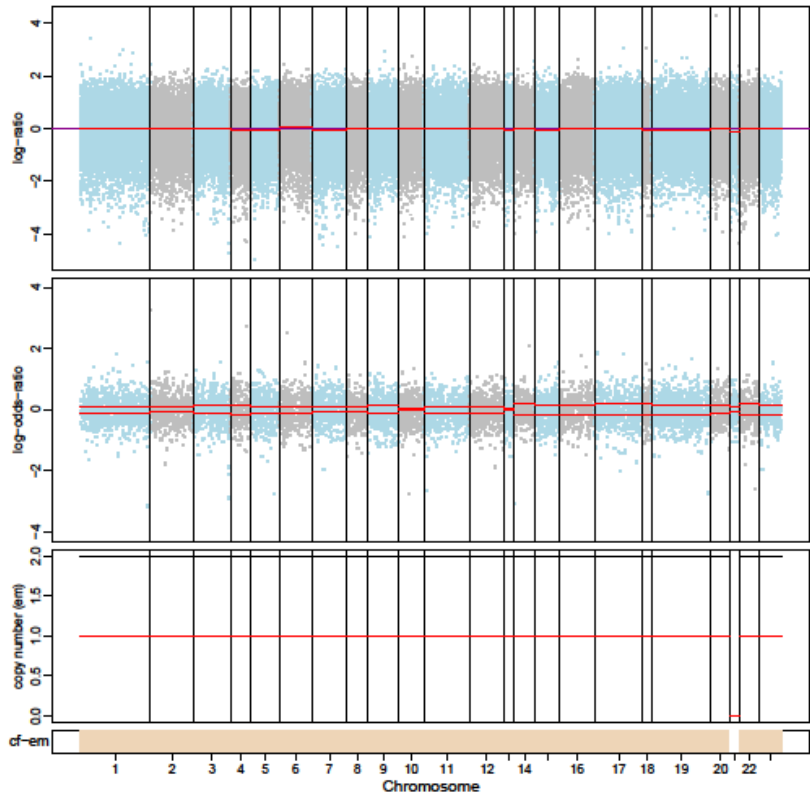
1195-P2



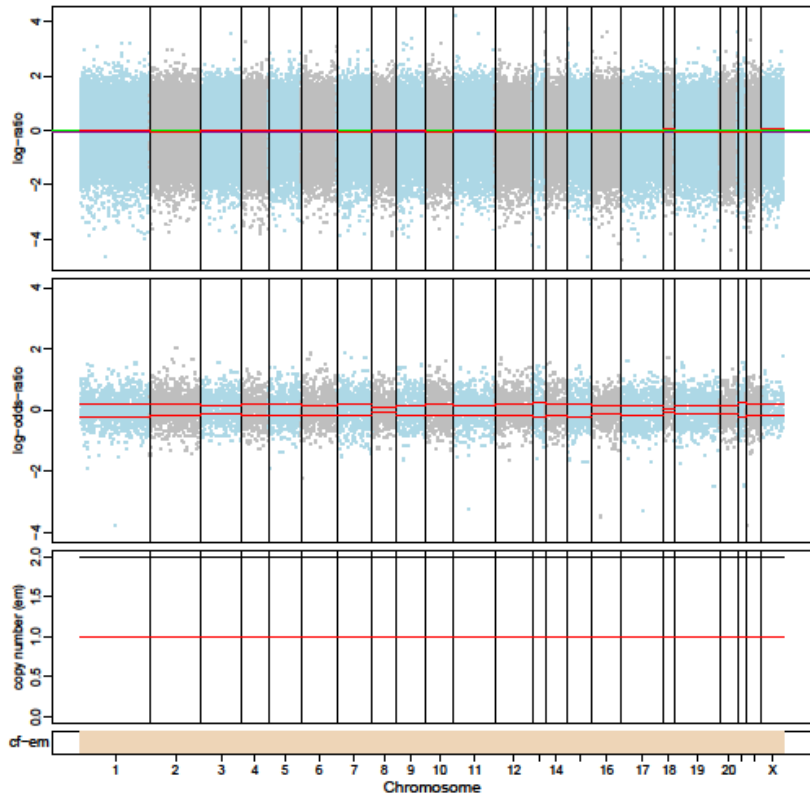
1196-P0



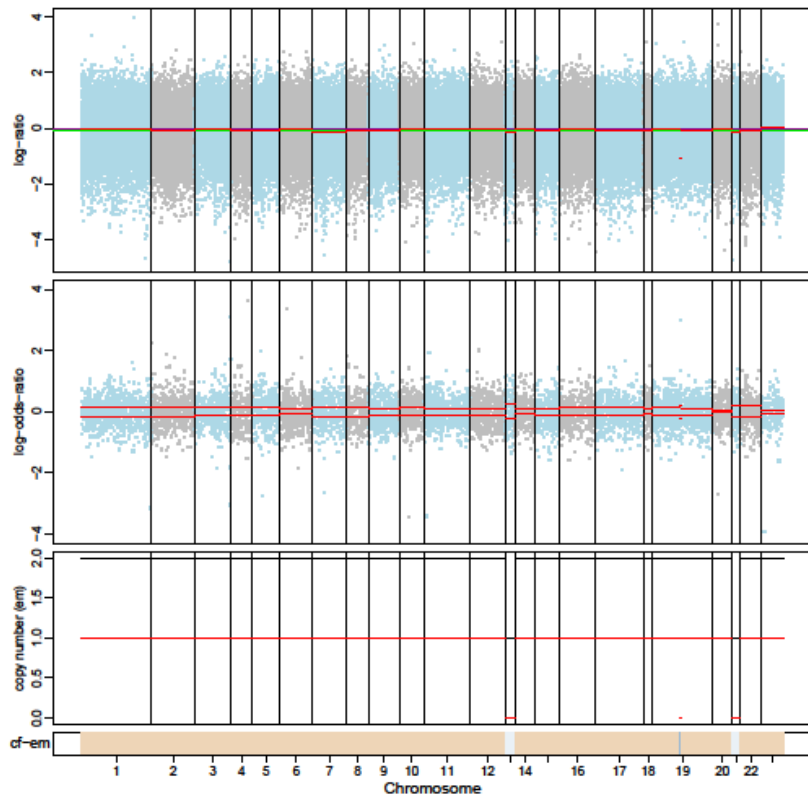
1196-P2



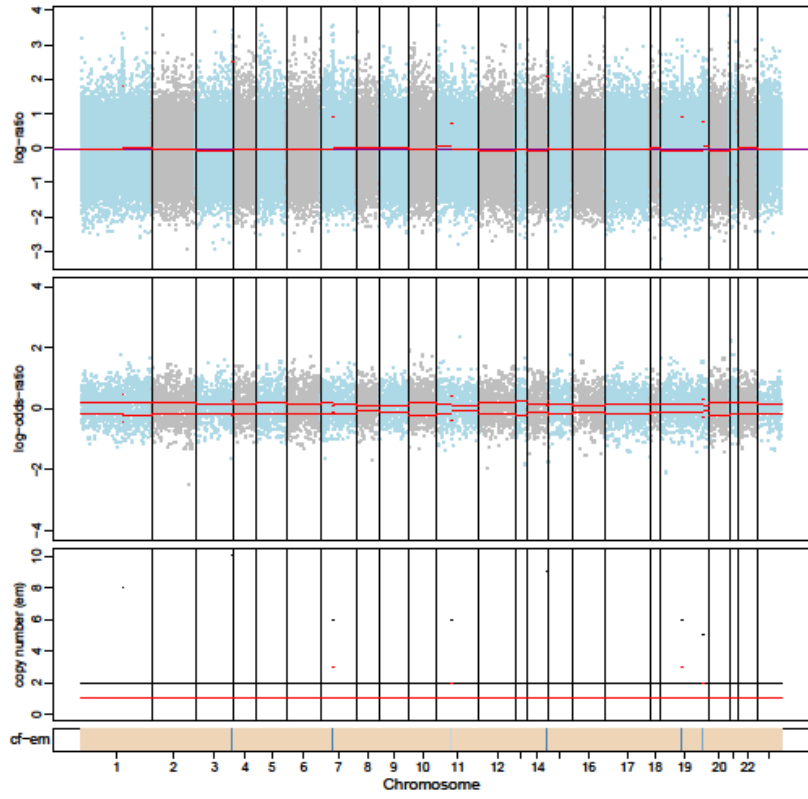
1198-P1



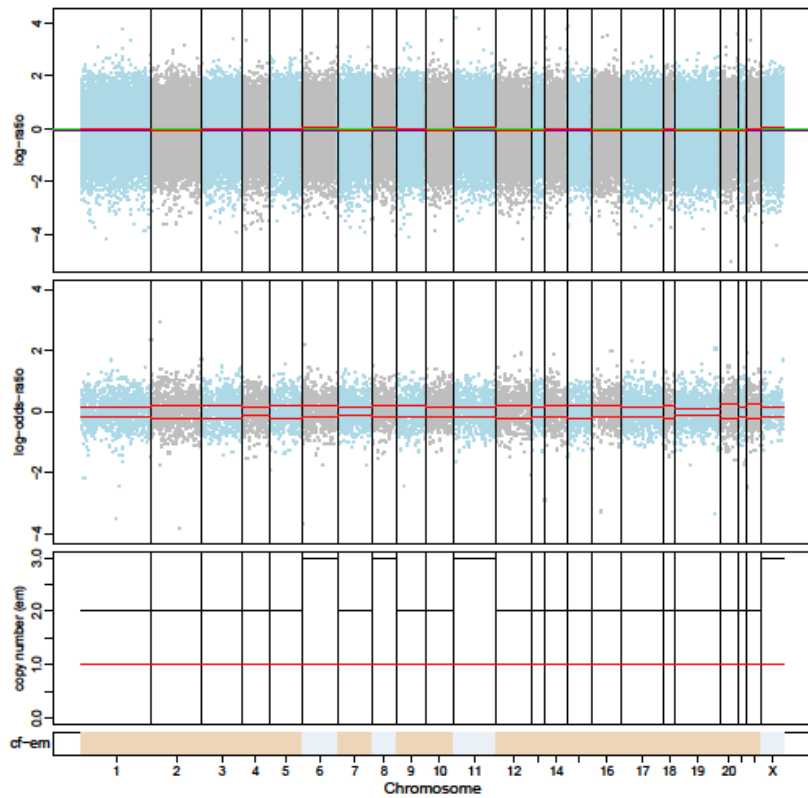
1196-P1



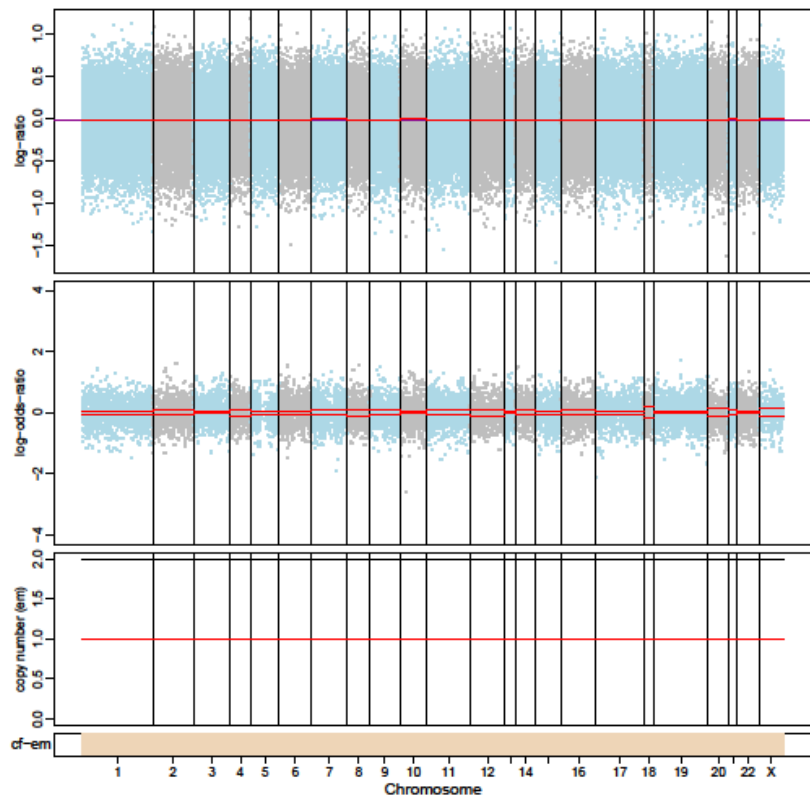
1198-P0



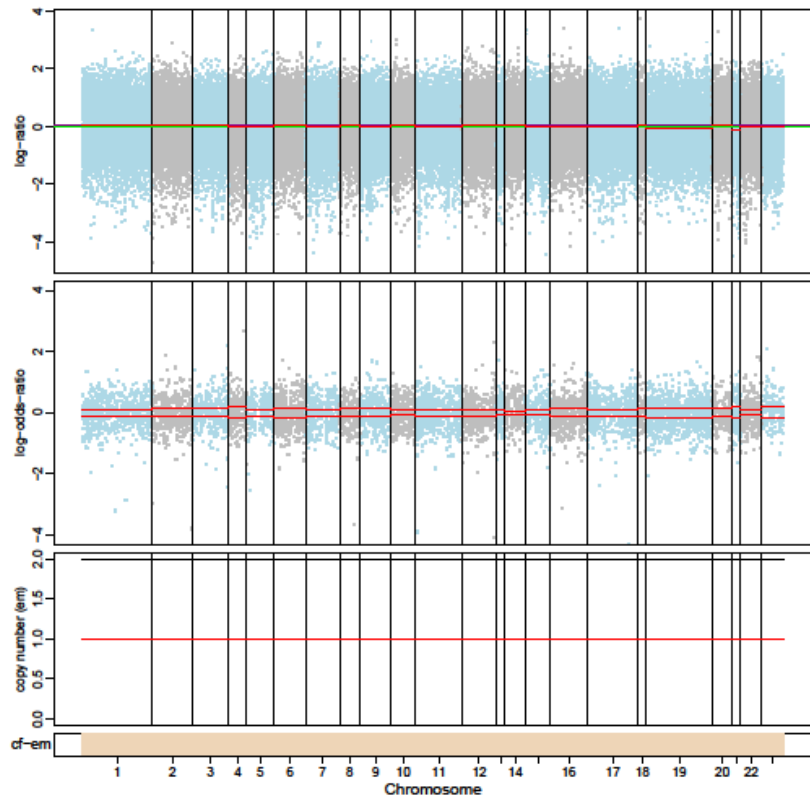
1198-P2



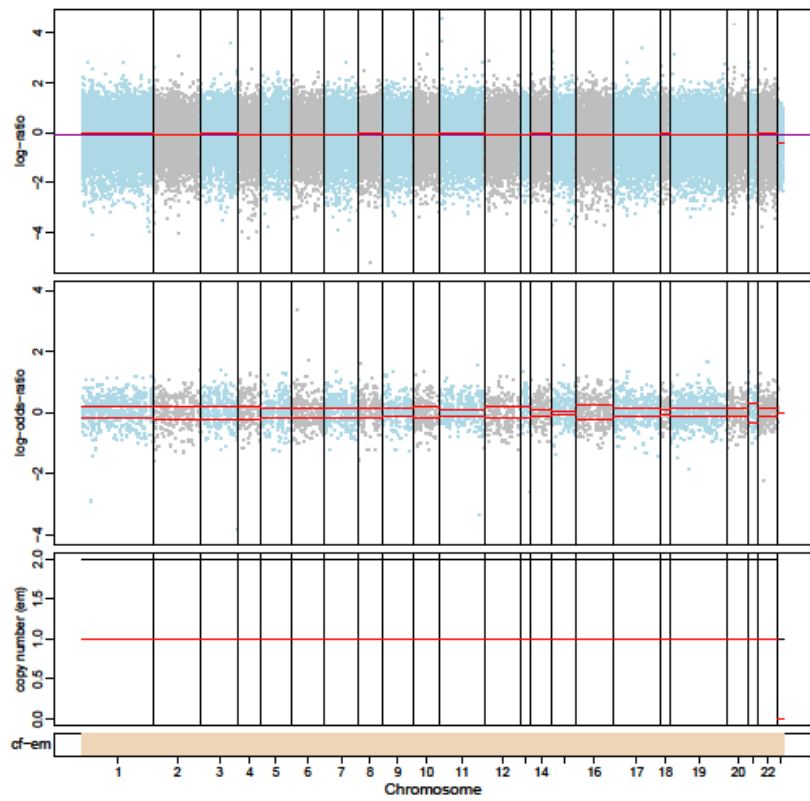
1199-P0



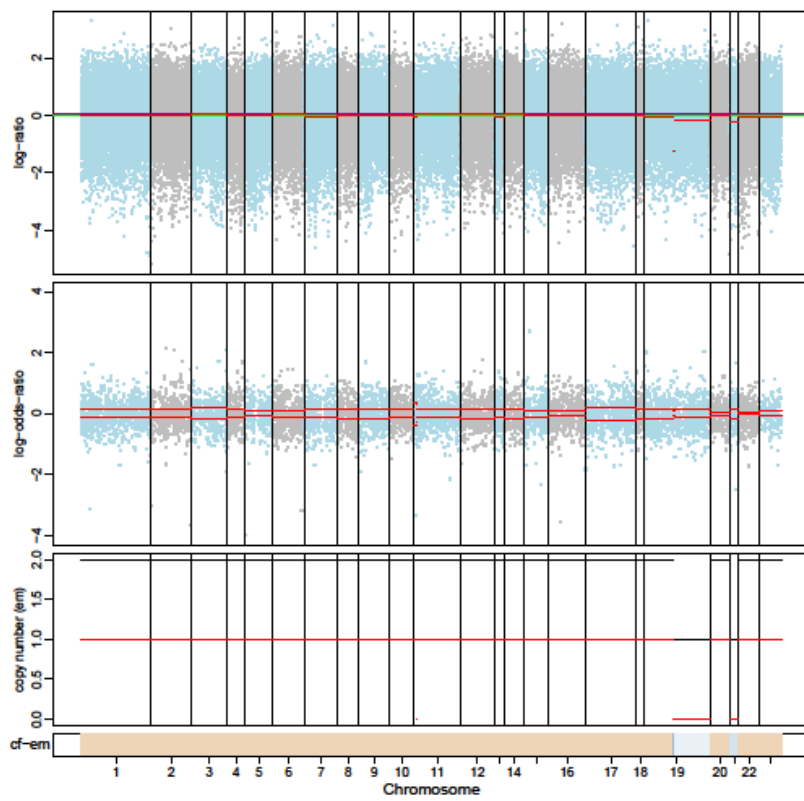
1199-P2



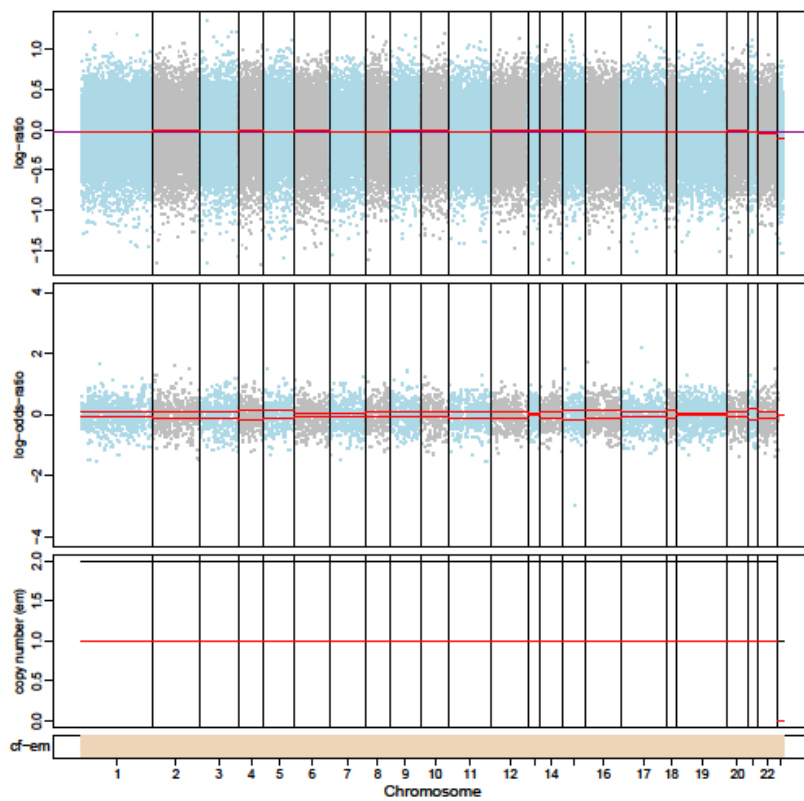
1200-P1



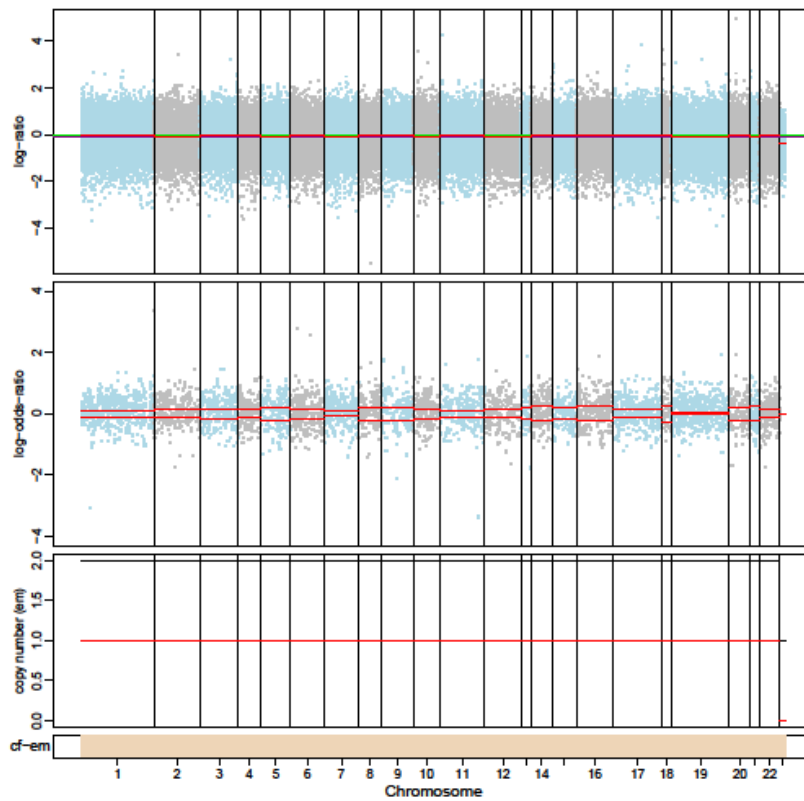
1199-P1



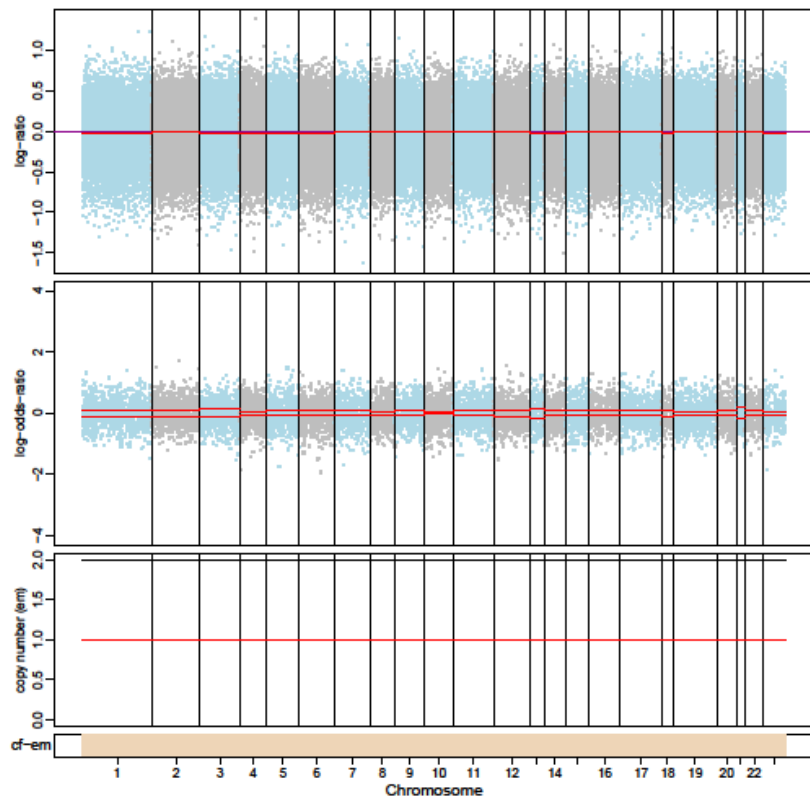
1200-P0



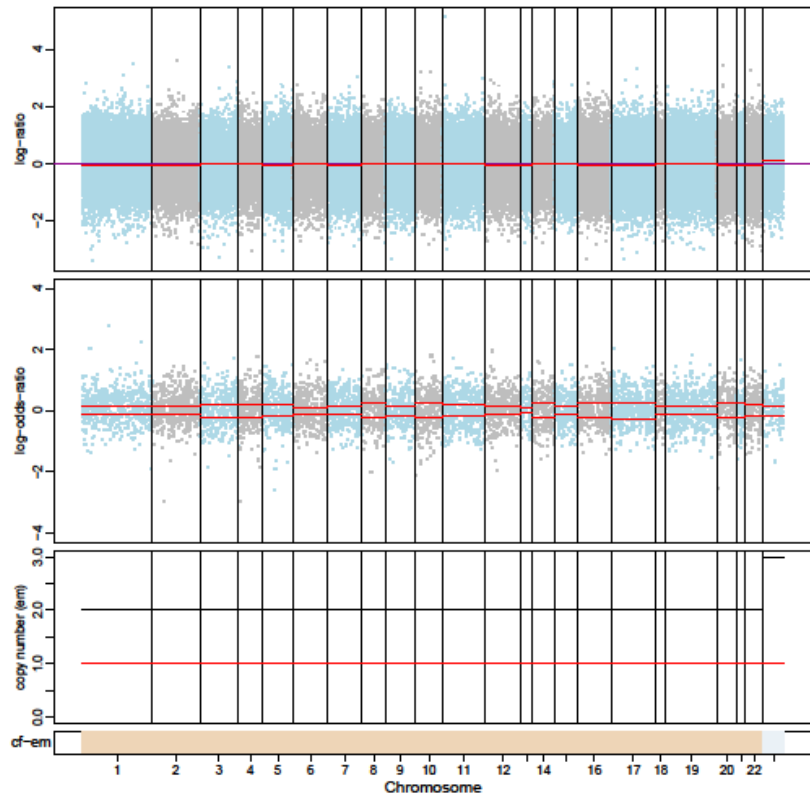
1200-P2



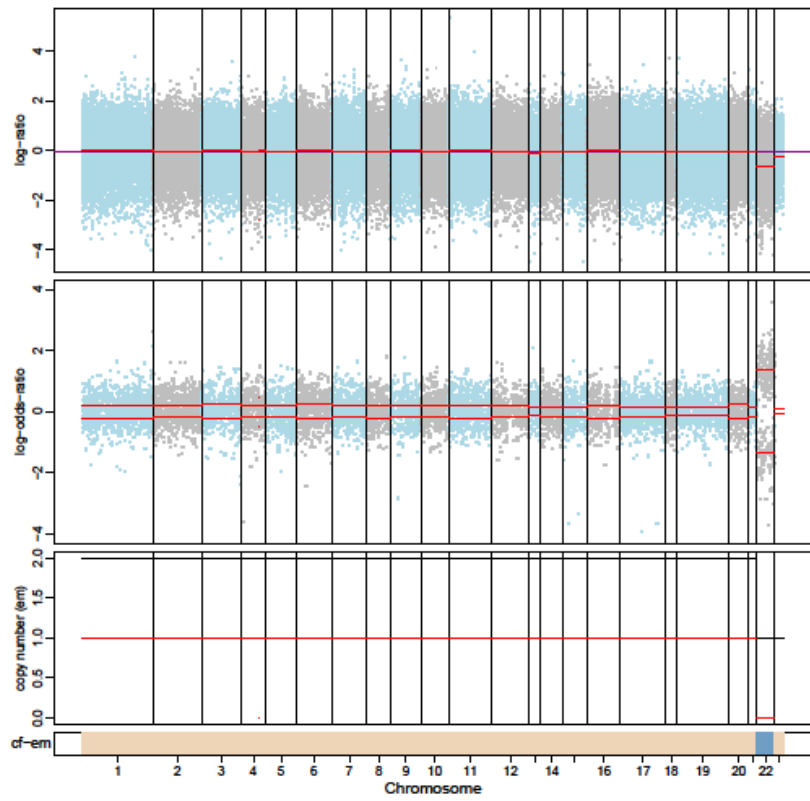
1201-P0



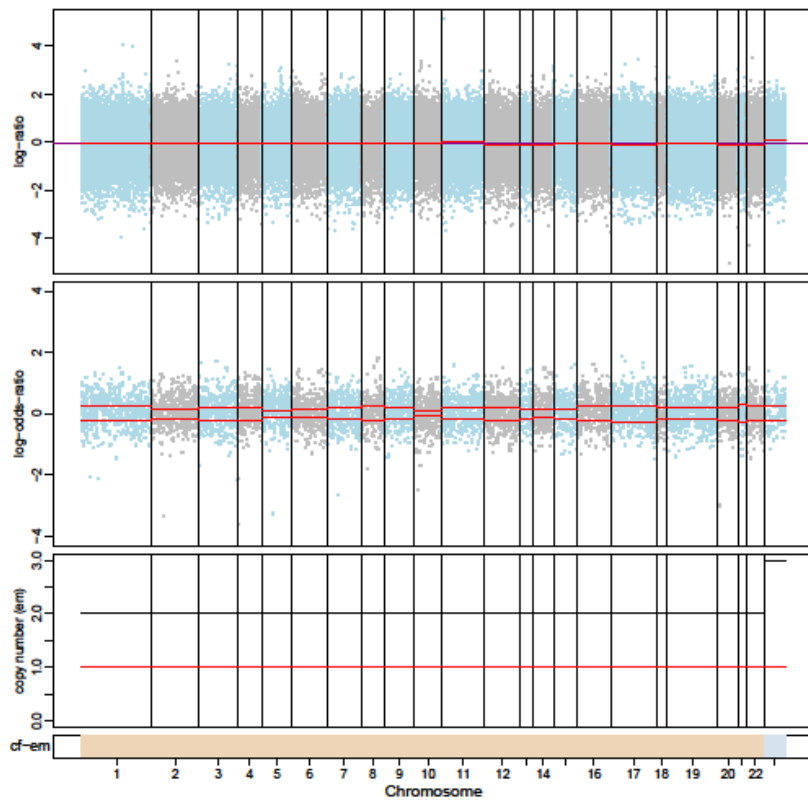
1201-P2



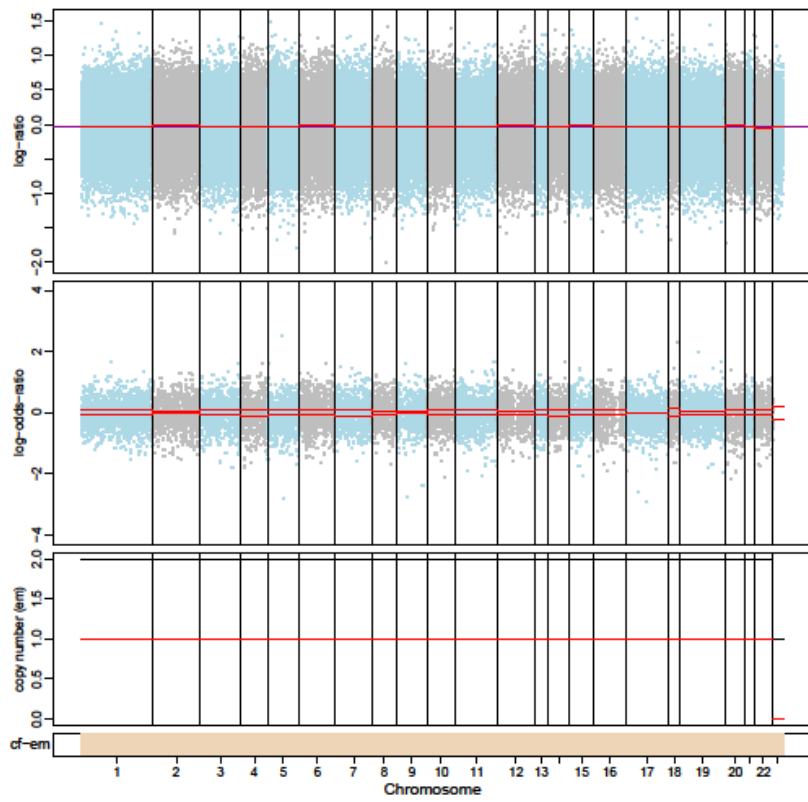
1400-P1



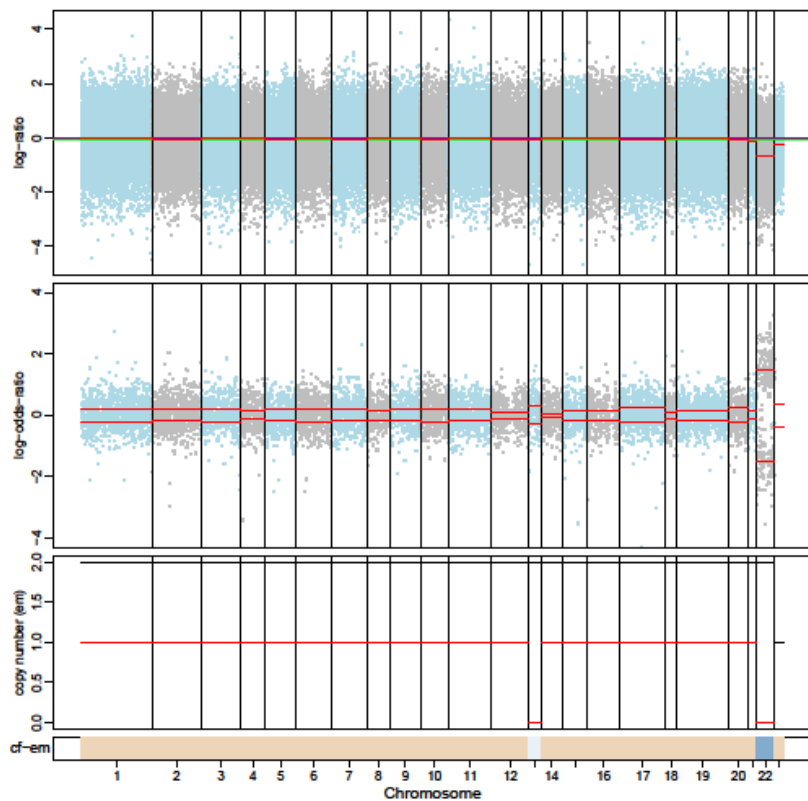
1201-P1



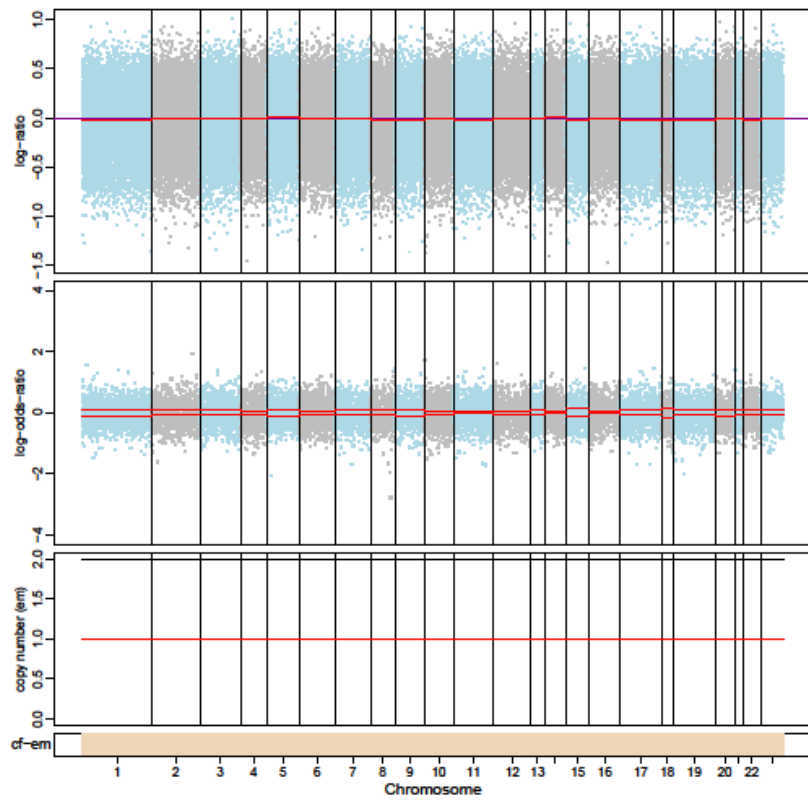
1400-P0



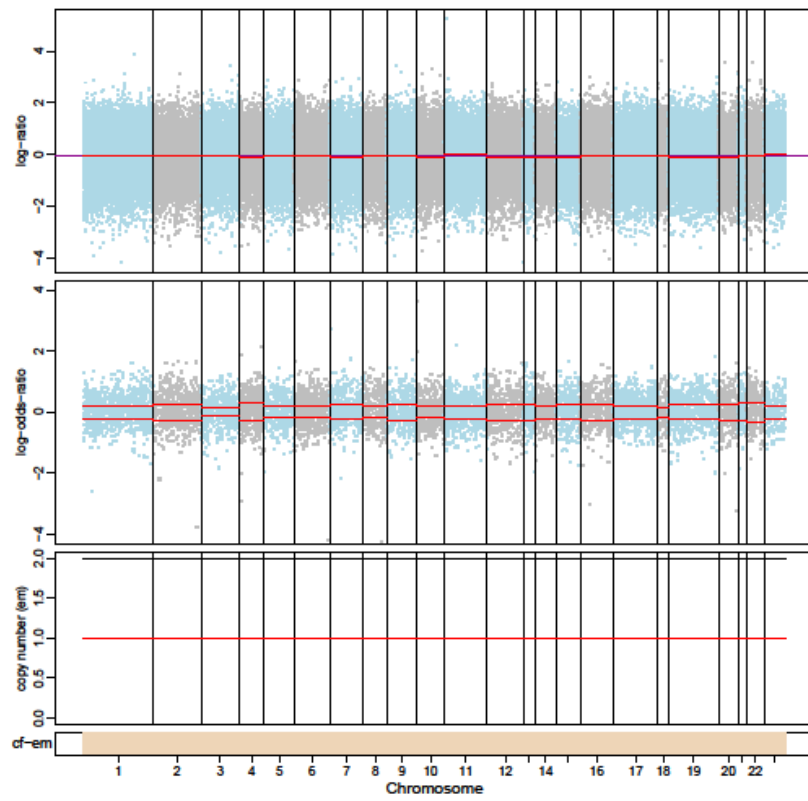
1400-P2



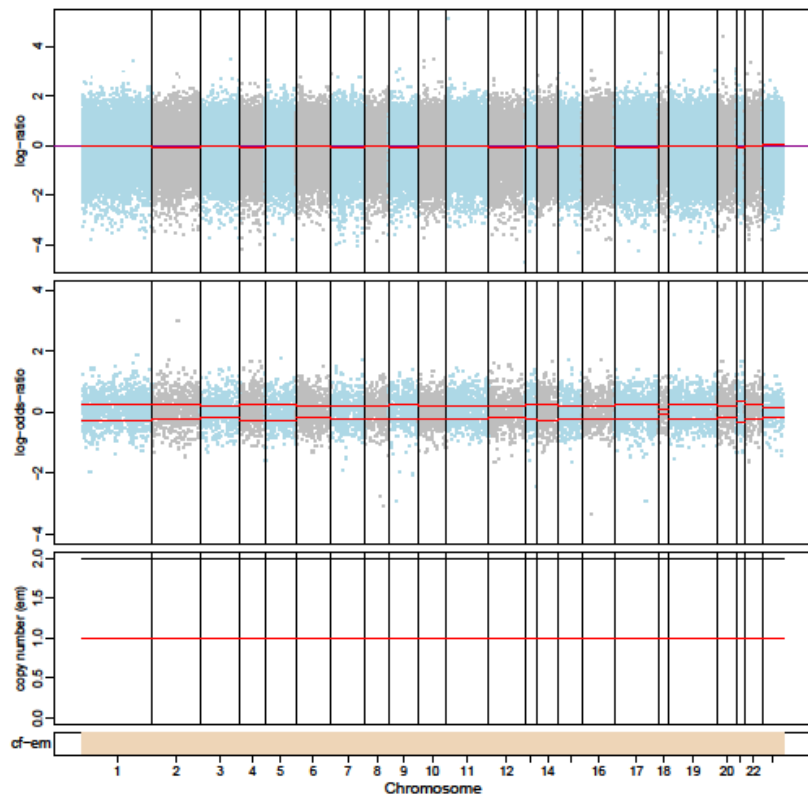
1403-P0



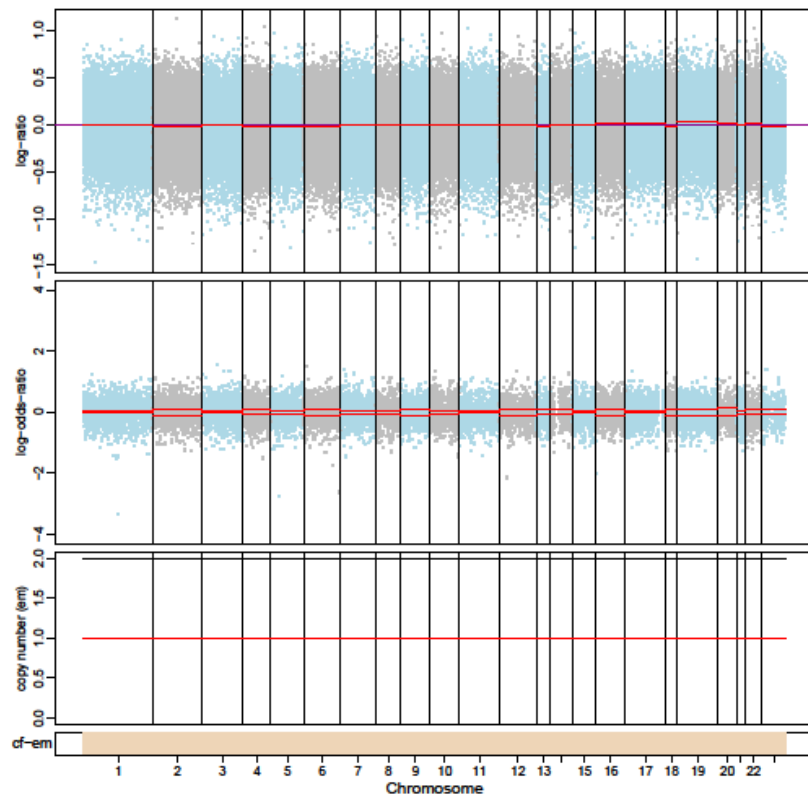
1403-P1



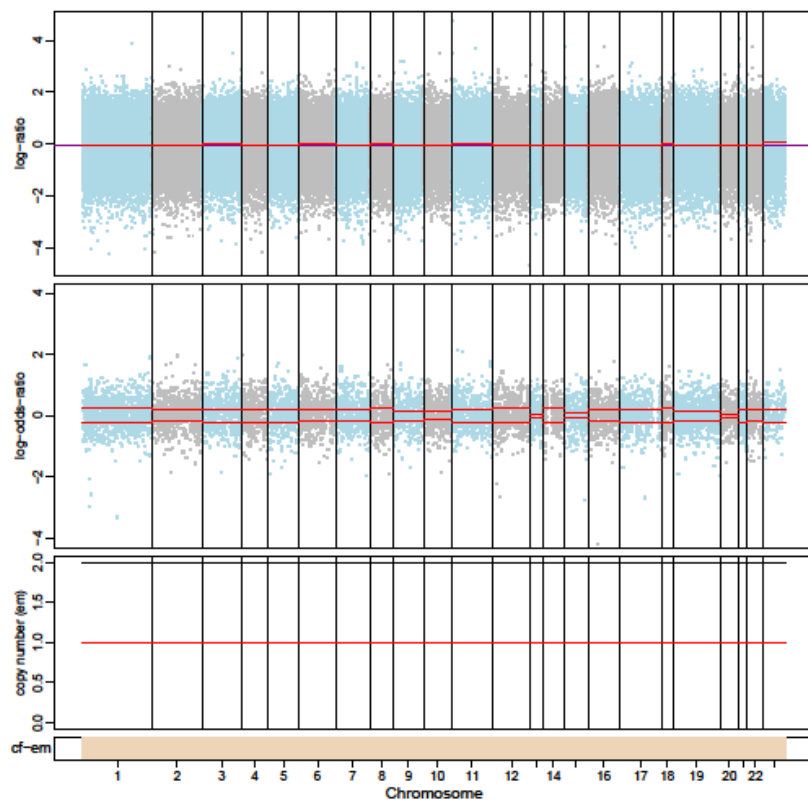
1403-P2



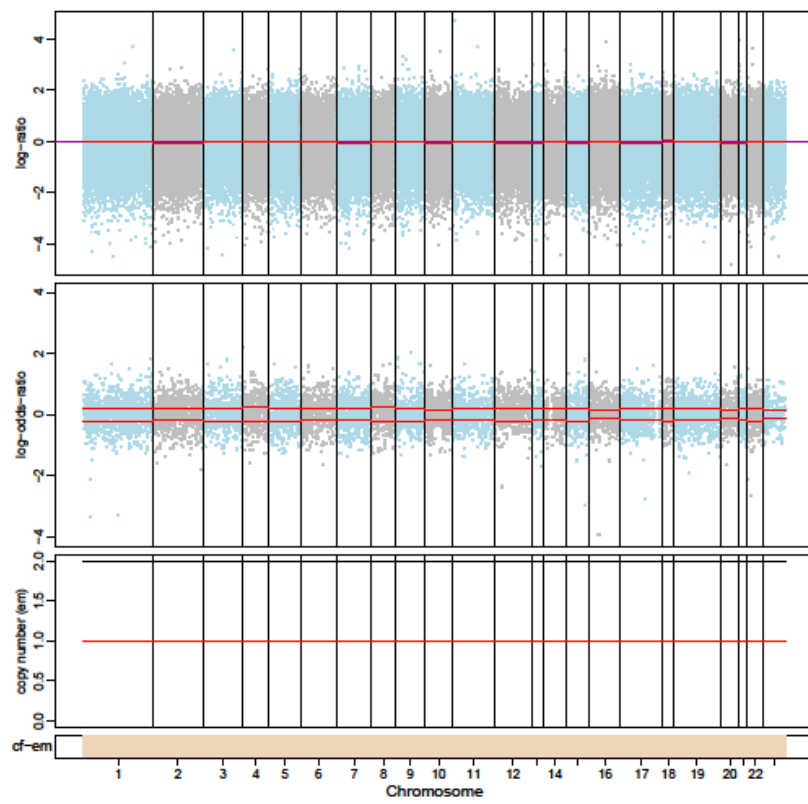
1426-P0



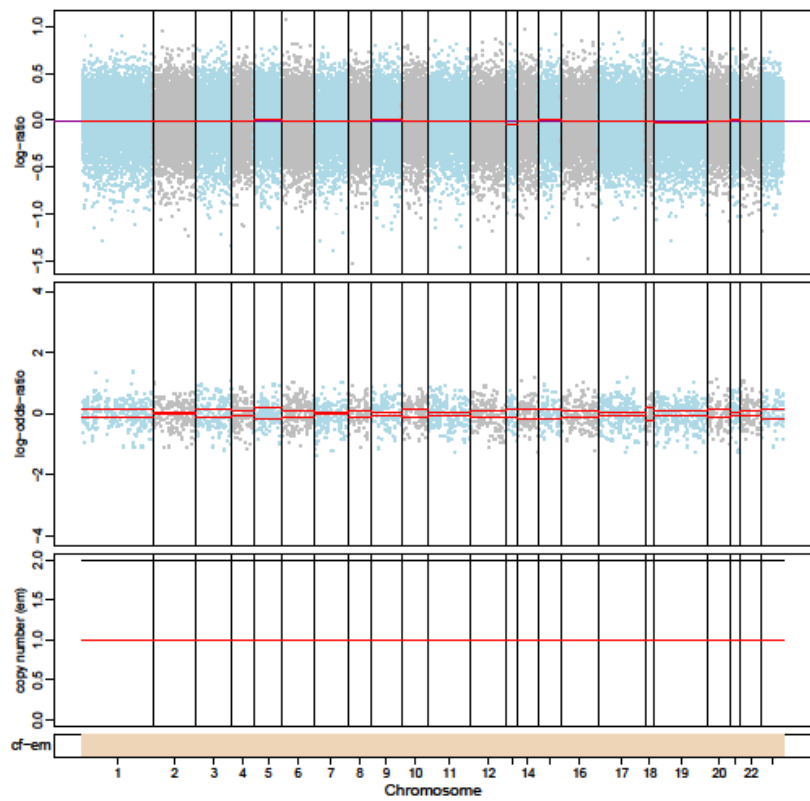
1426-P1



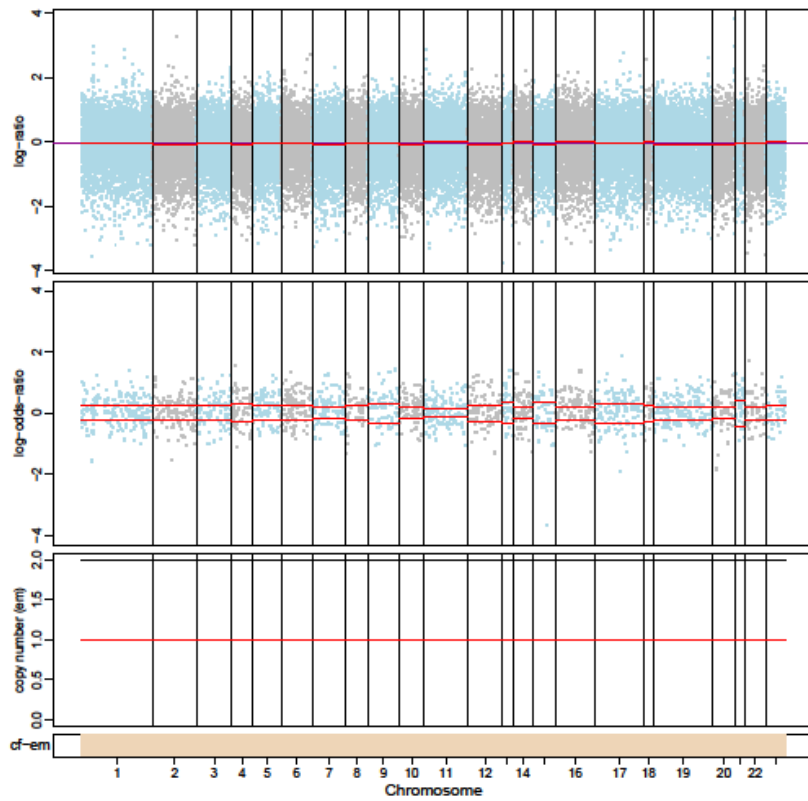
1426-P2



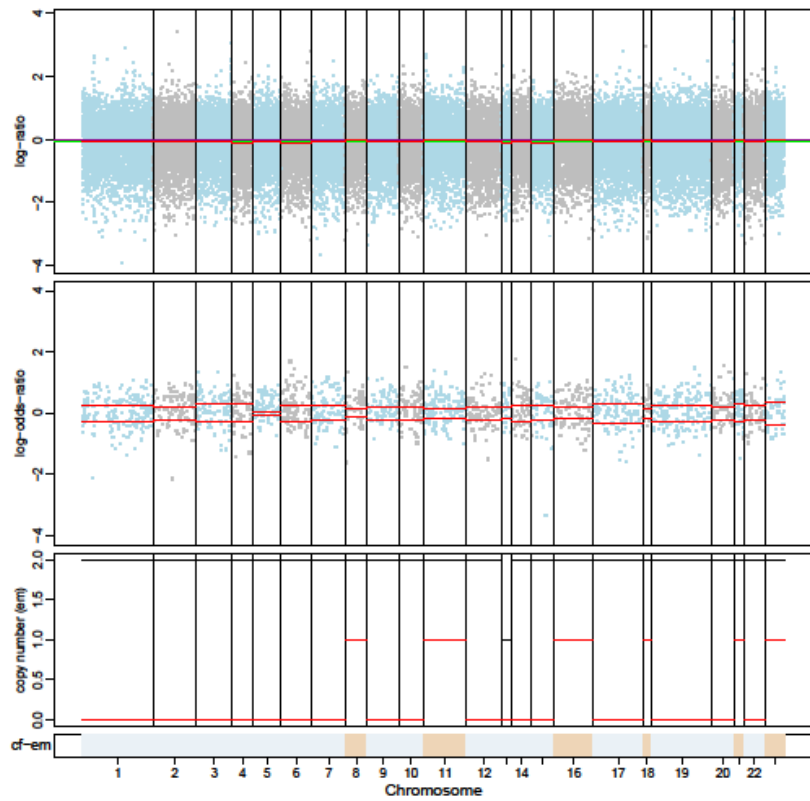
1428-P0



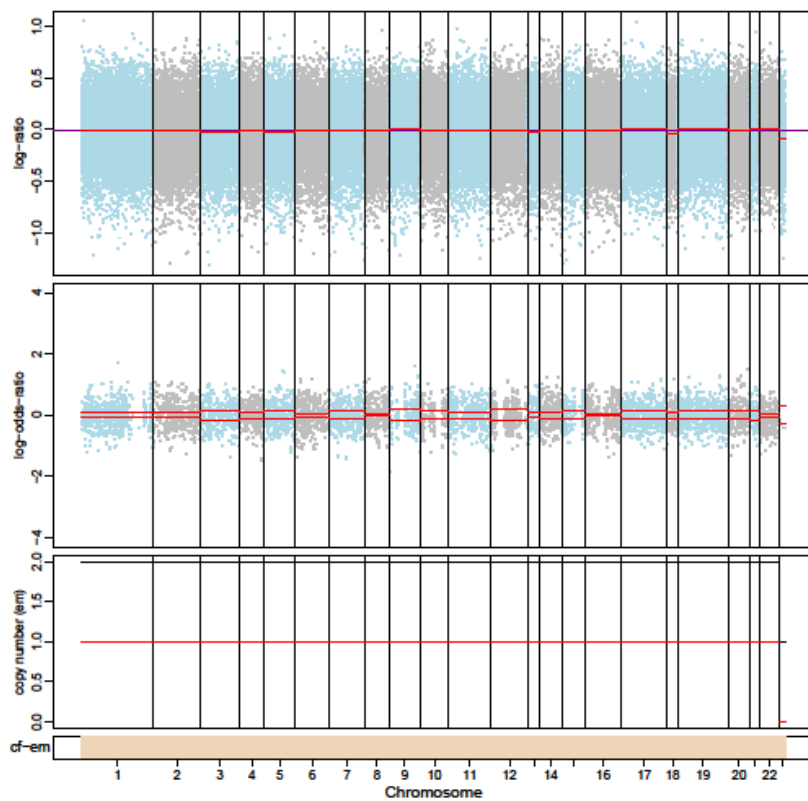
1428-P1



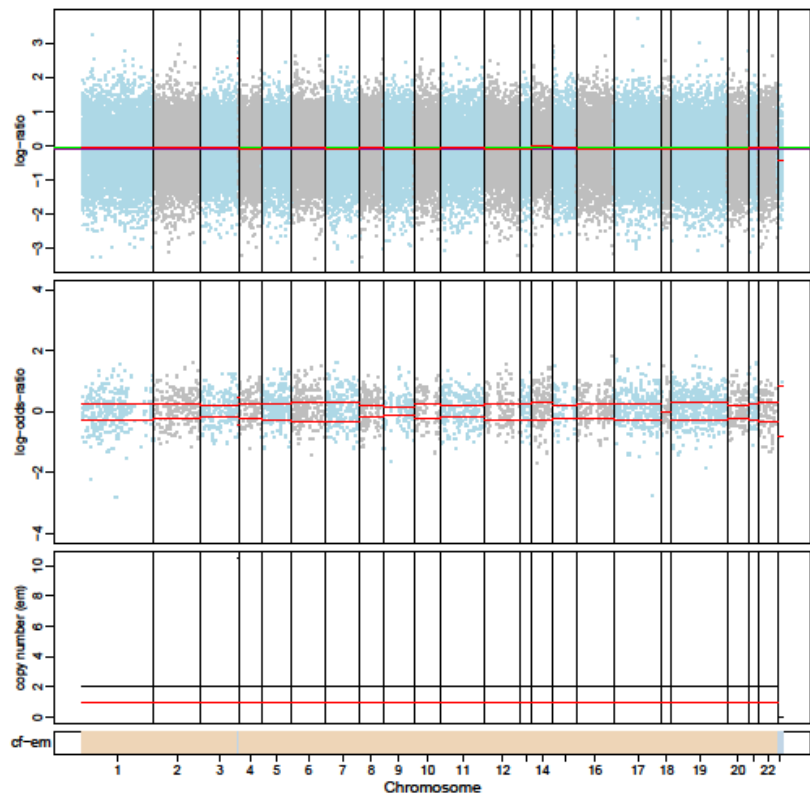
1428-P2



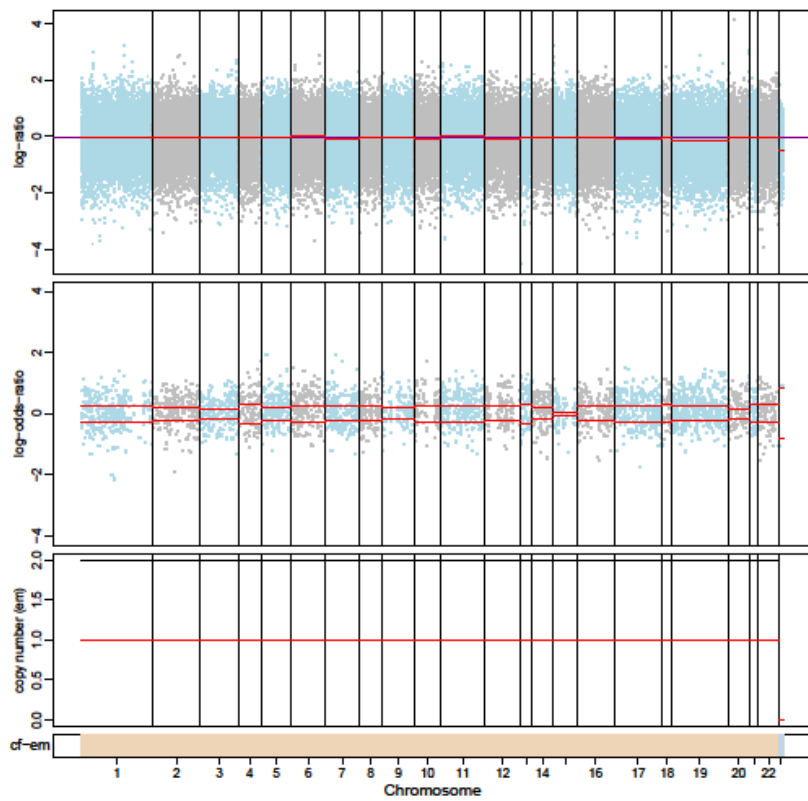
1437-P0



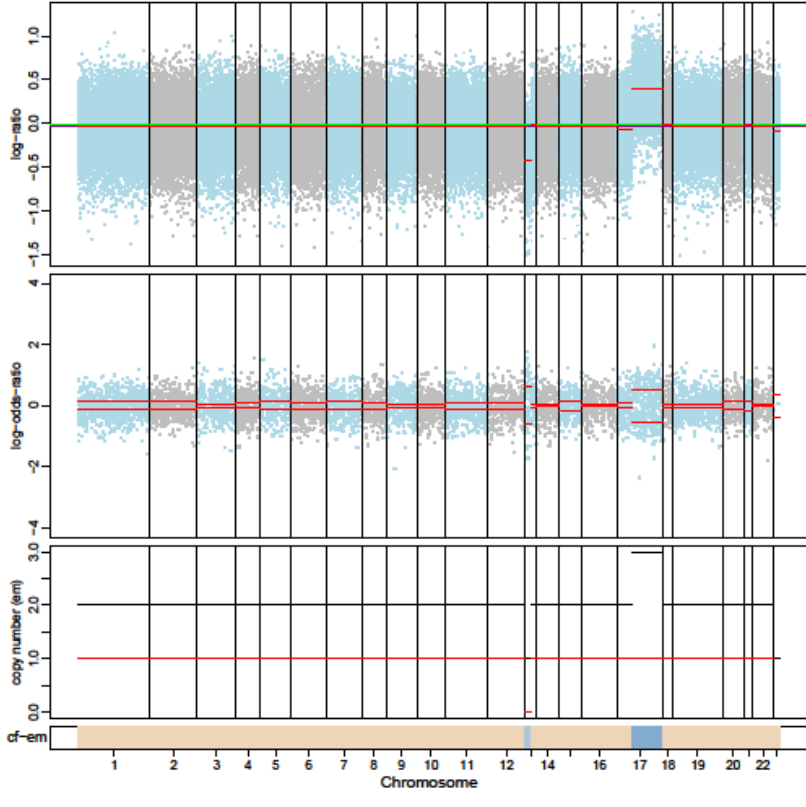
1437-P1



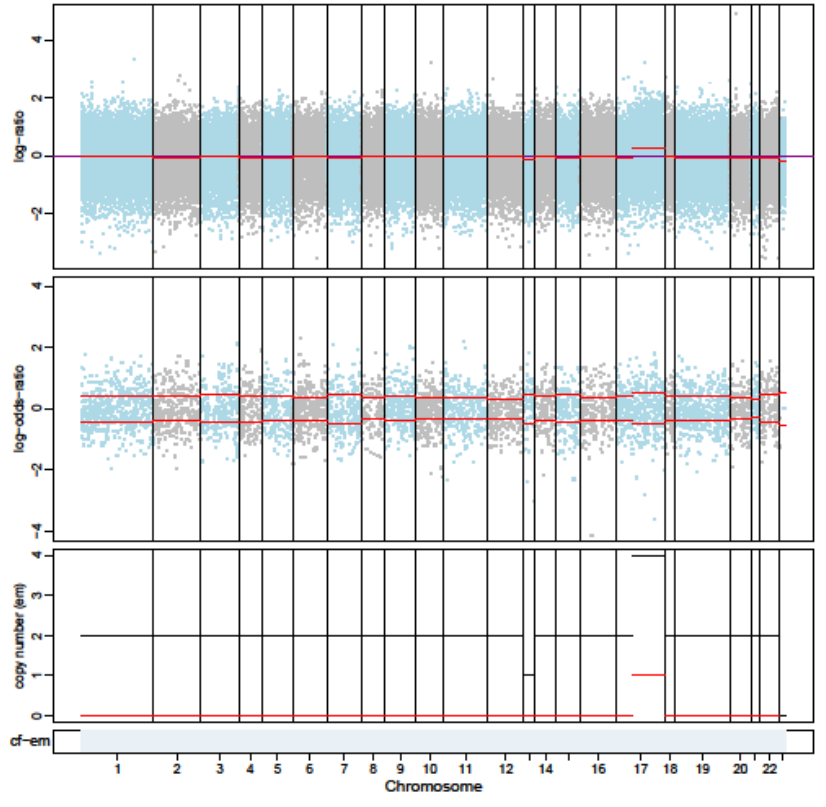
1437-P2



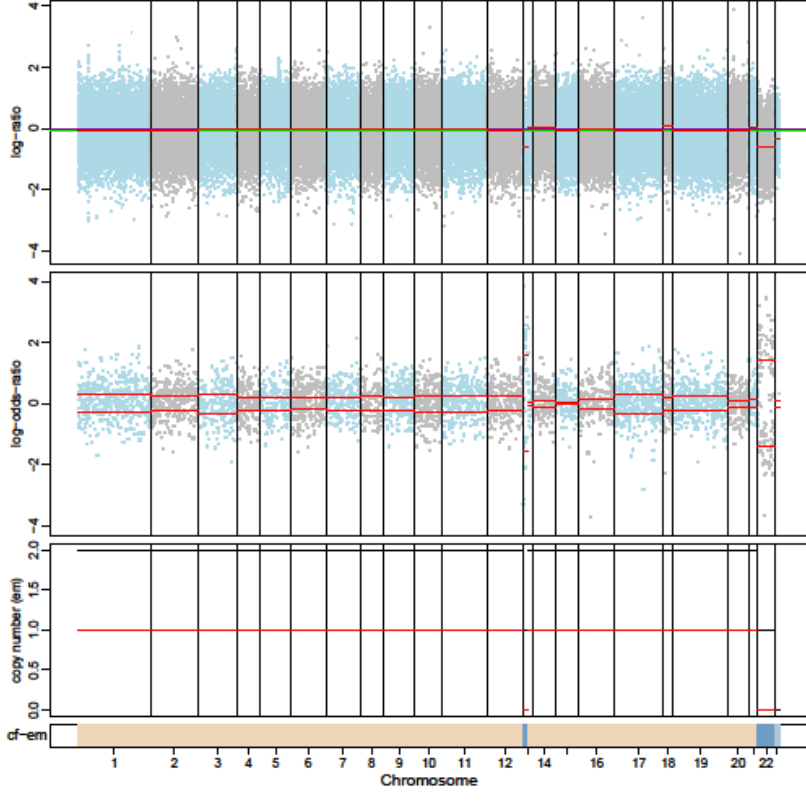
1438-P0



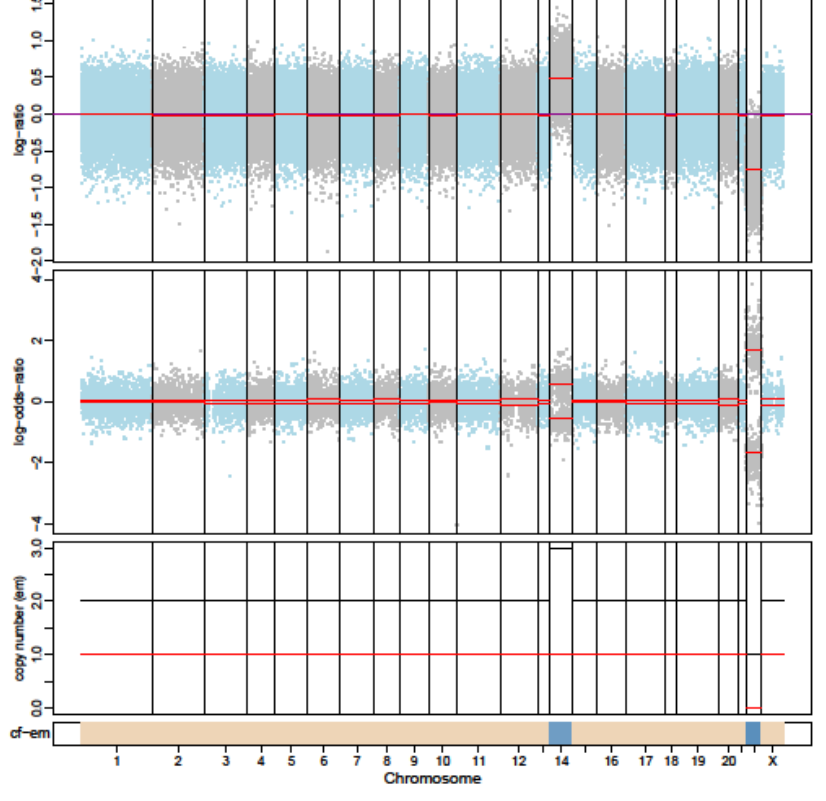
1438-P1



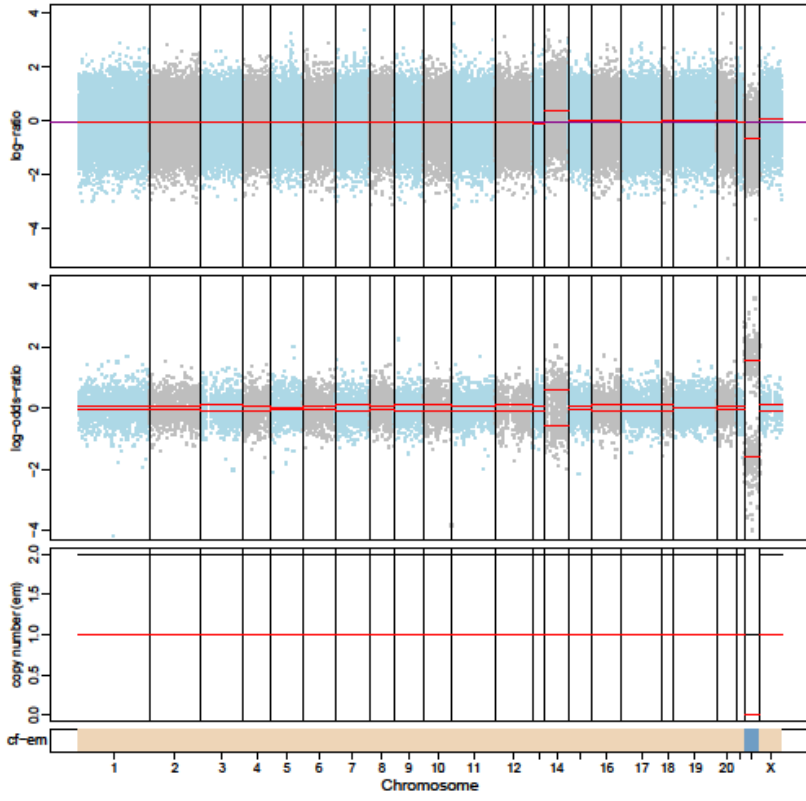
1438-P2



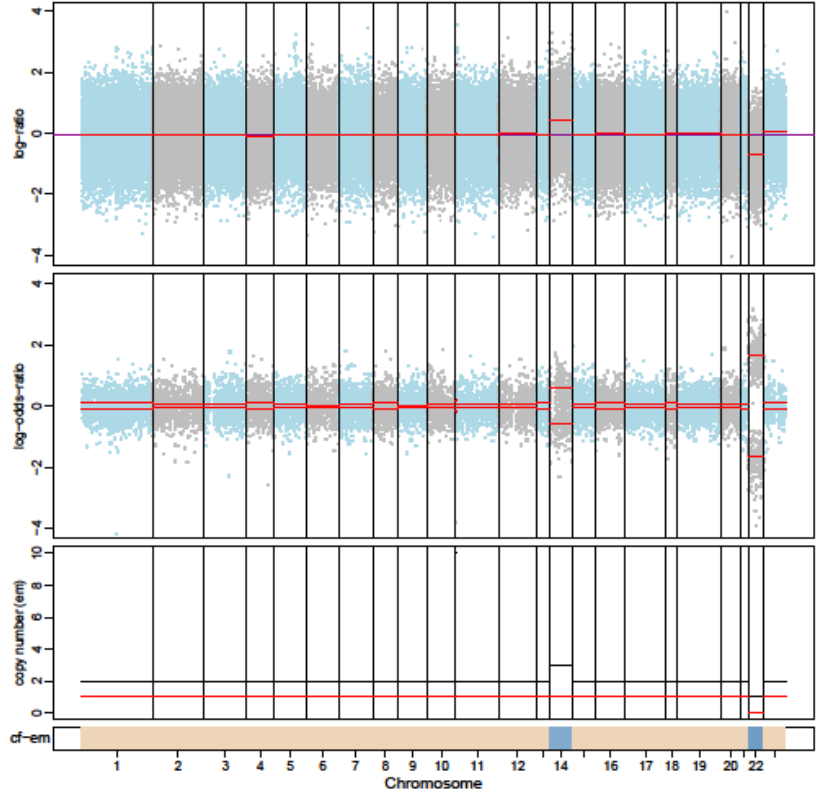
1443-P0



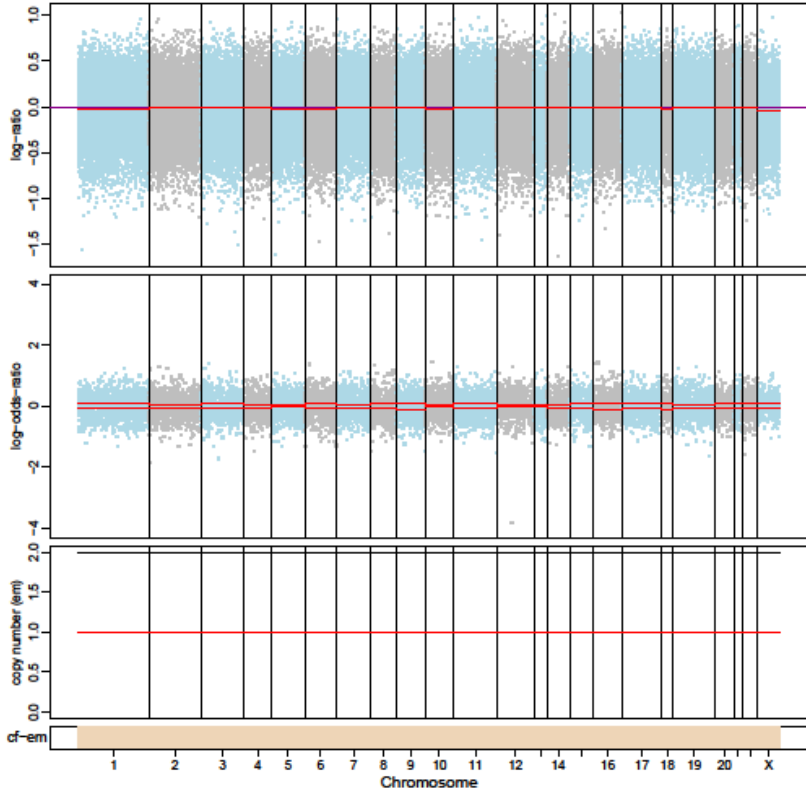
1443-P1



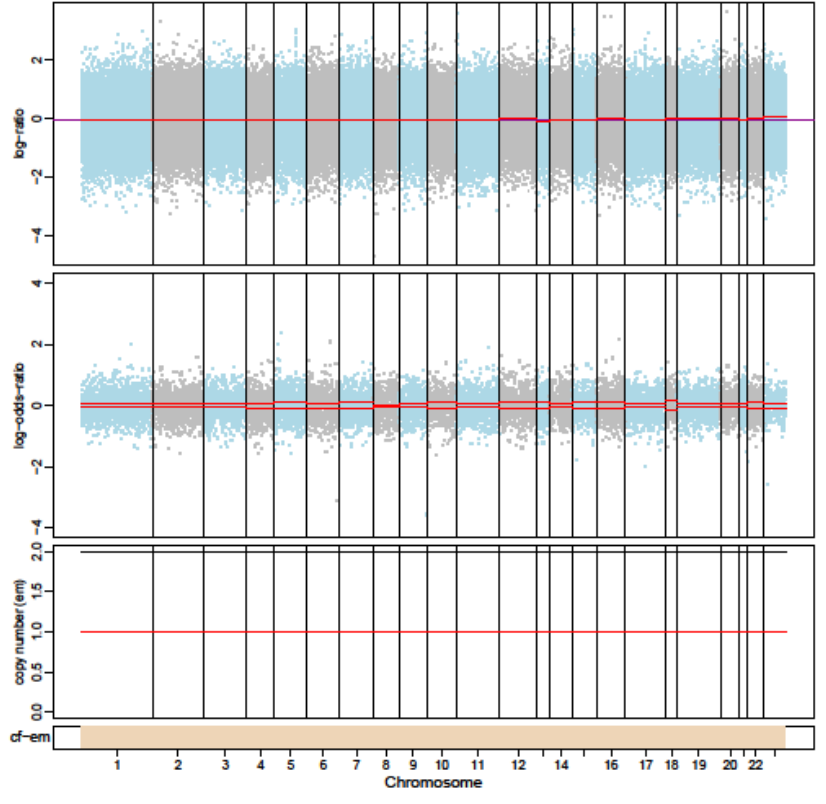
1443-P2



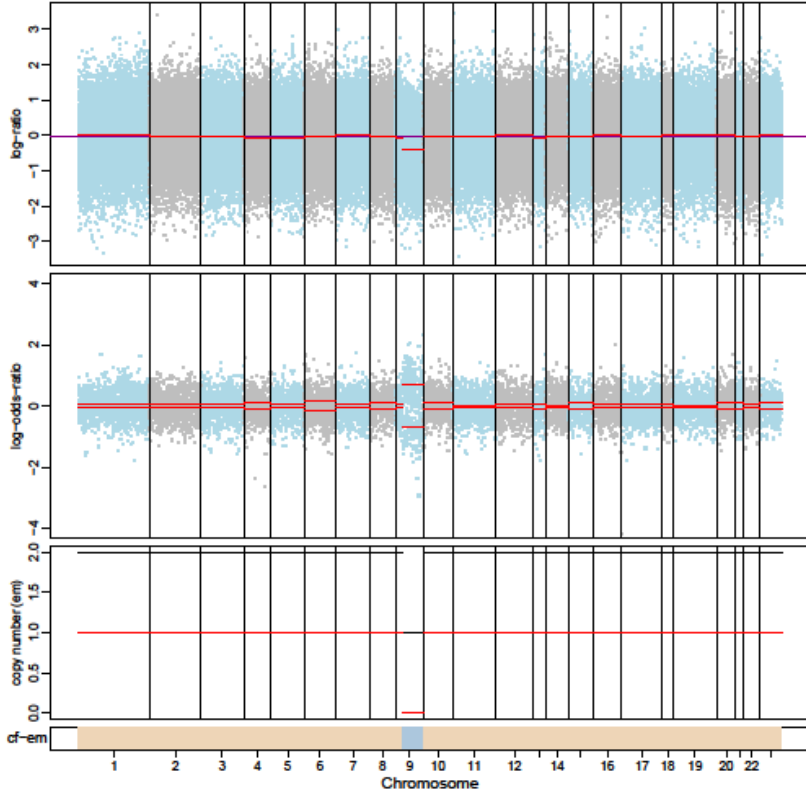
1454-P0



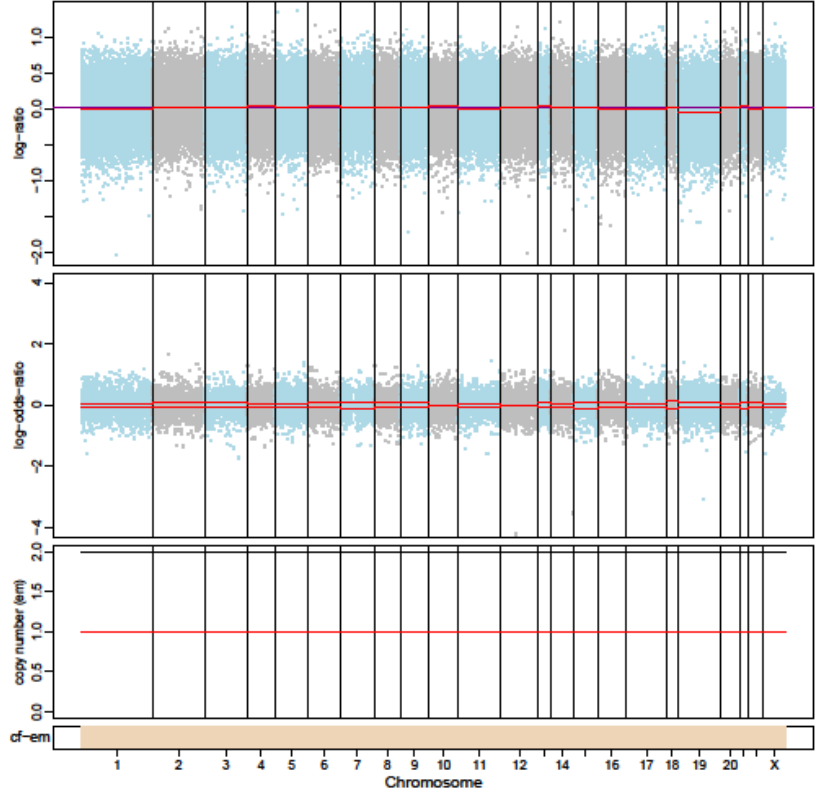
1454-P1



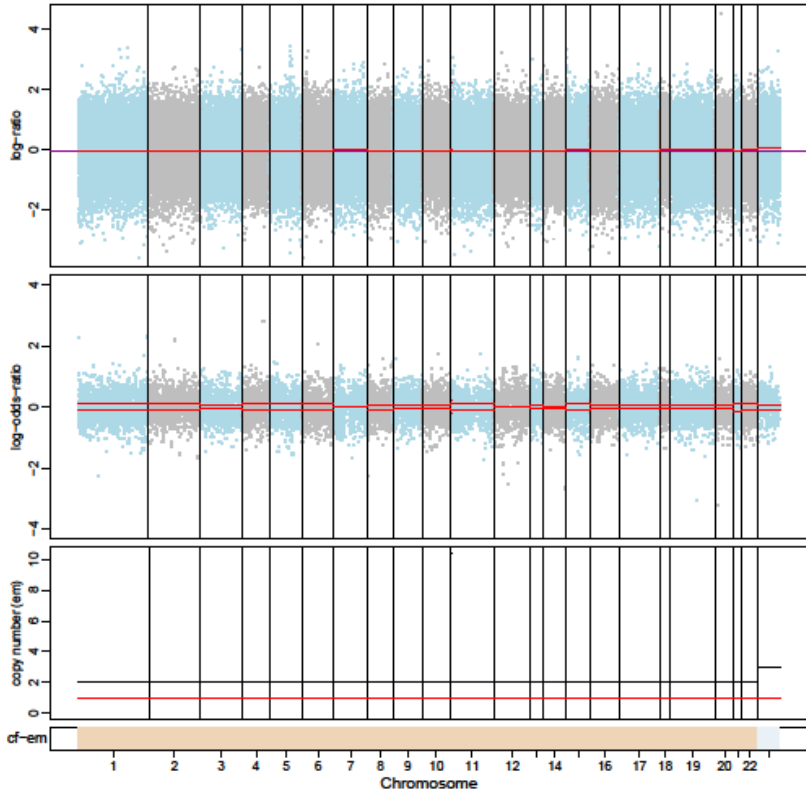
1454-P2



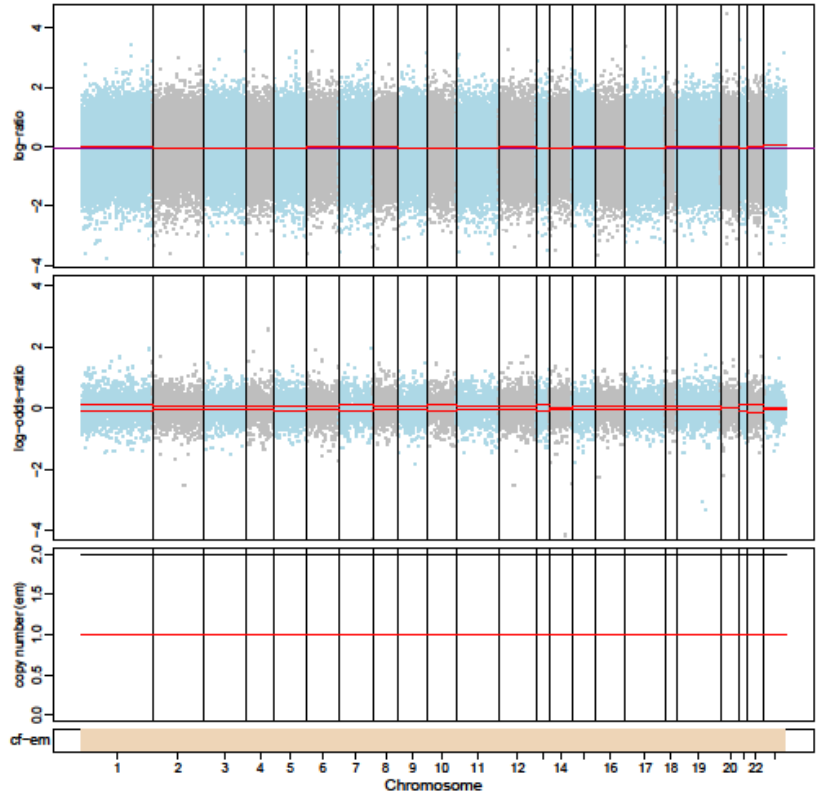
1458-P0



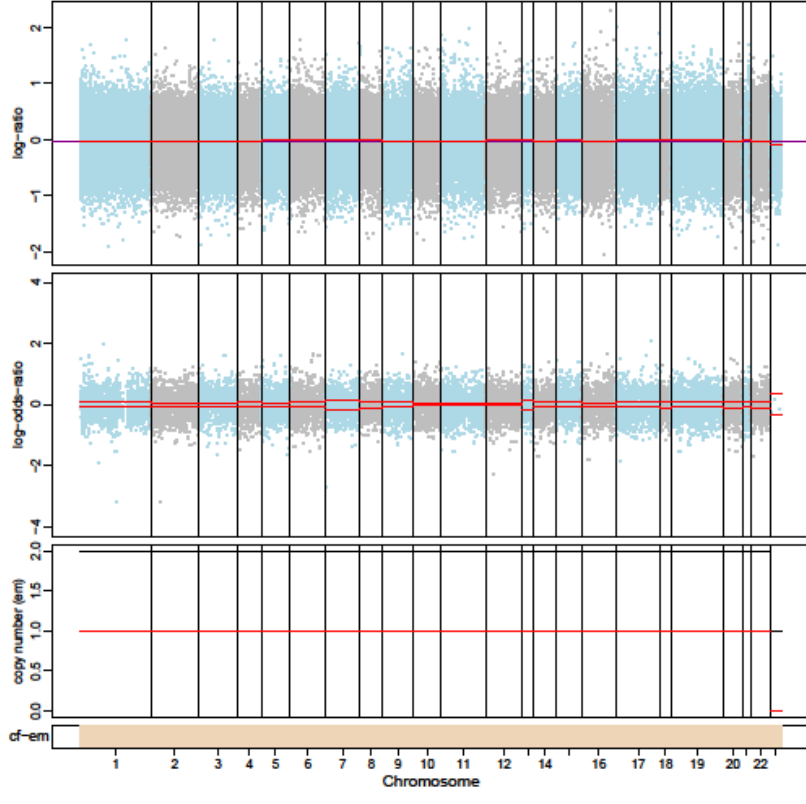
1458-P1



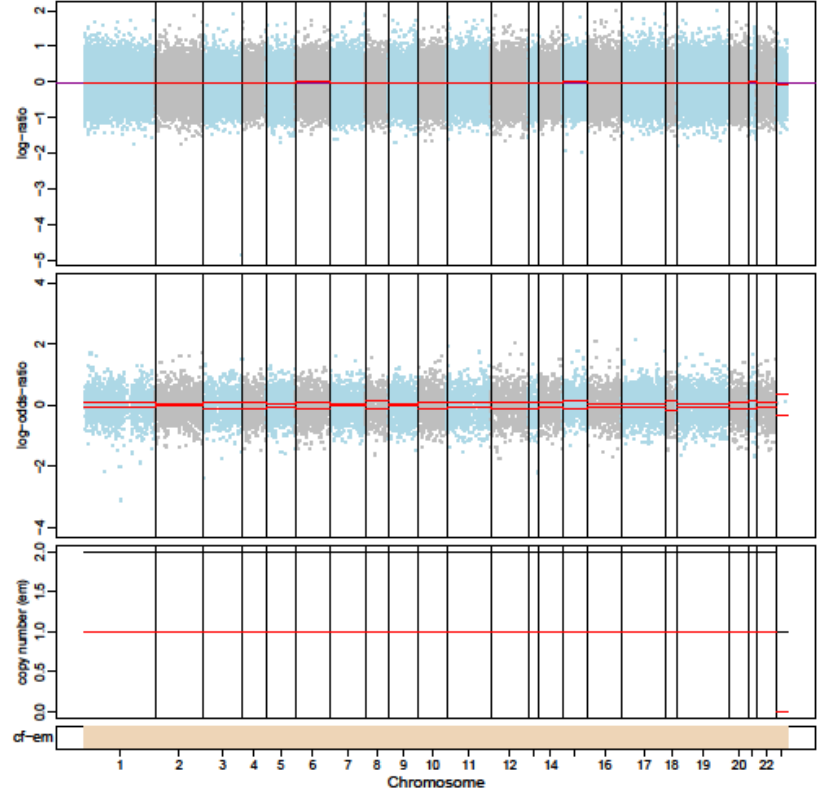
1458-P2



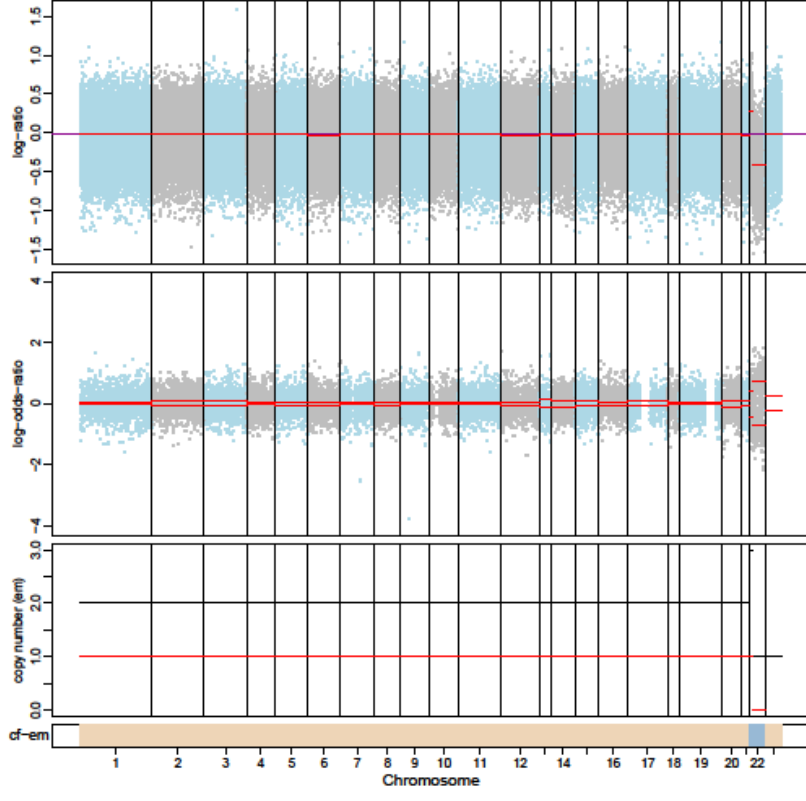
1182-P0



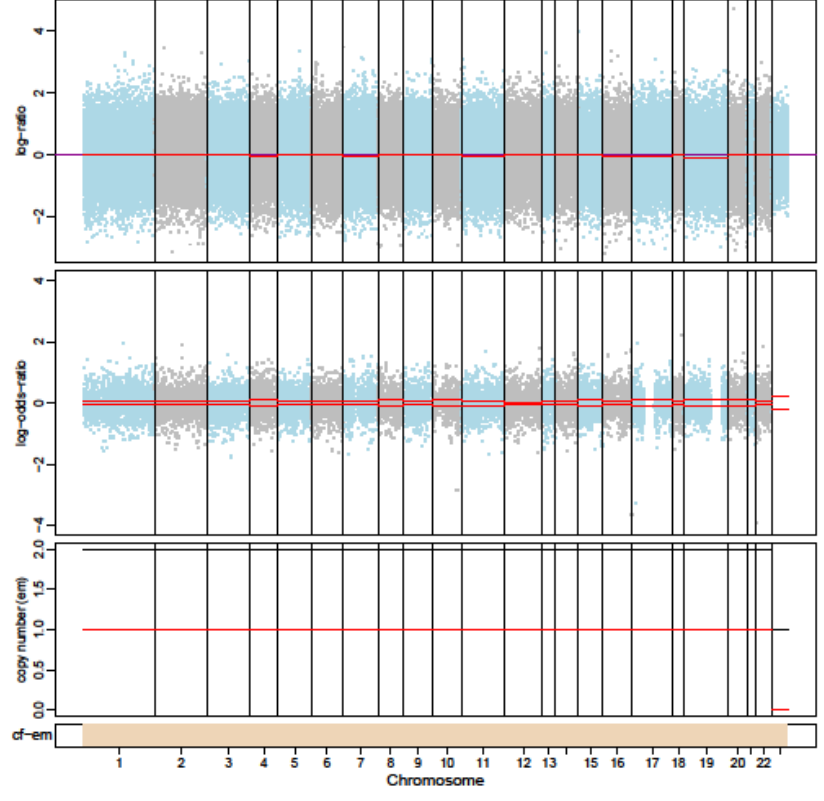
1182-P1



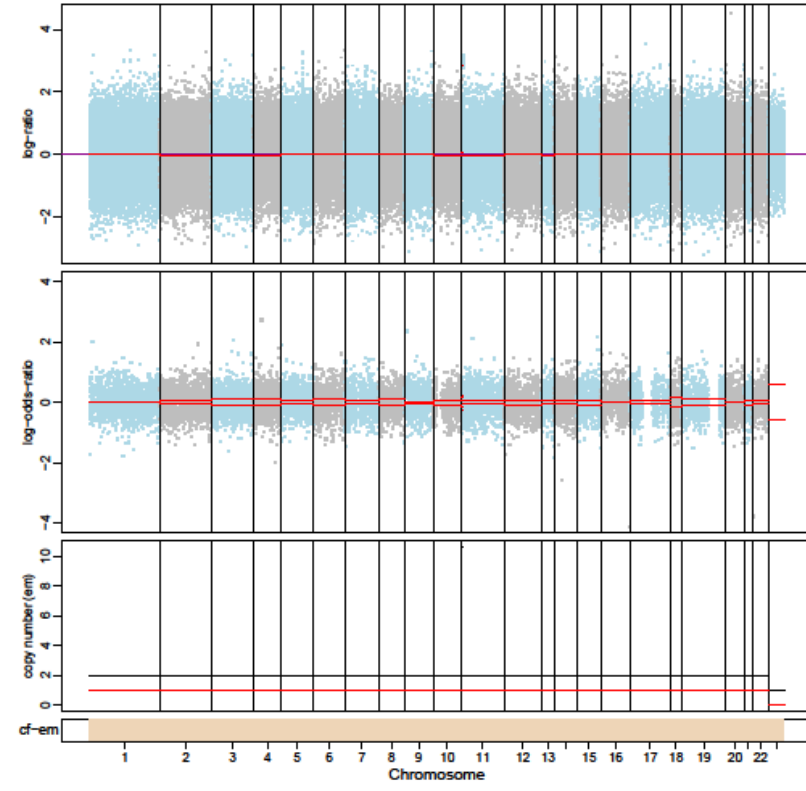
1482-P0



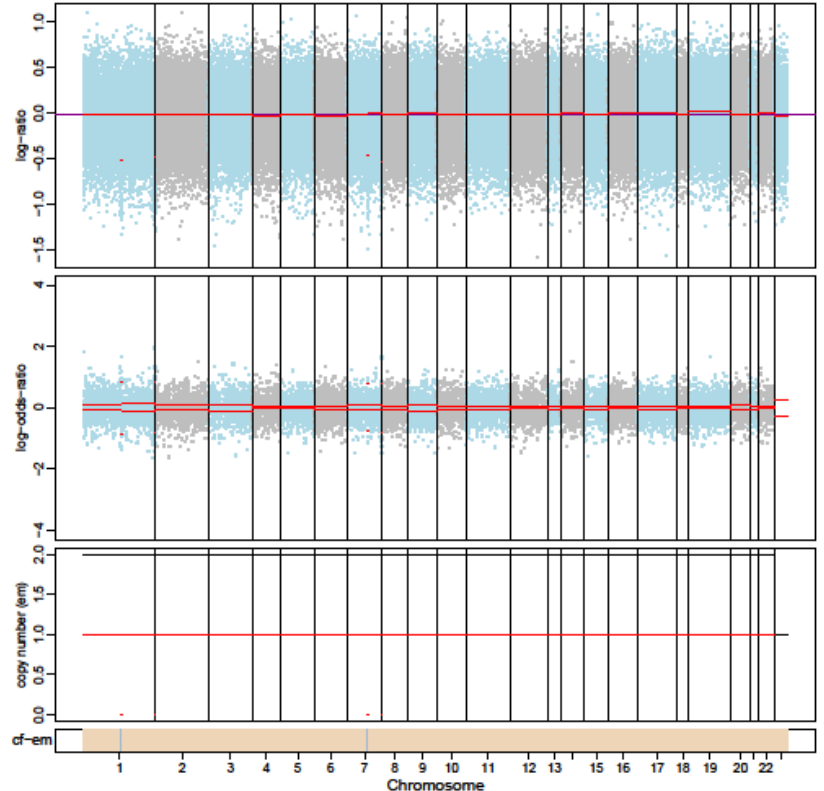
1482-P1



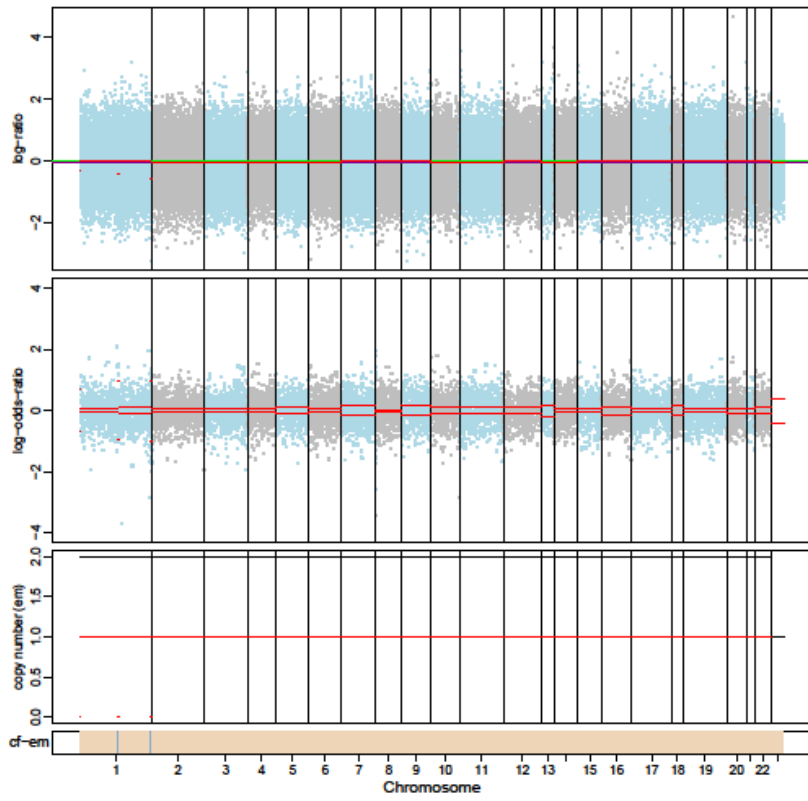
1482-P2



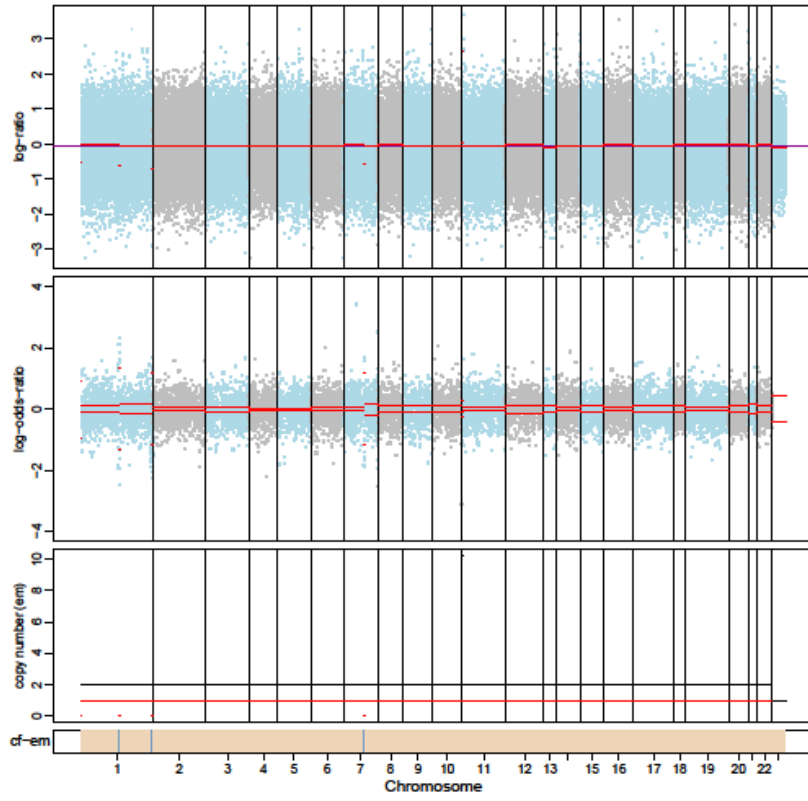
1491-P0



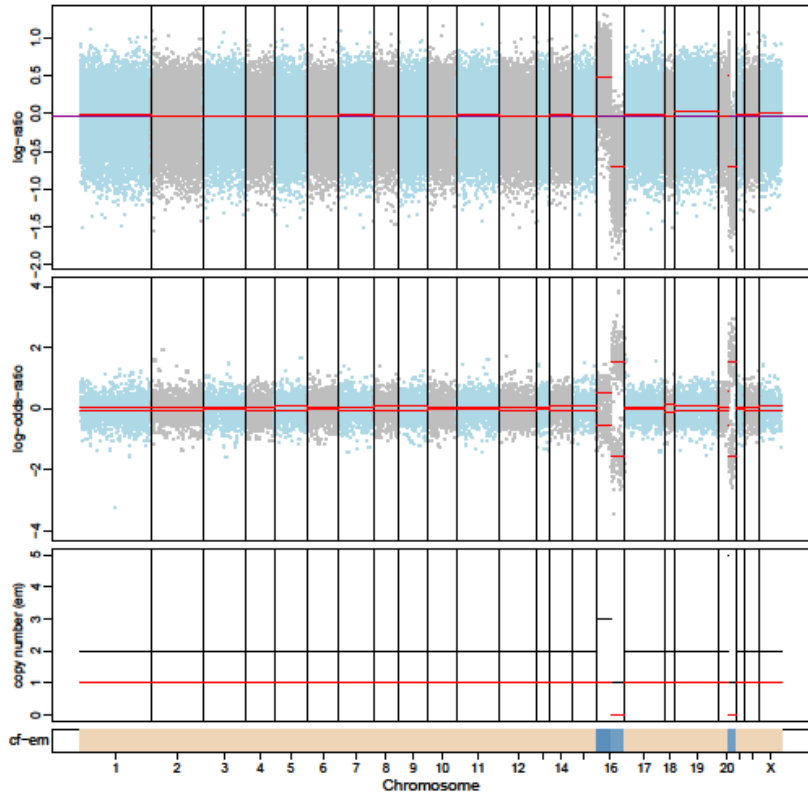
1491-P1



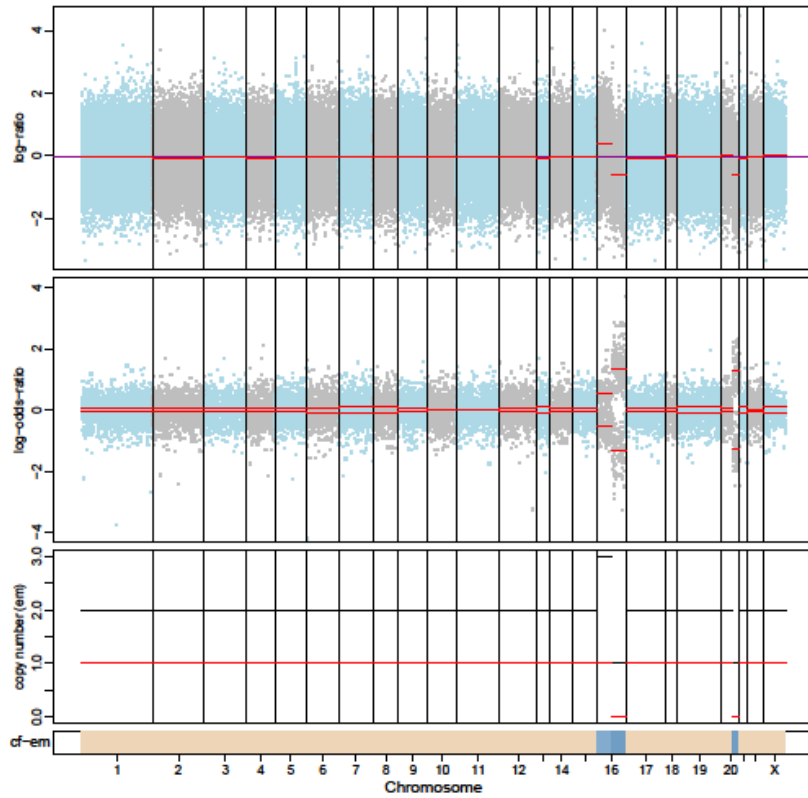
1491-P2



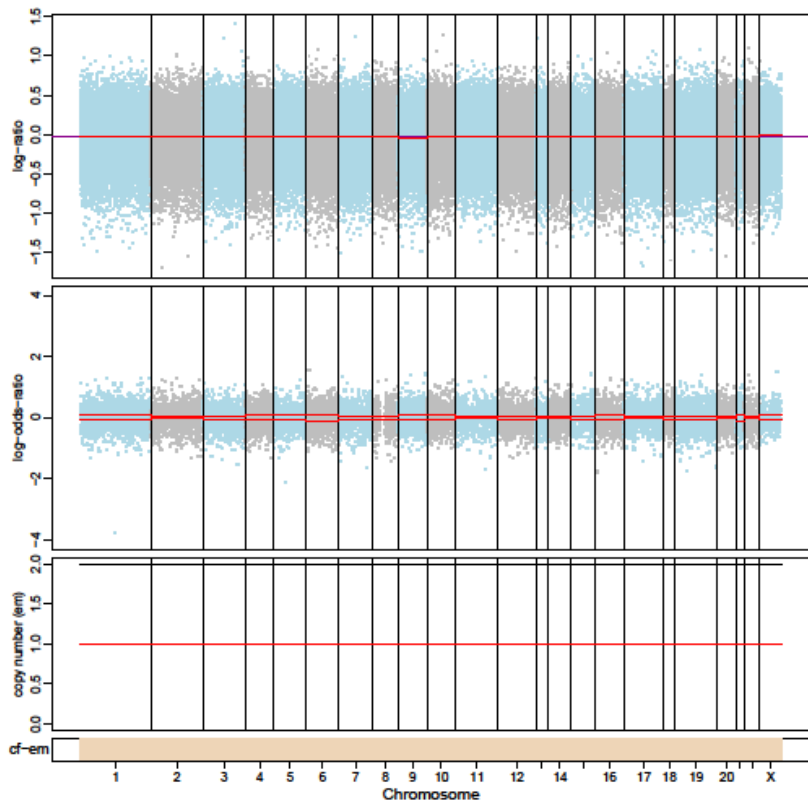
1497-P0



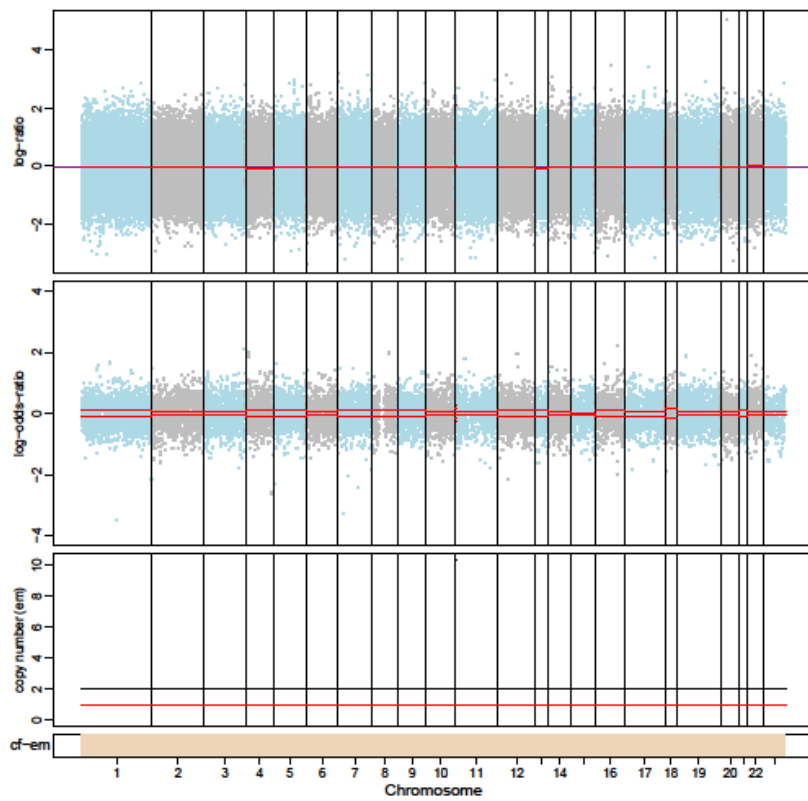
1497-P2



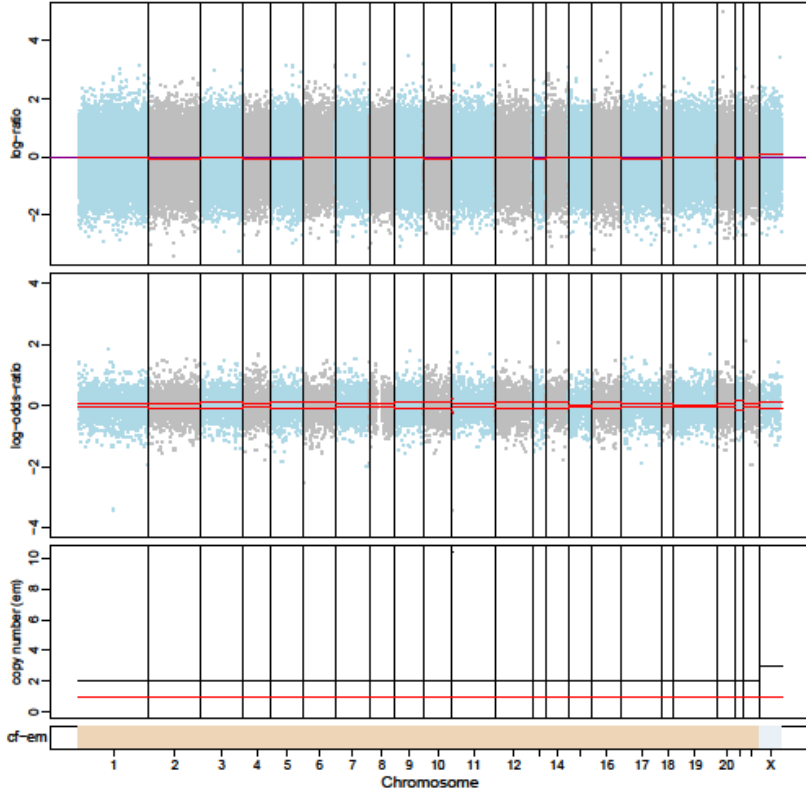
1499-P0



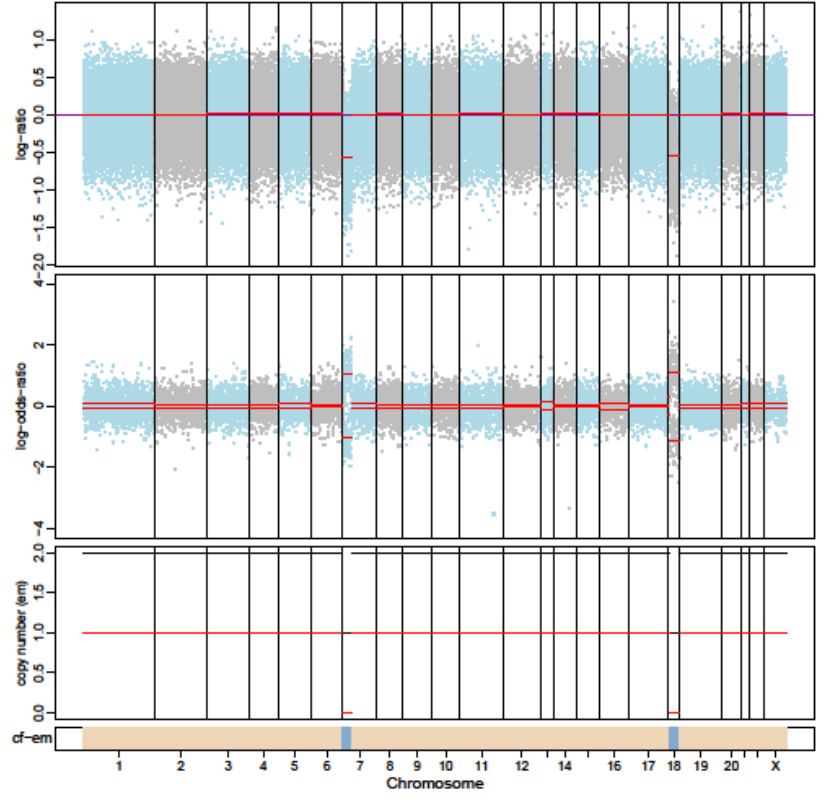
1499-P1



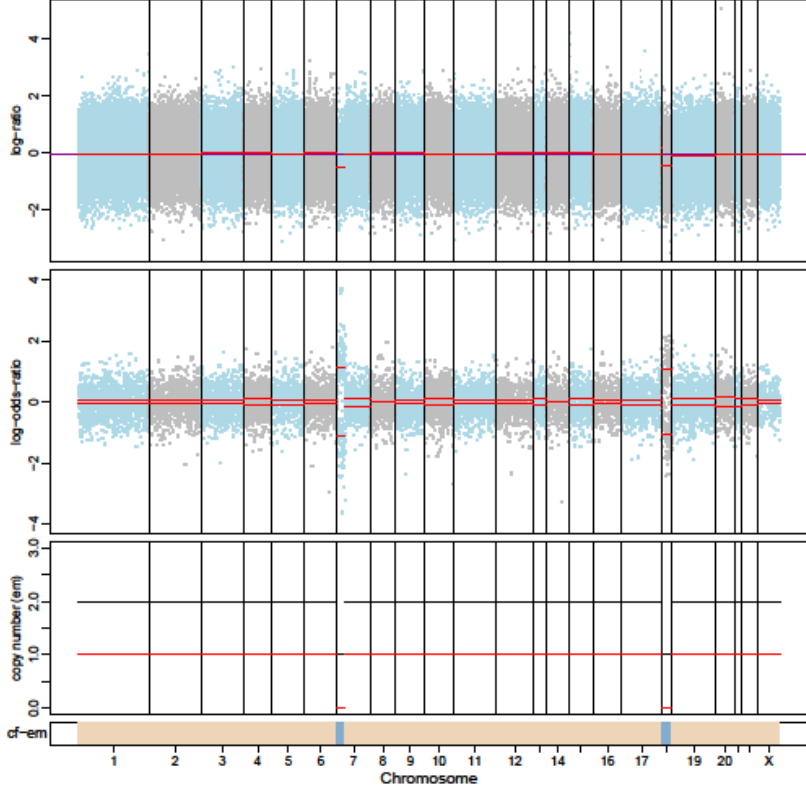
1499-P2



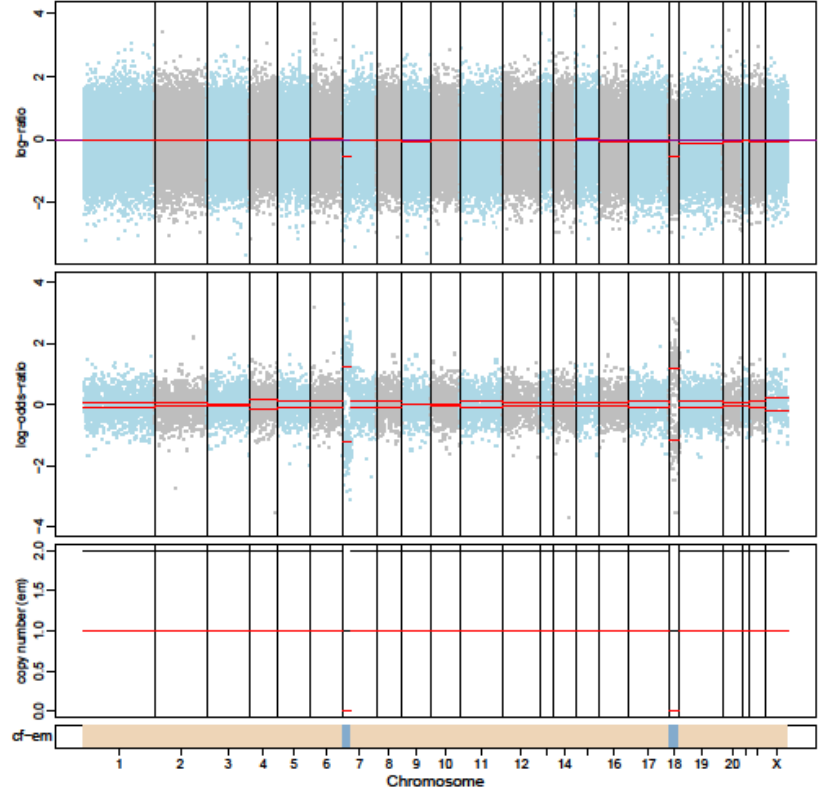
1502-P0



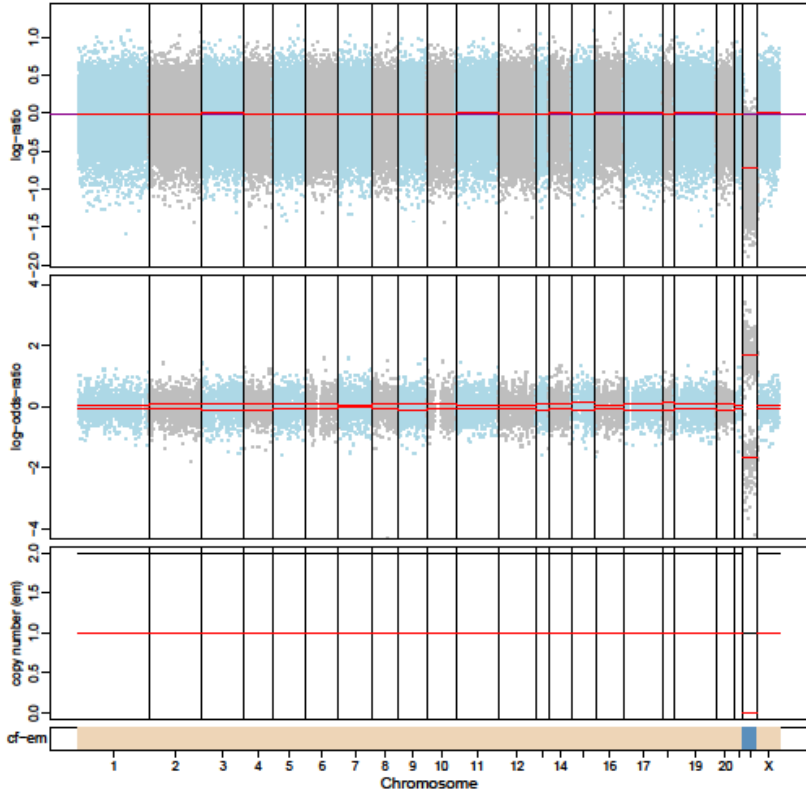
1502-P1



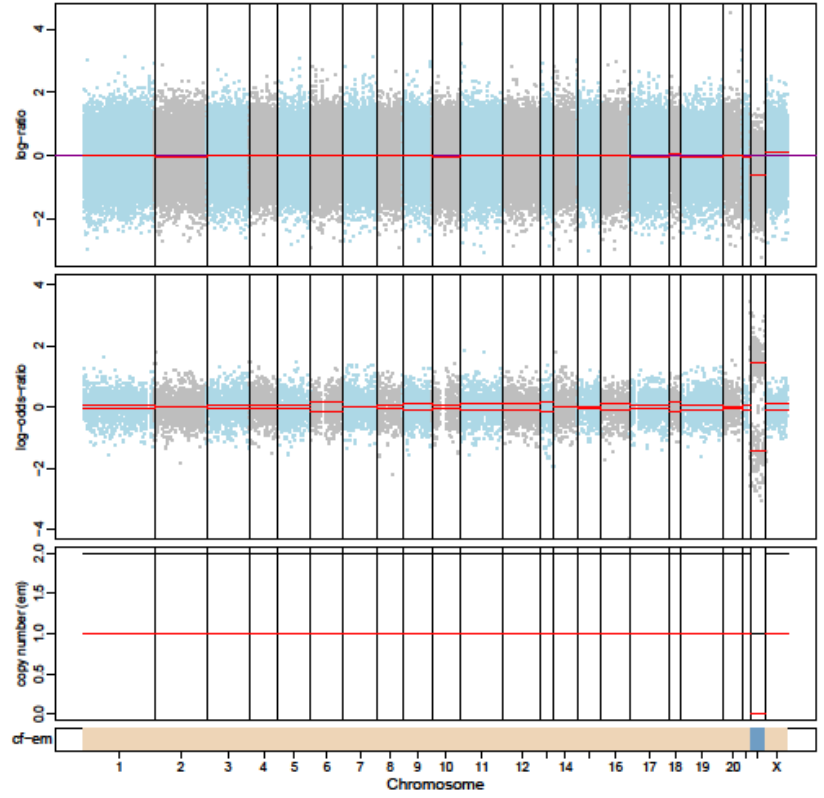
1502-P2



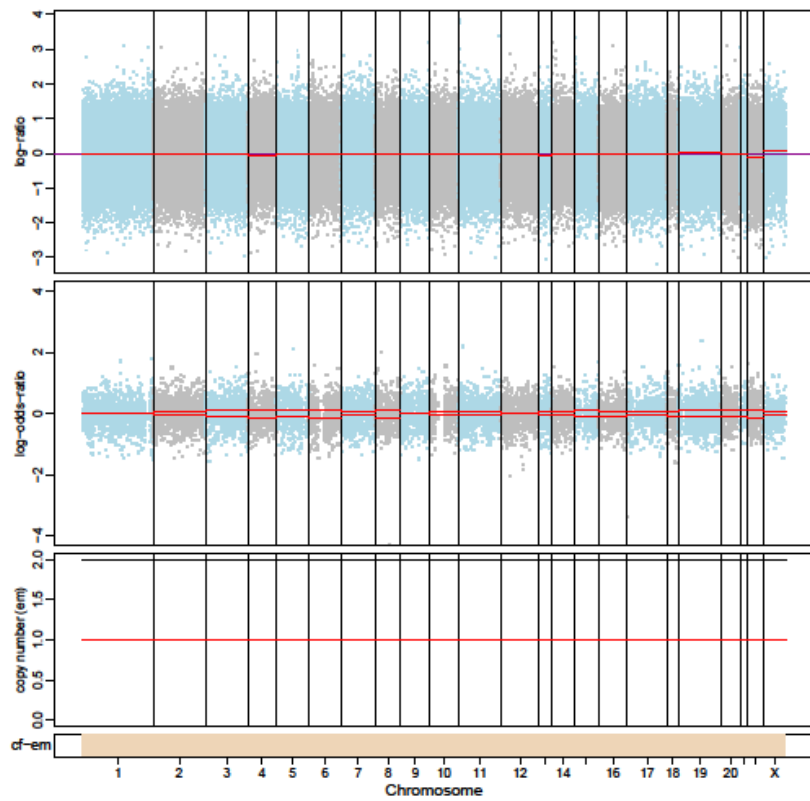
1504-P0



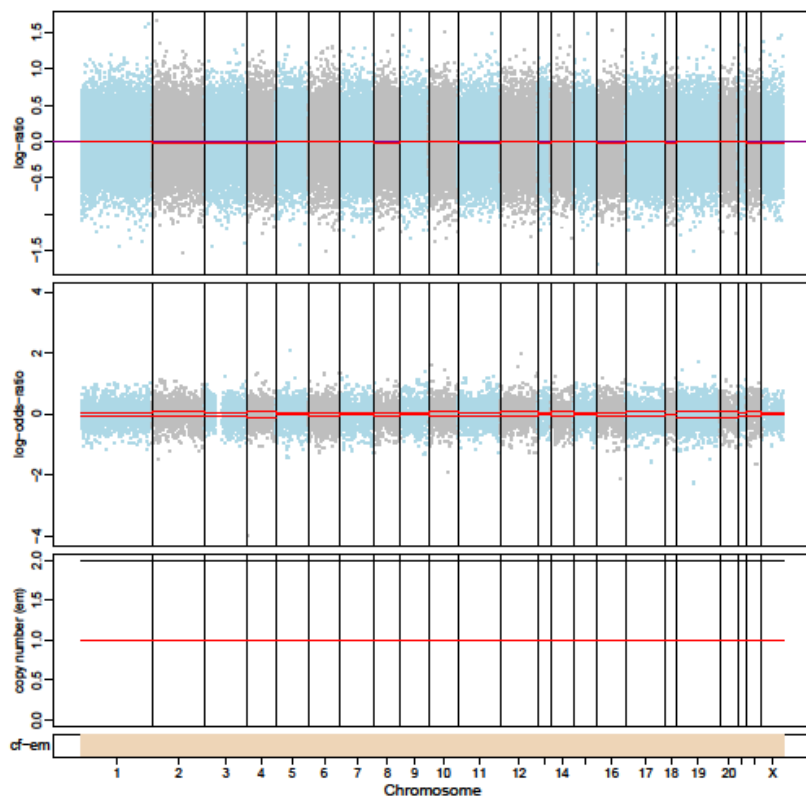
1504-P1



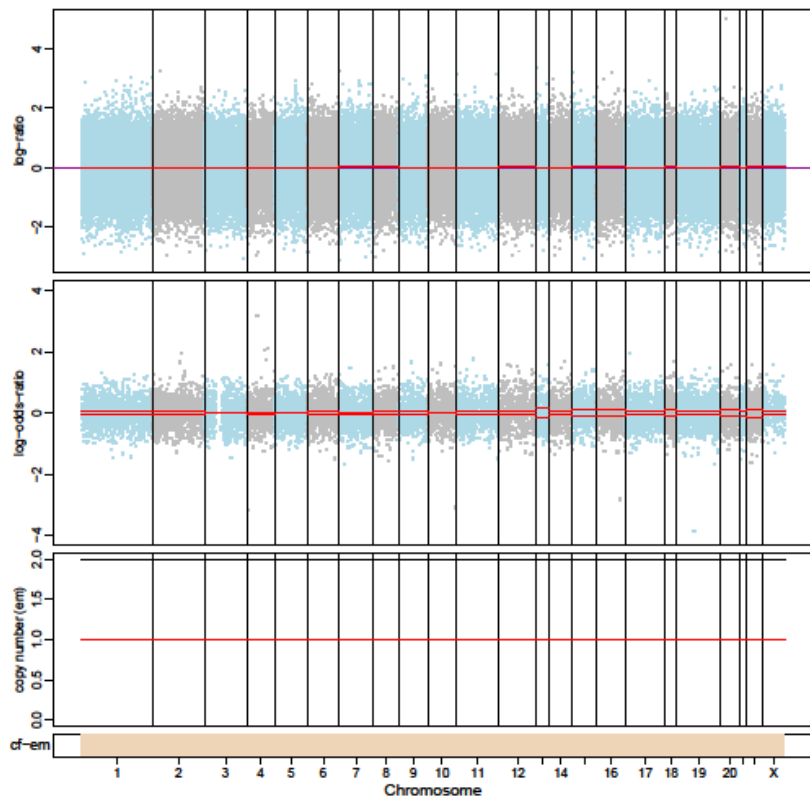
1504-P2



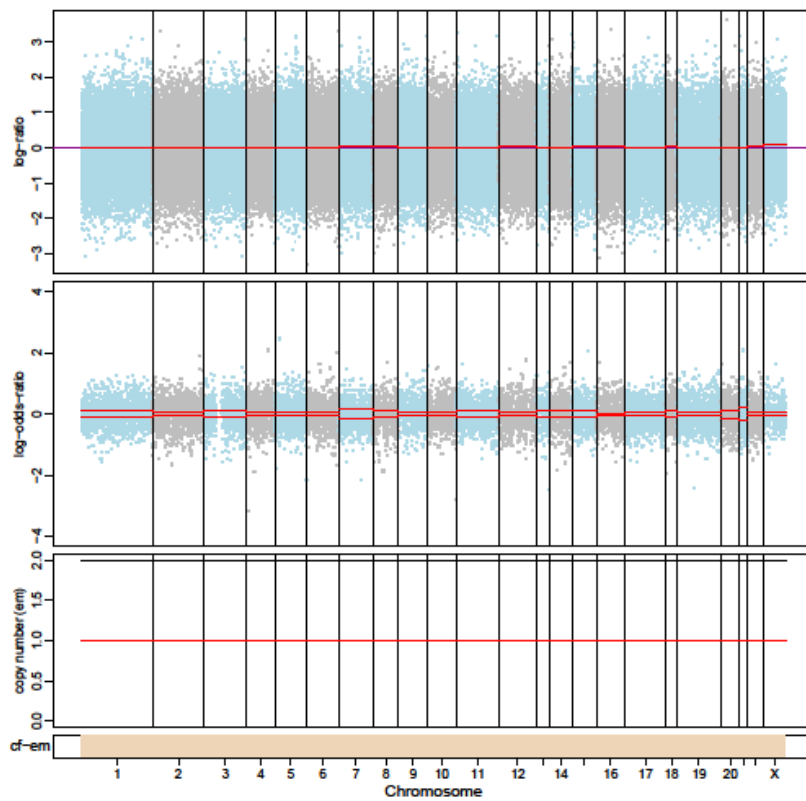
1508-P0



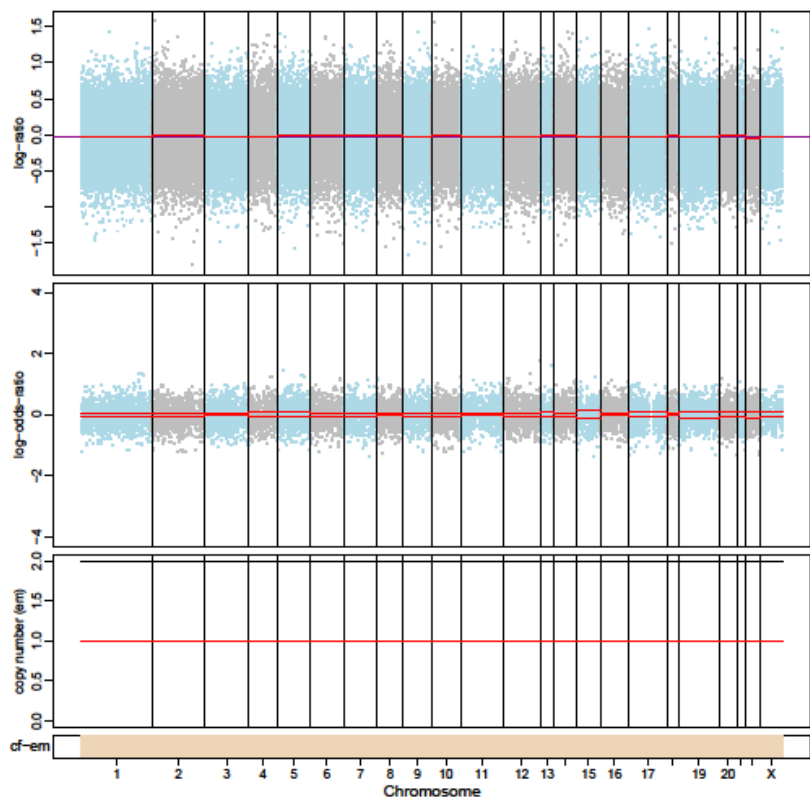
1508-P1



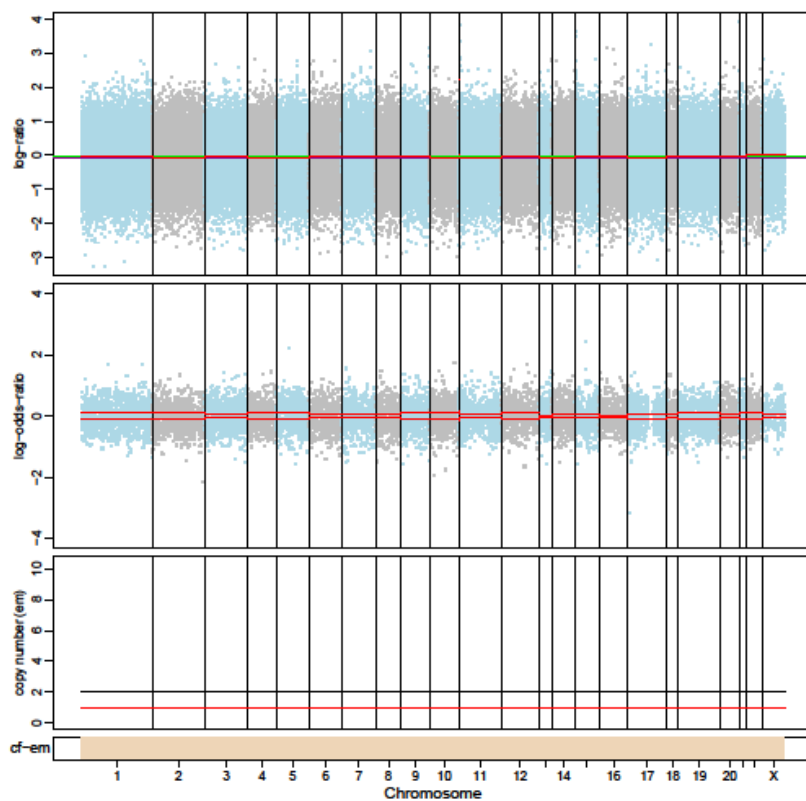
1508-P2



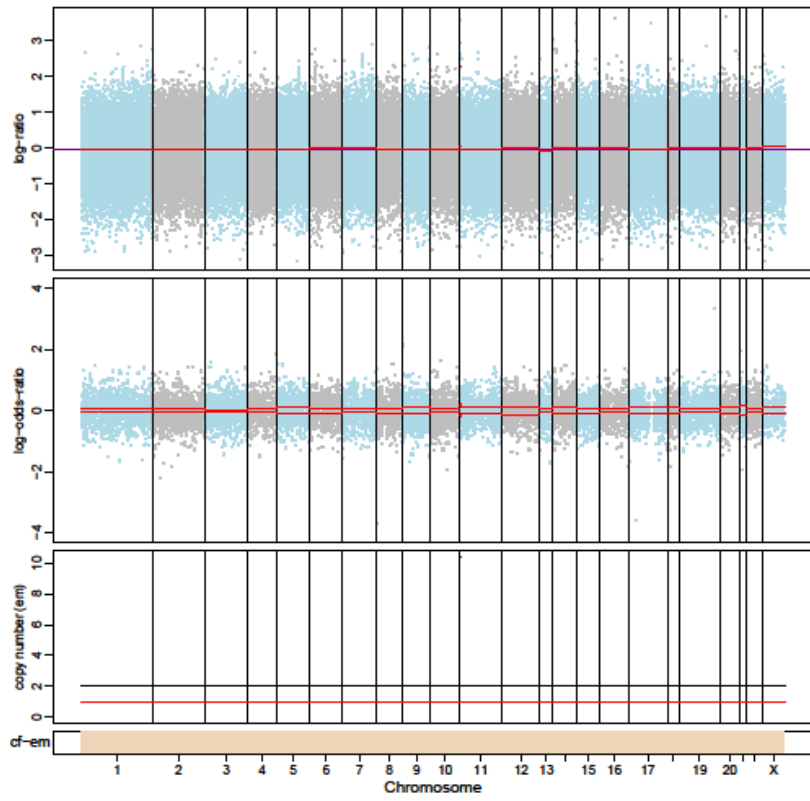
1510-P0



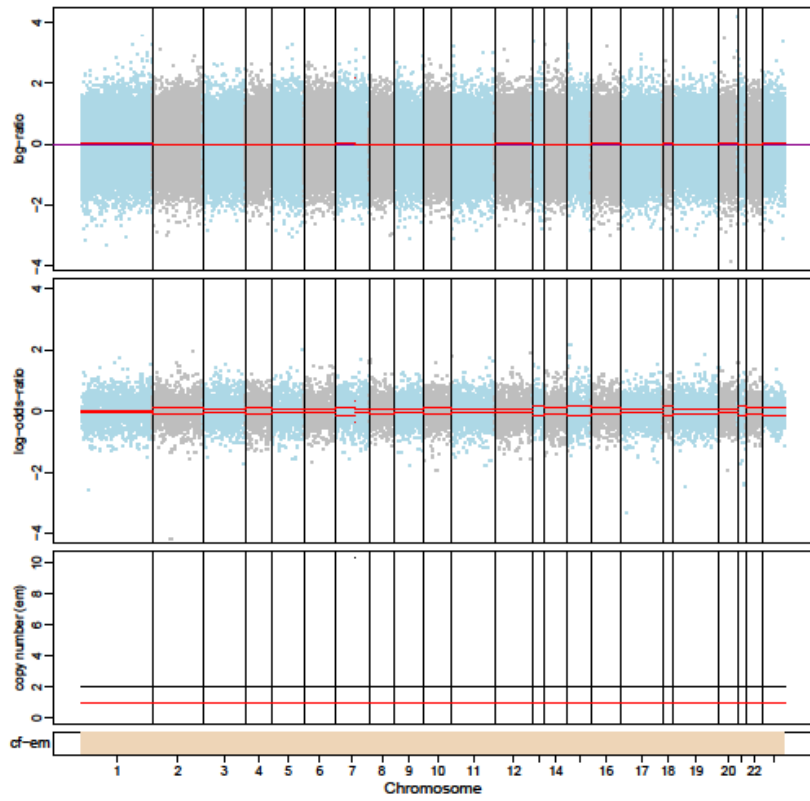
1510-P1



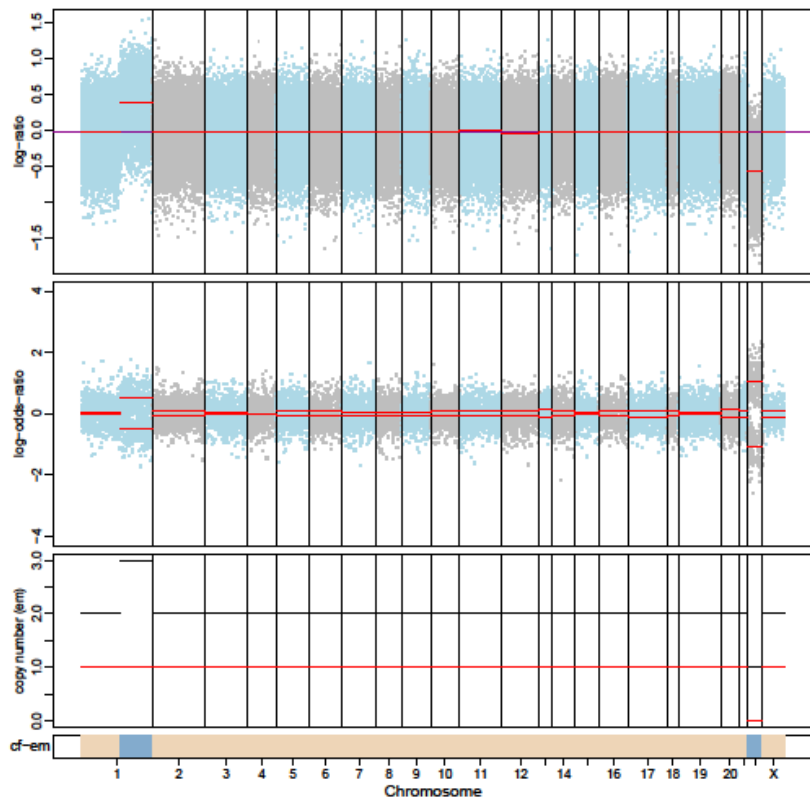
1510-P2



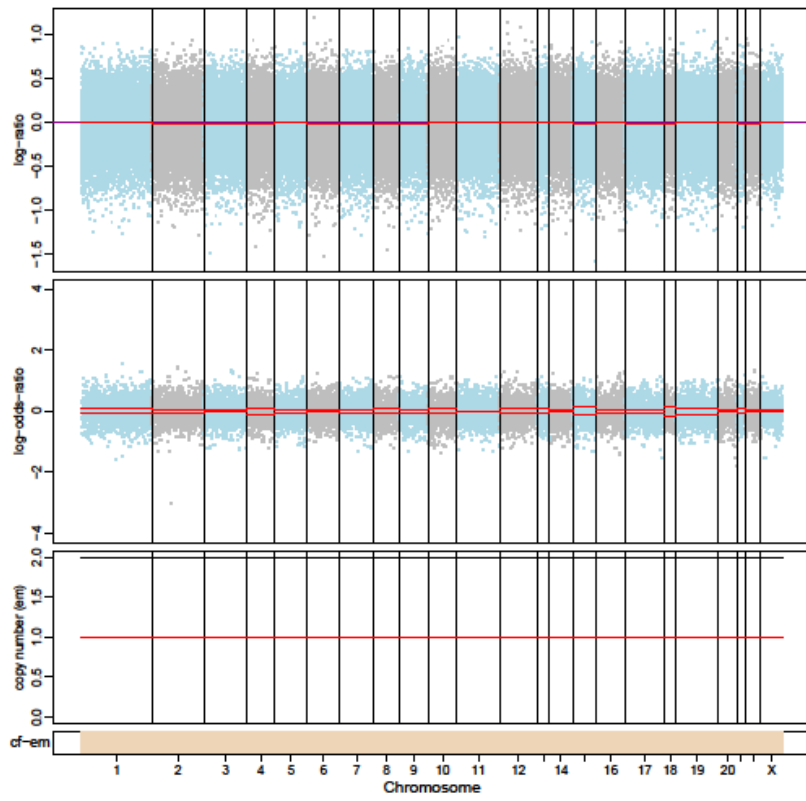
1526-P1



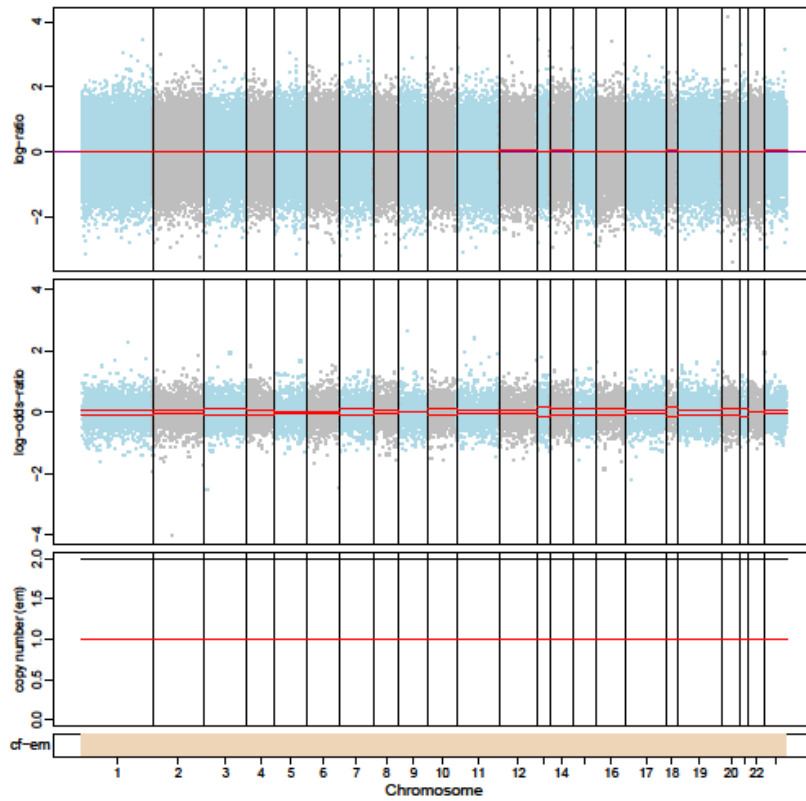
1537-P0



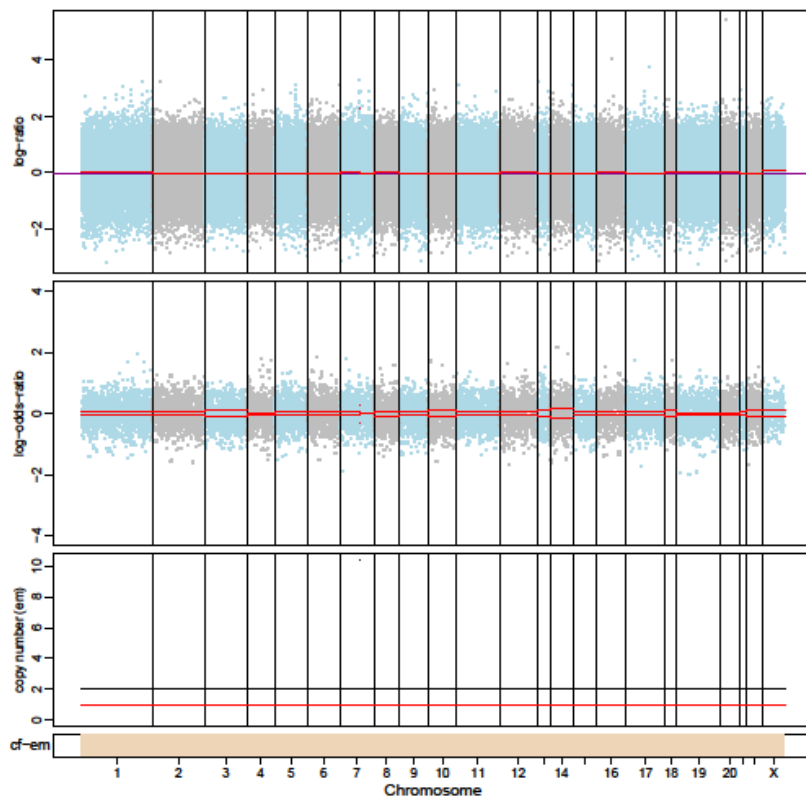
1526-P0



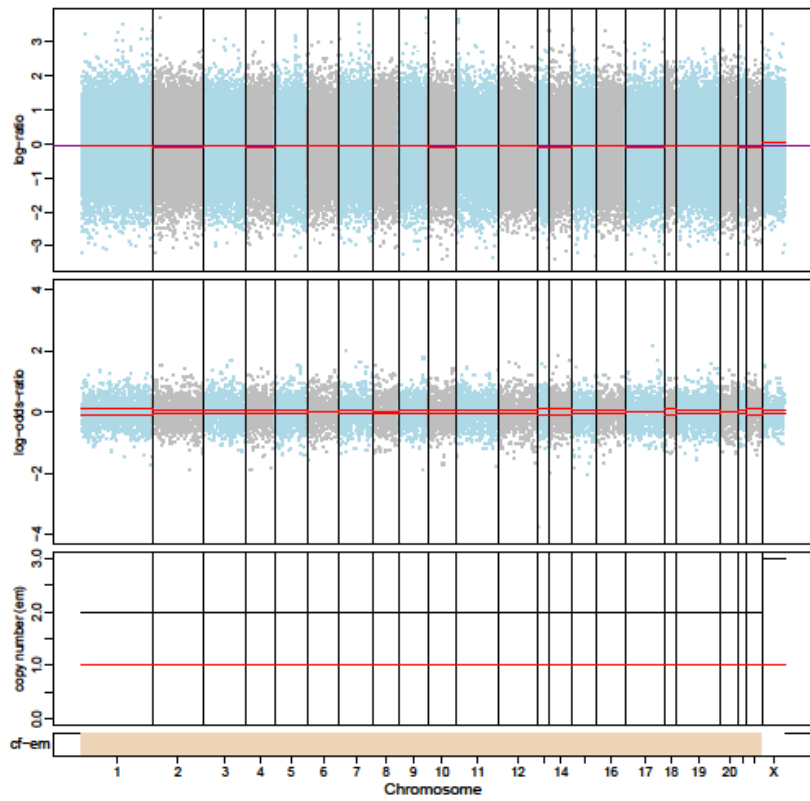
1526-P2



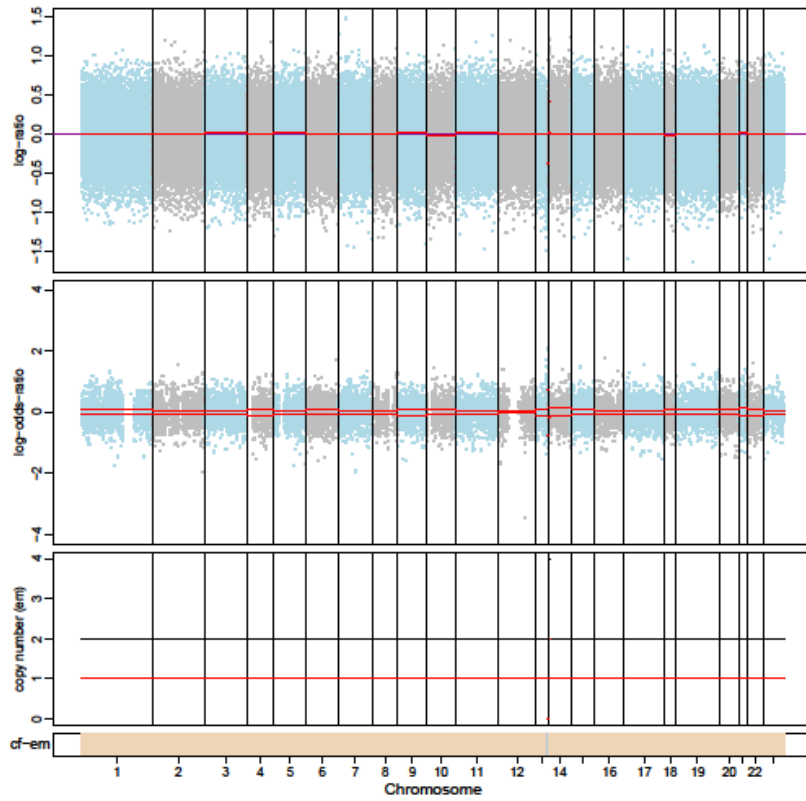
1537-P1



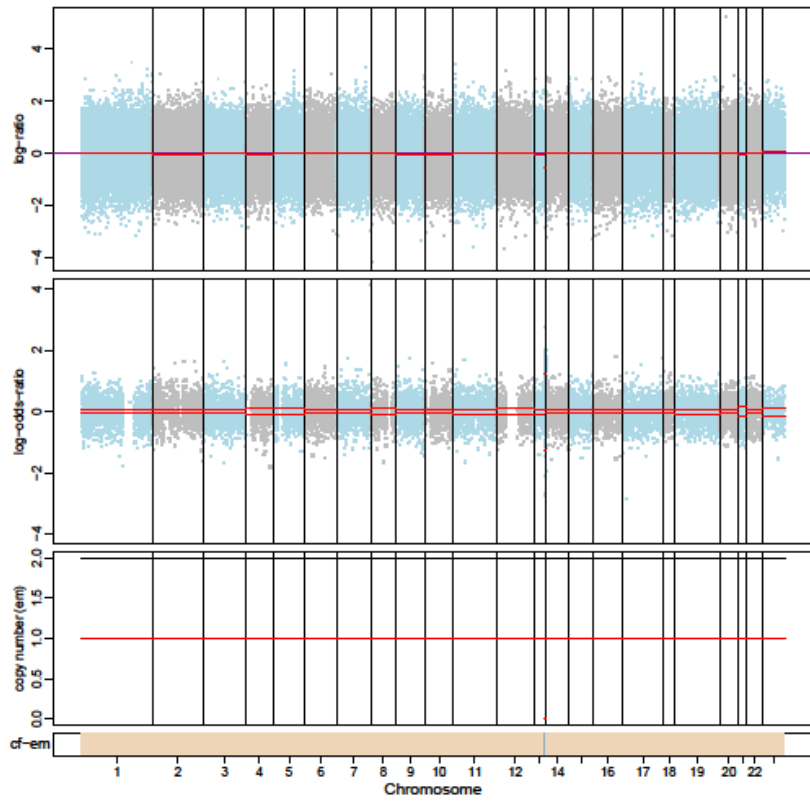
1537-P2



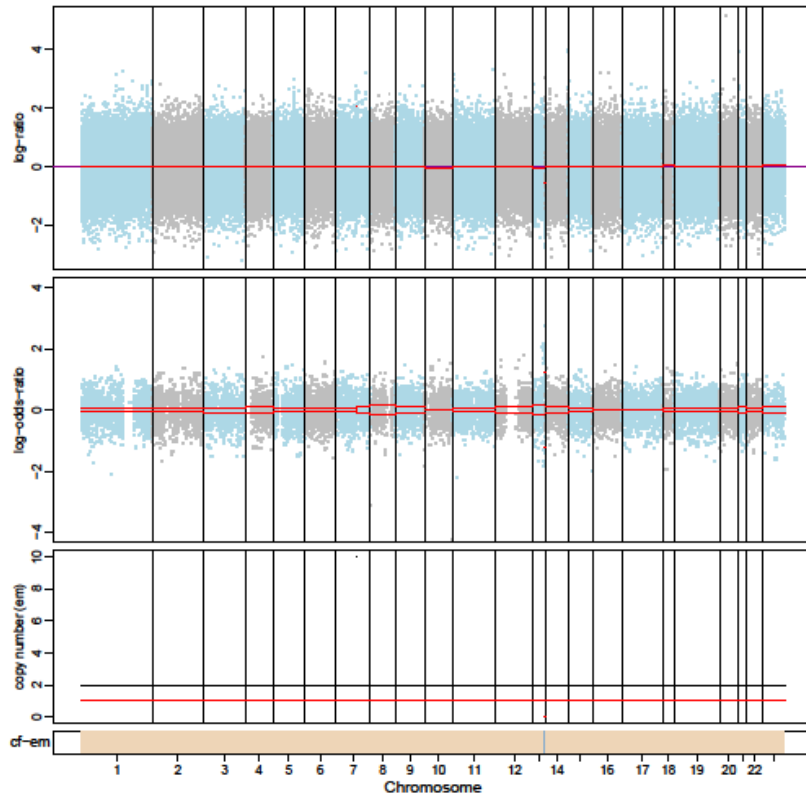
1542-P0



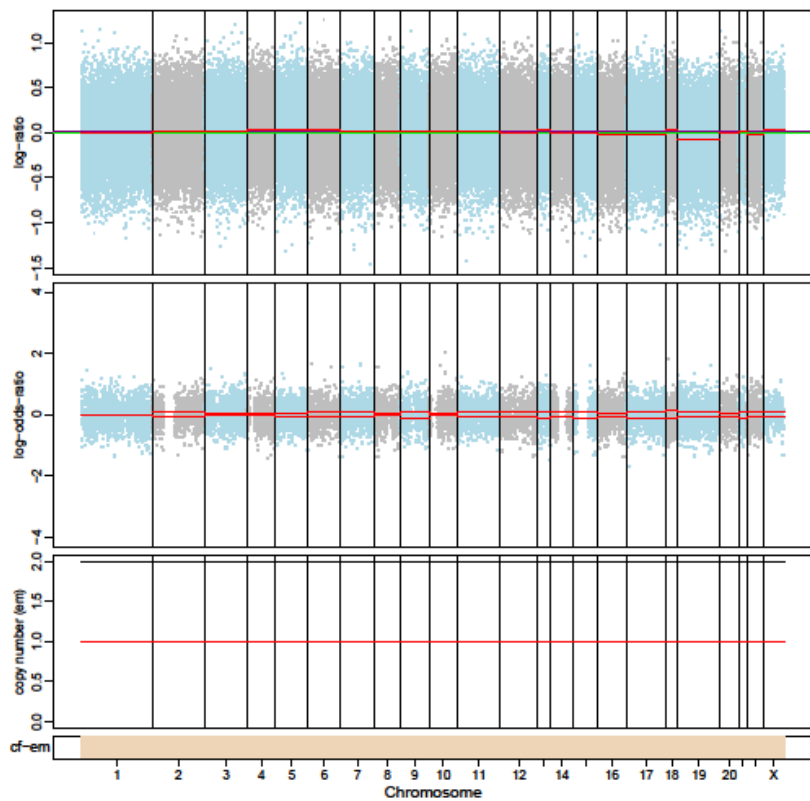
1542-P1



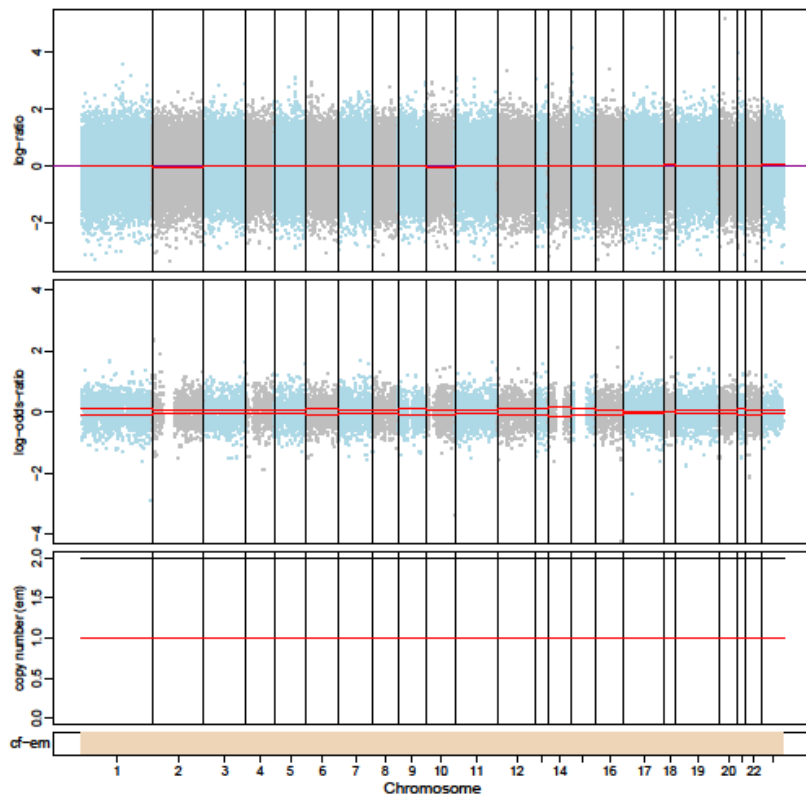
1542-P2



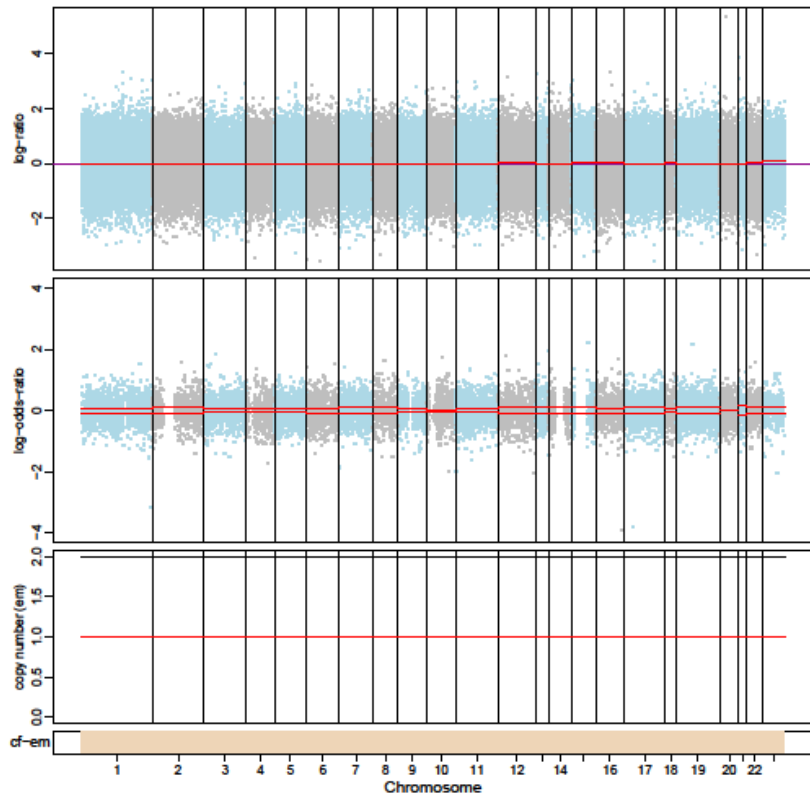
1544-P0



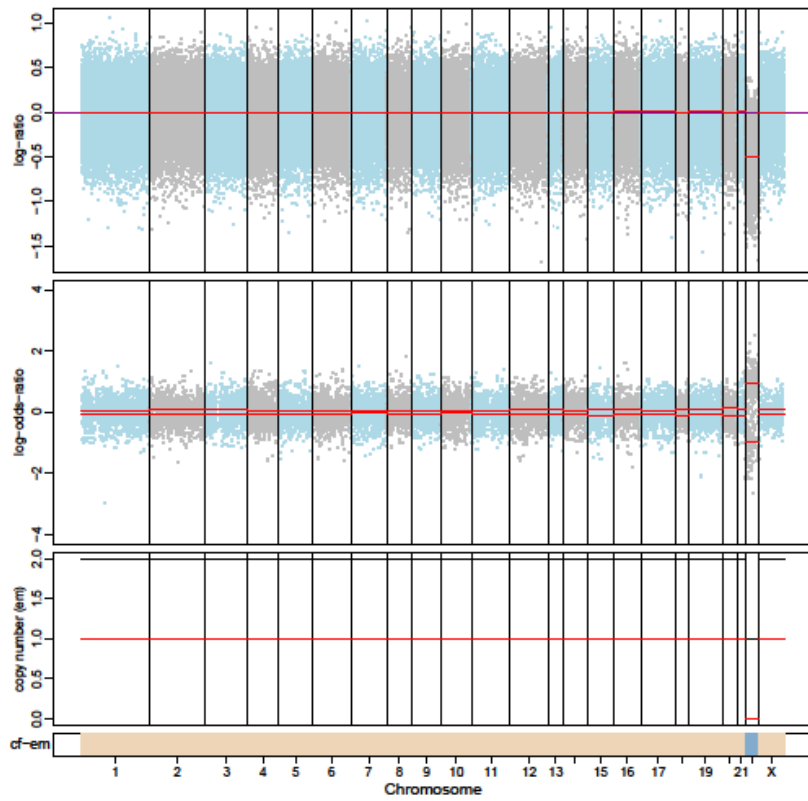
1544-P1



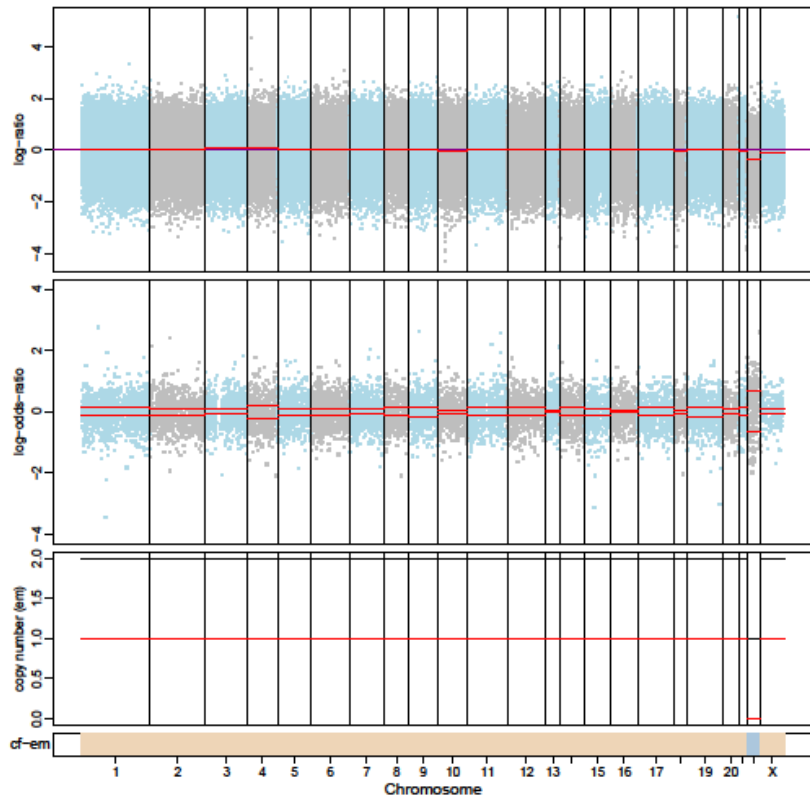
1544-P2



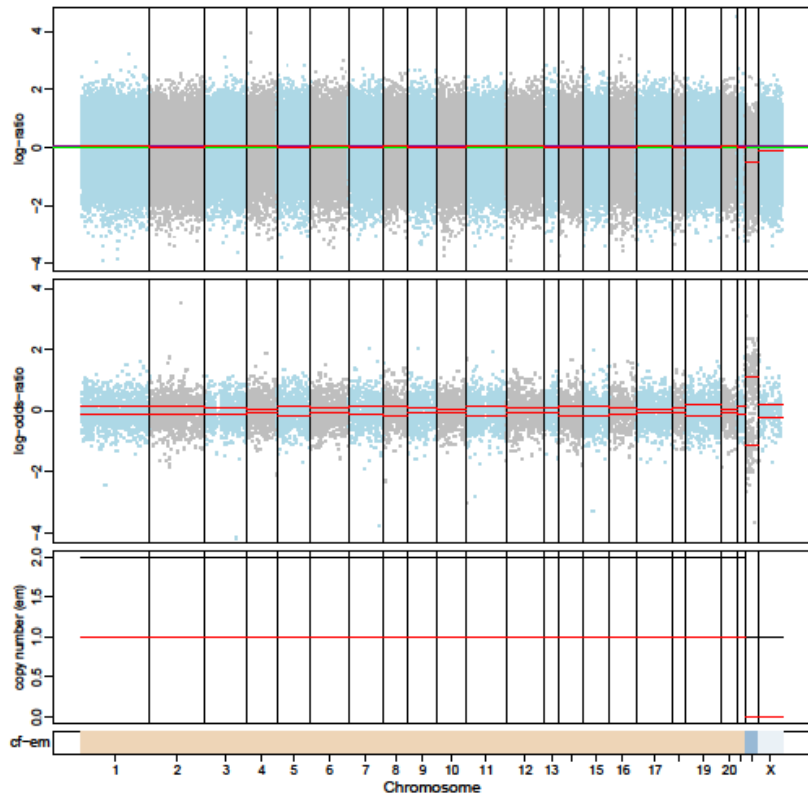
1560-P0



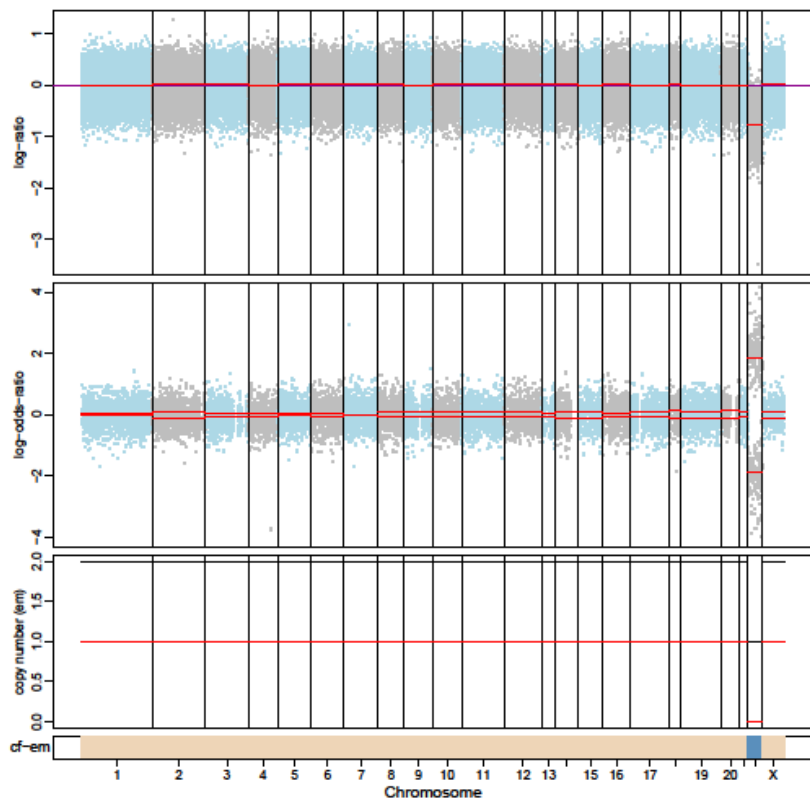
1560-P1



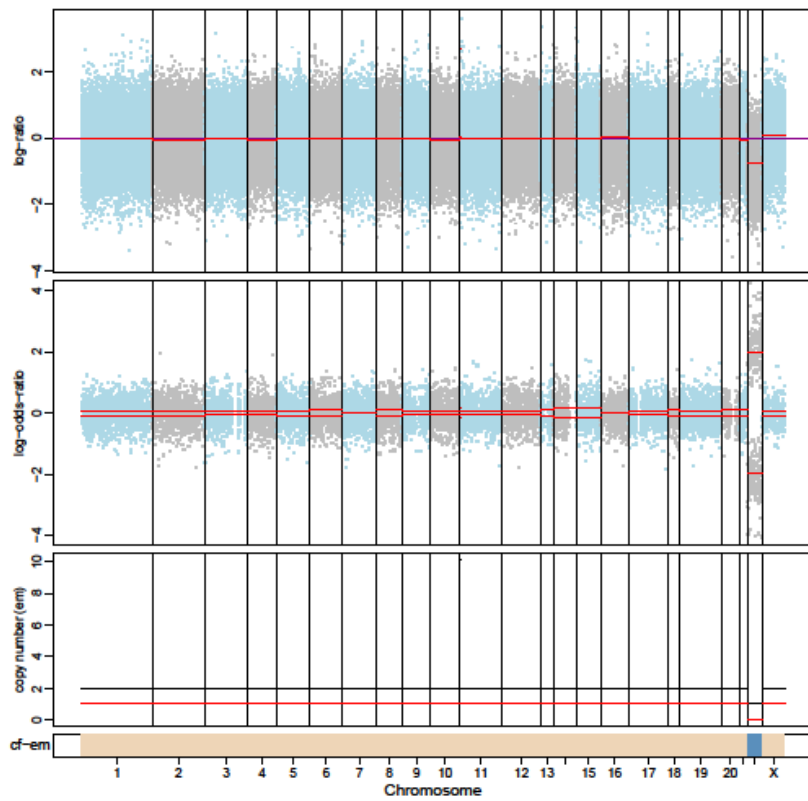
1560-P2



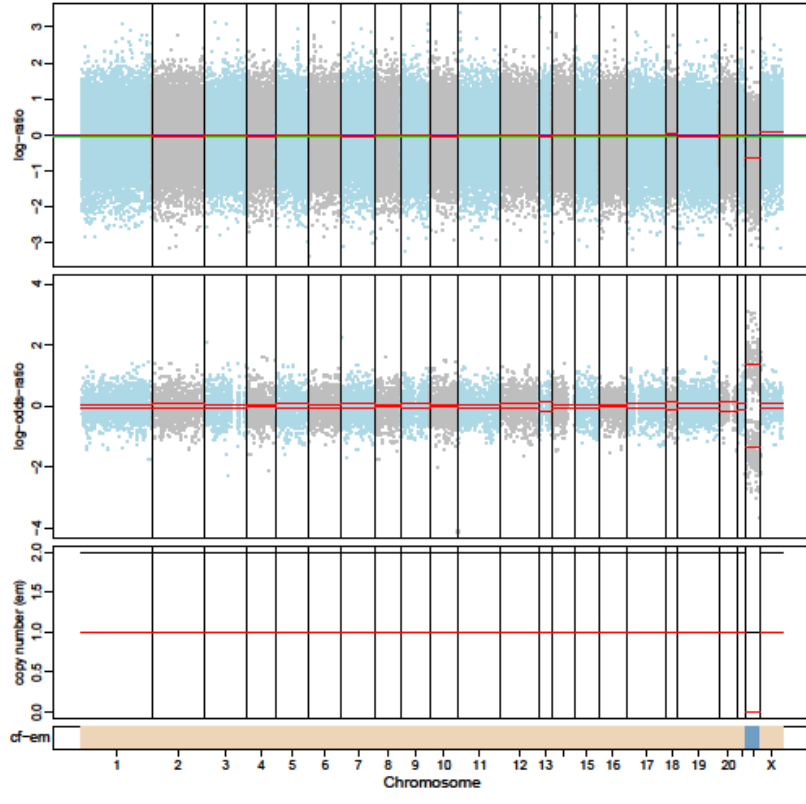
1565-P0



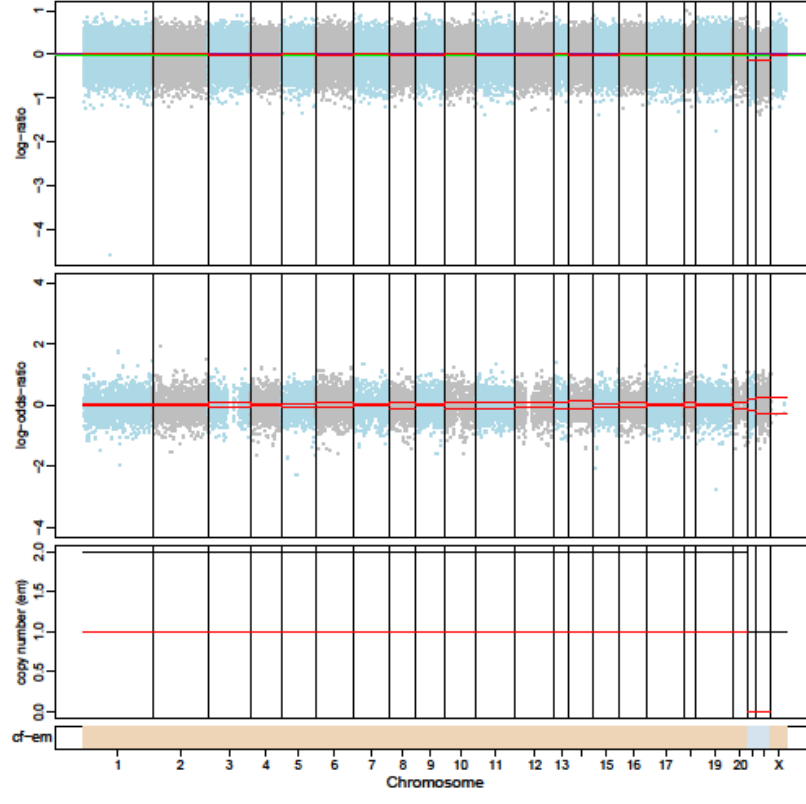
1565-P1



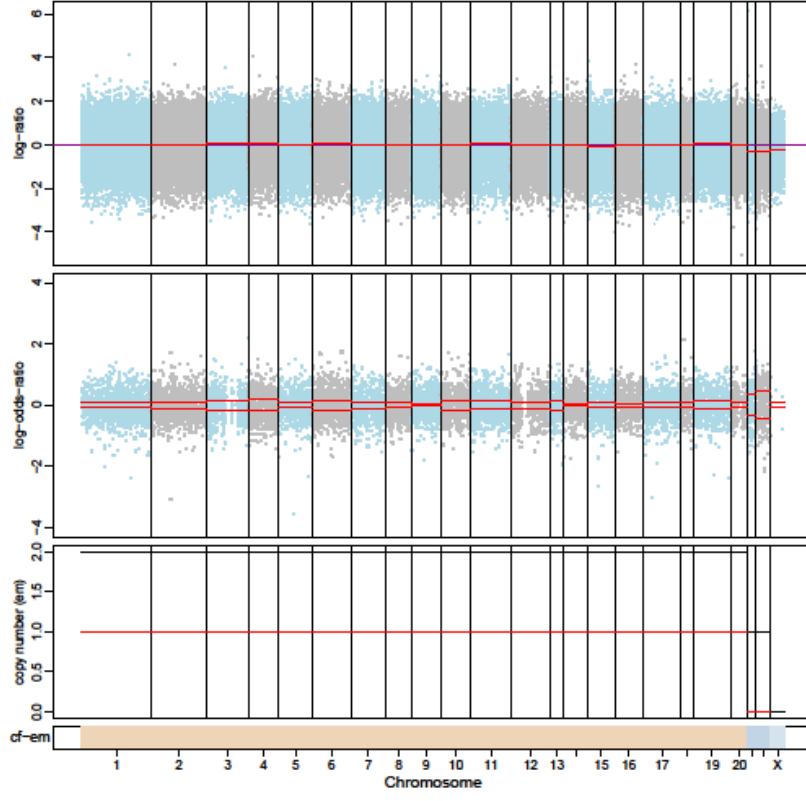
1565-P2



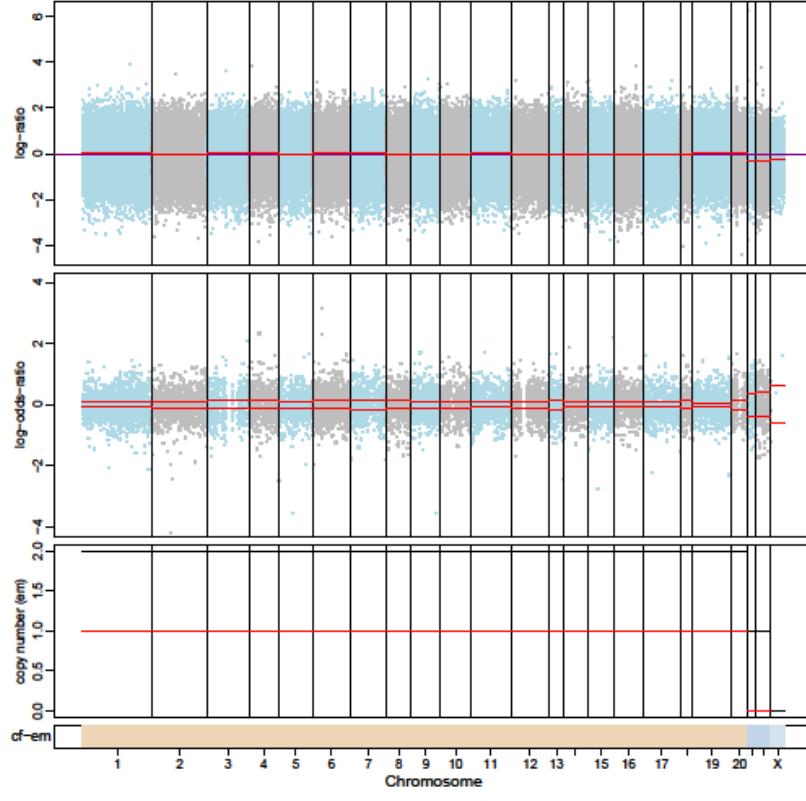
1575-P0



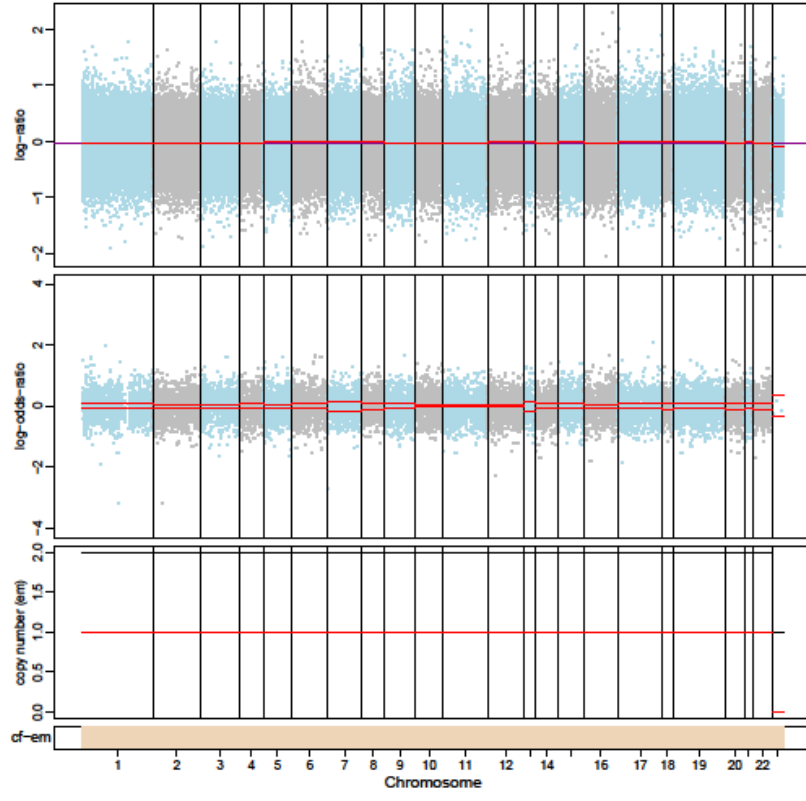
1575-P1



1575-P2



1182-P2



1168-P2

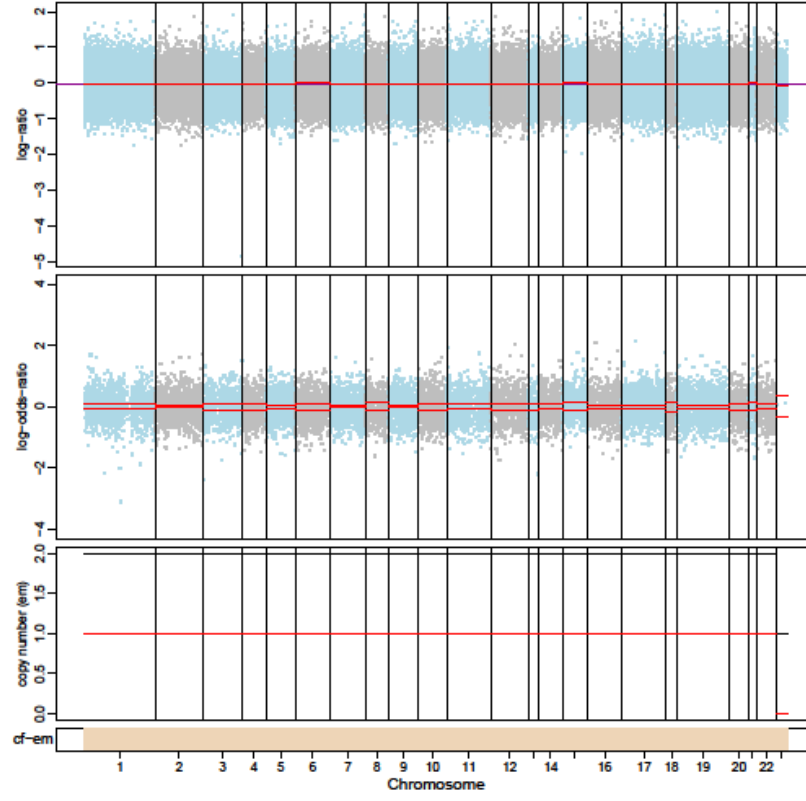


Figure S1: Copy number plots. Raw copy number plots using Facets. The top panel in each case is the total copy number log-ratio (logR), and the second panel is allele-specific log-odds-ratio data (logOR) with chromosomes in blue and gray color. Third panel is the plot of corresponding integer (total, minor) copy number changes.

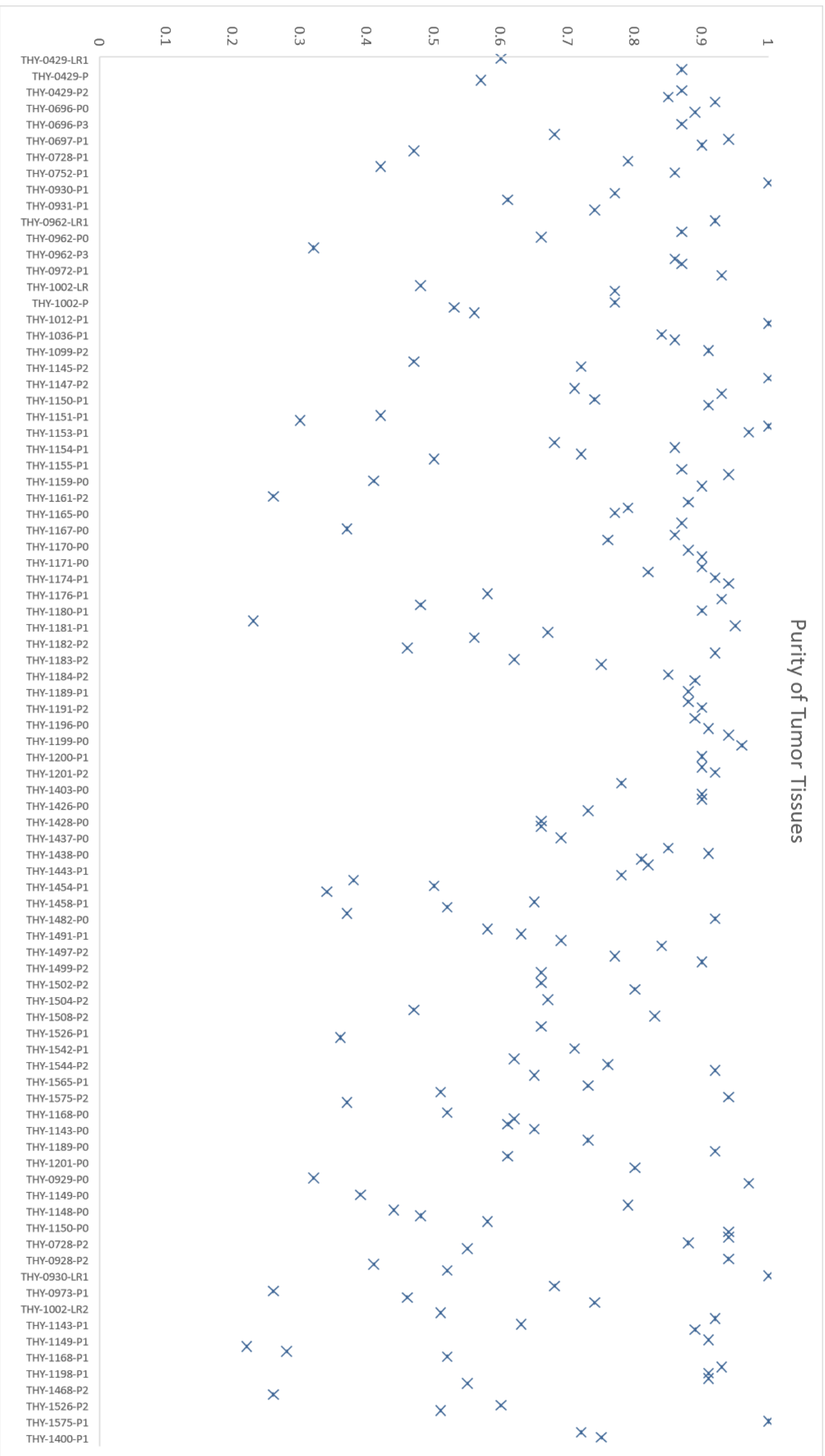
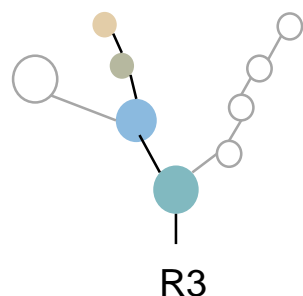
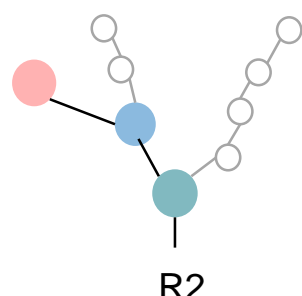
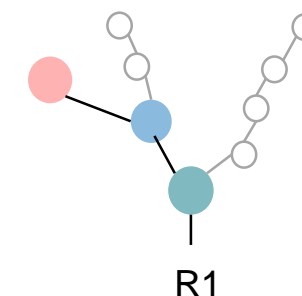
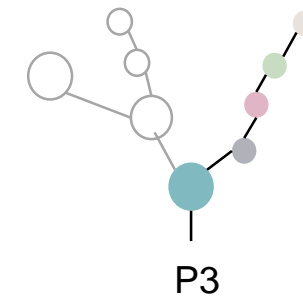
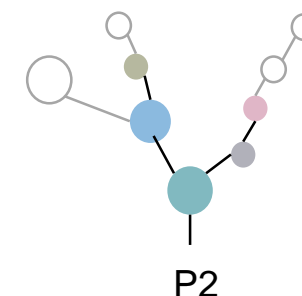
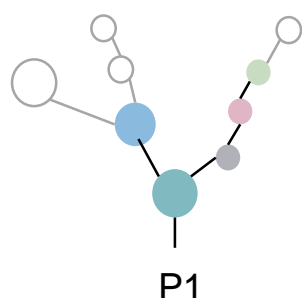
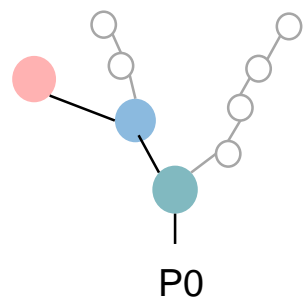
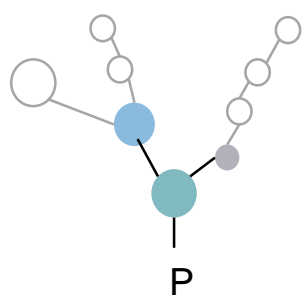
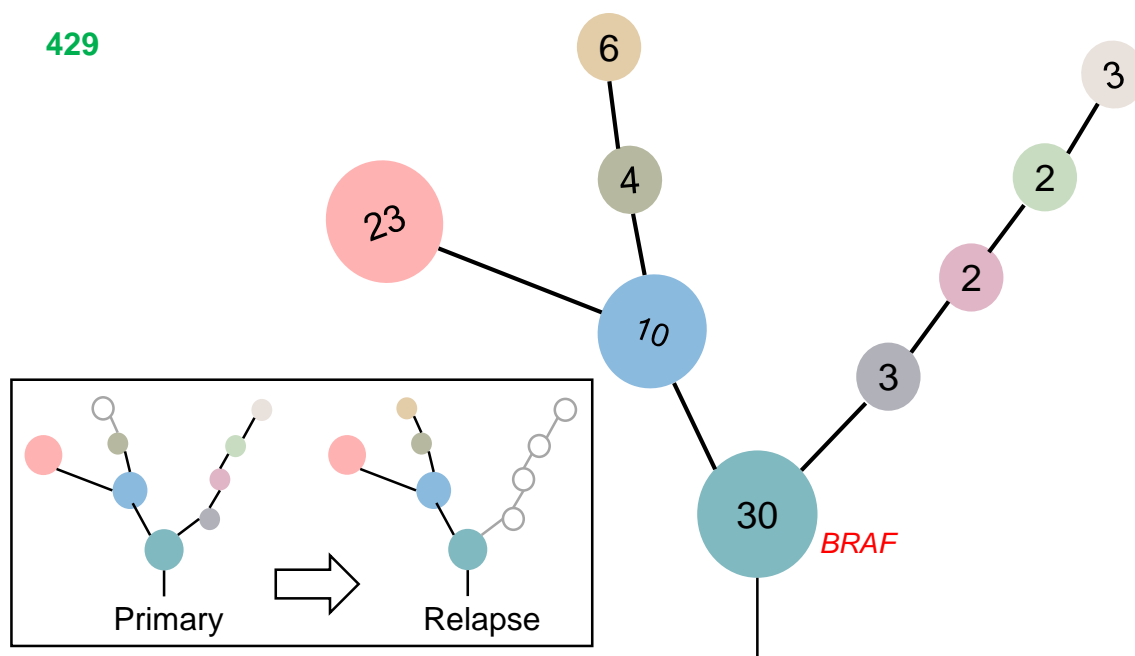
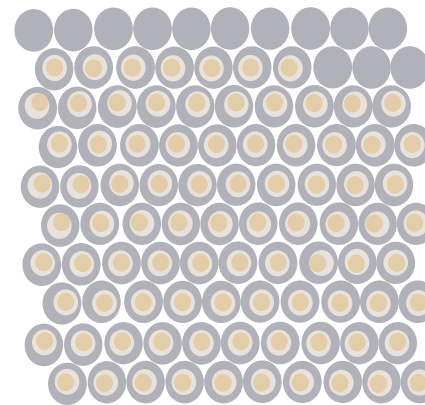
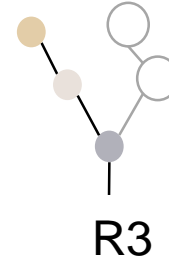
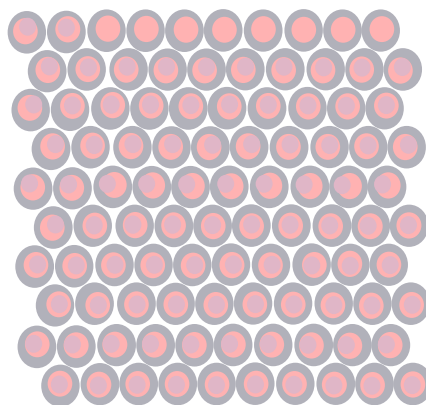
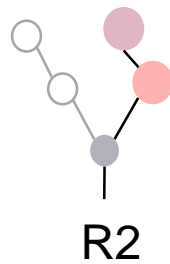
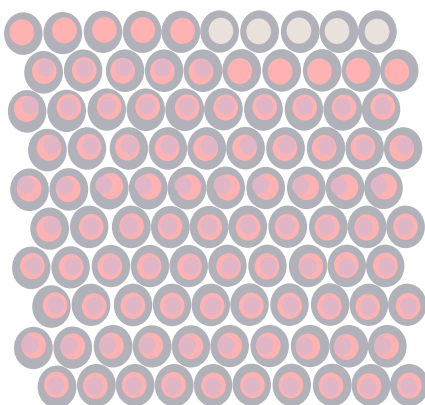
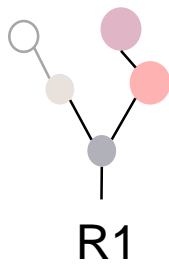
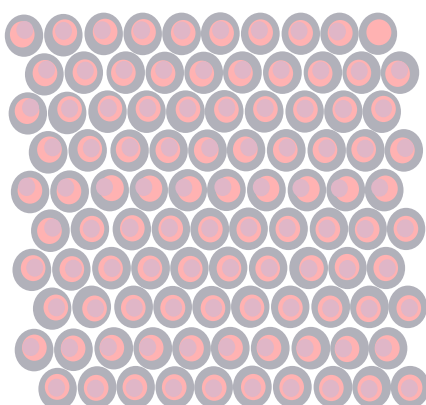
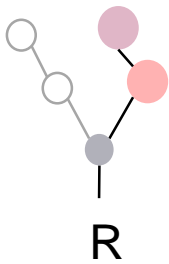
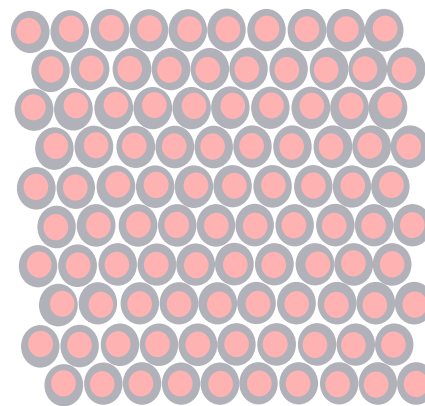
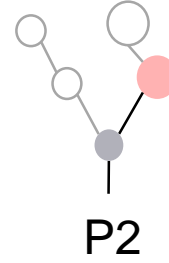
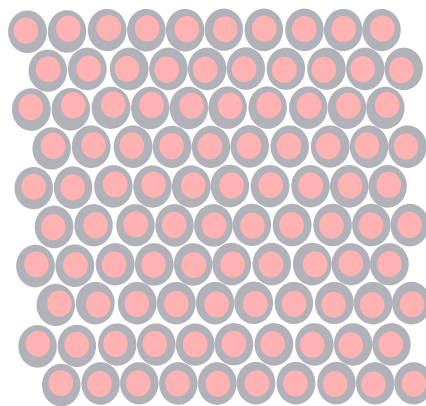
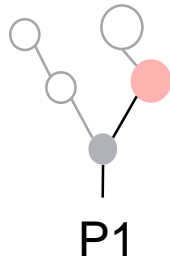
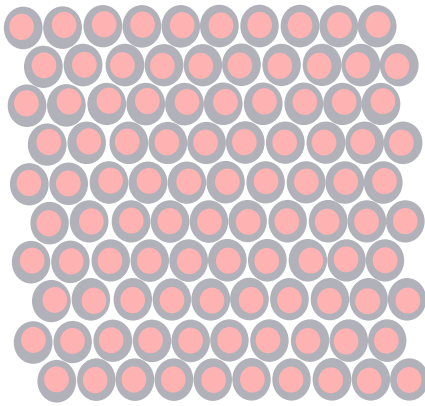
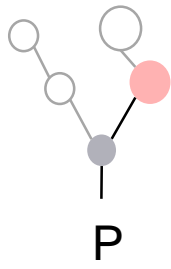
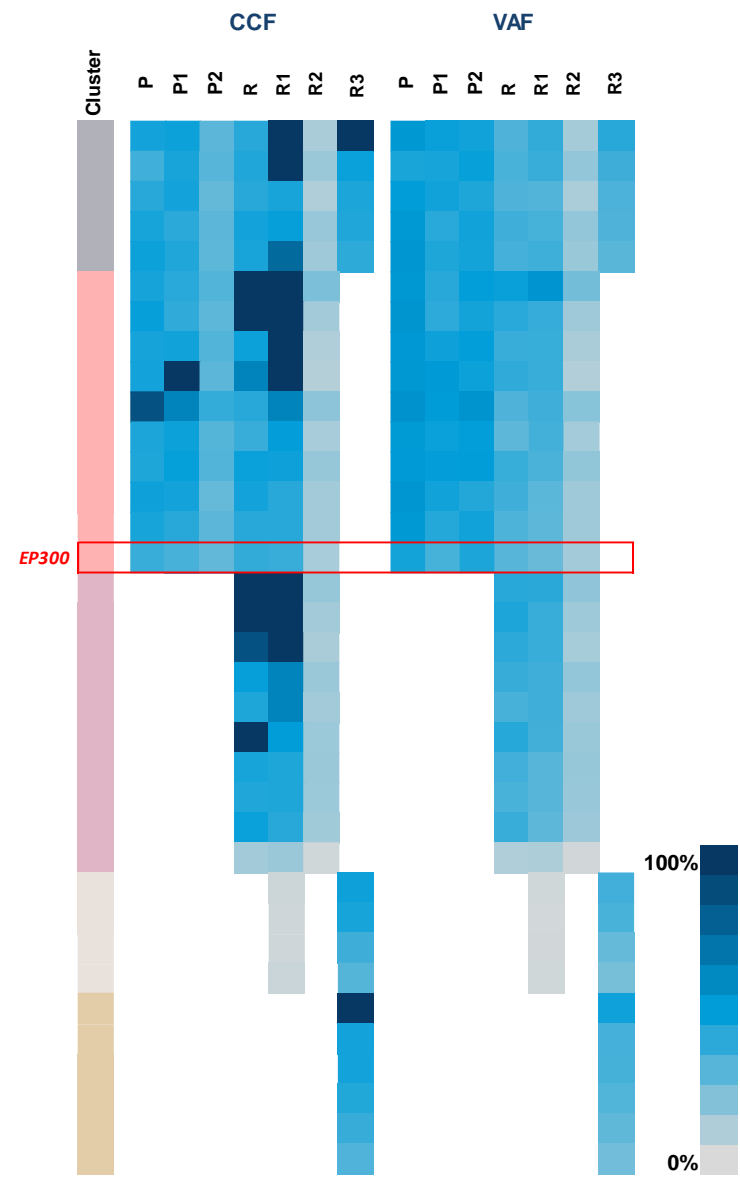
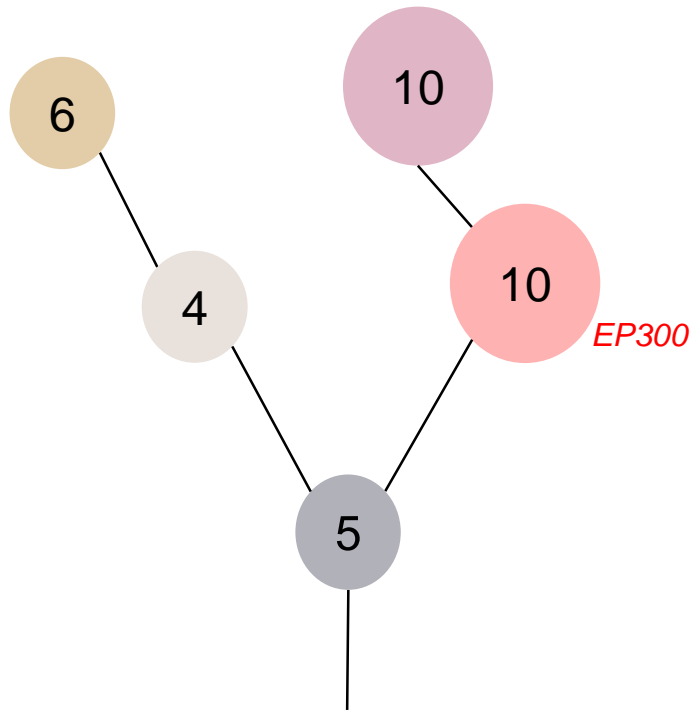
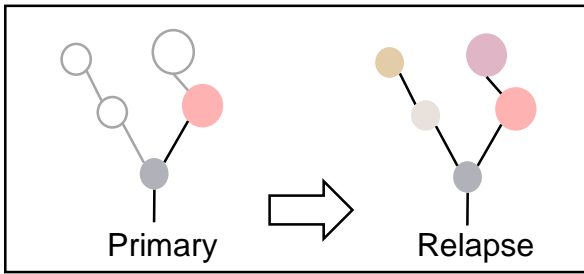


Figure S2: Purity estimation in PTC cohort. Purity estimation of each cancer tissue.

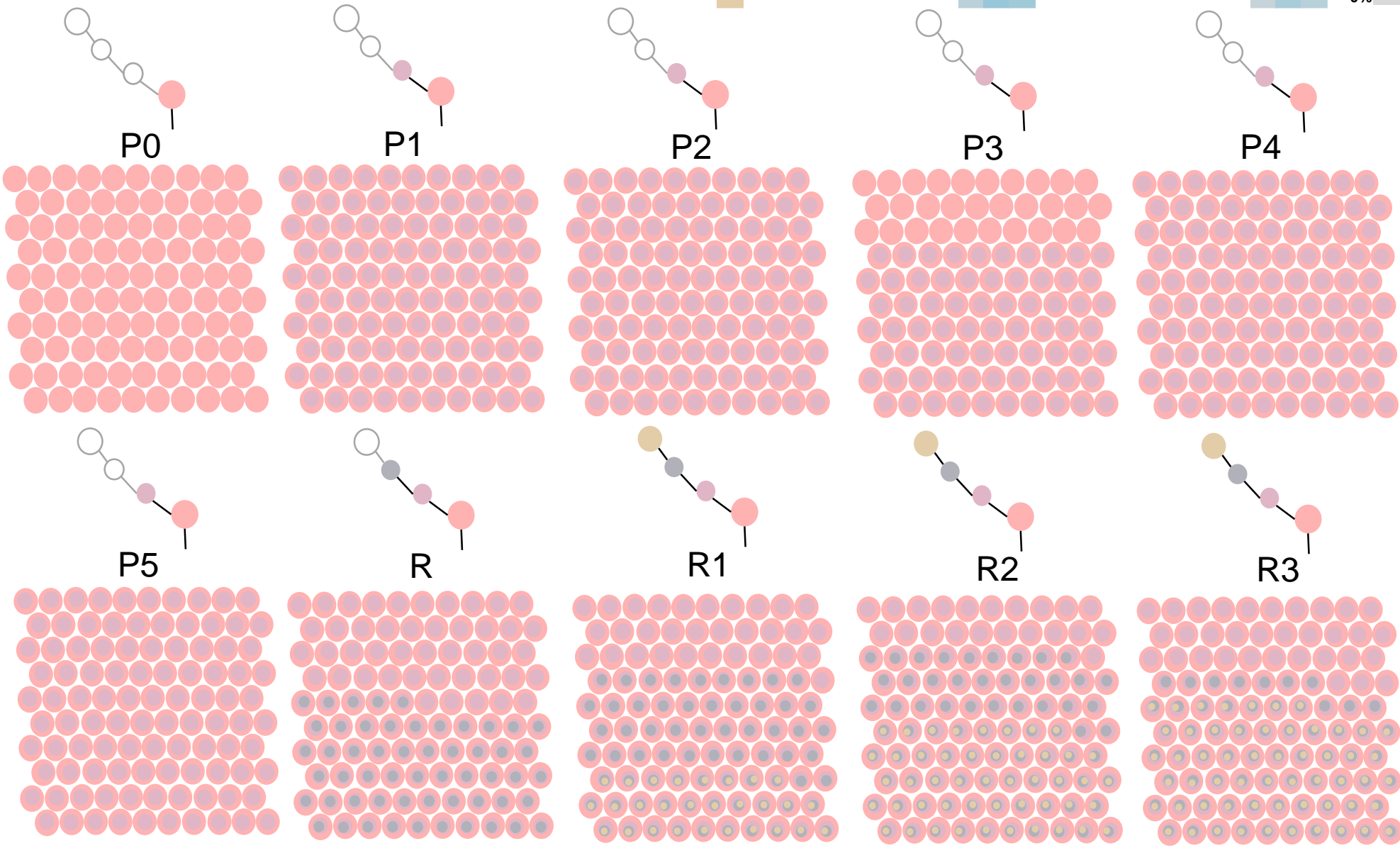
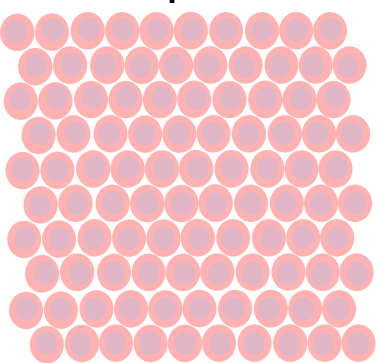
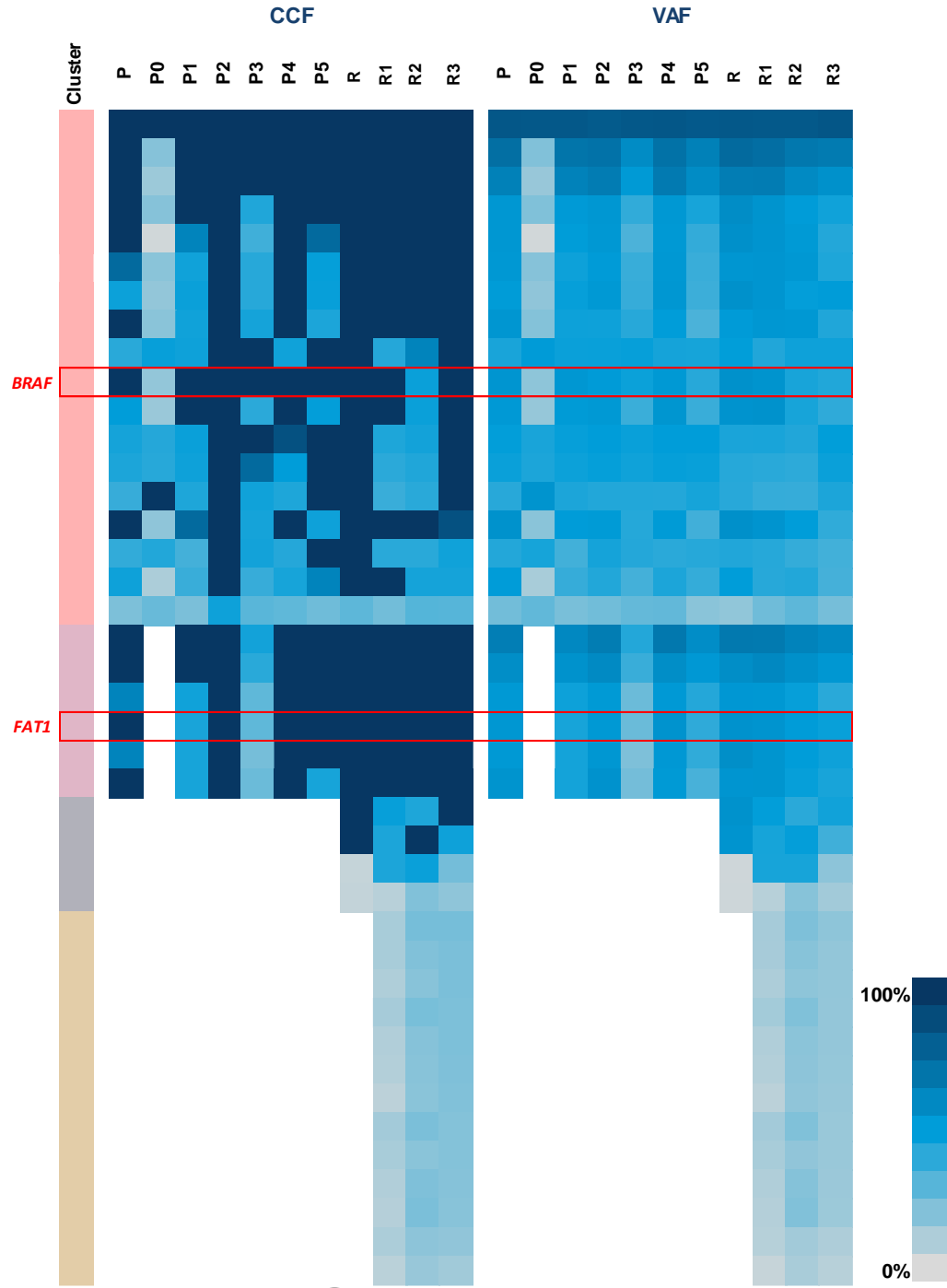
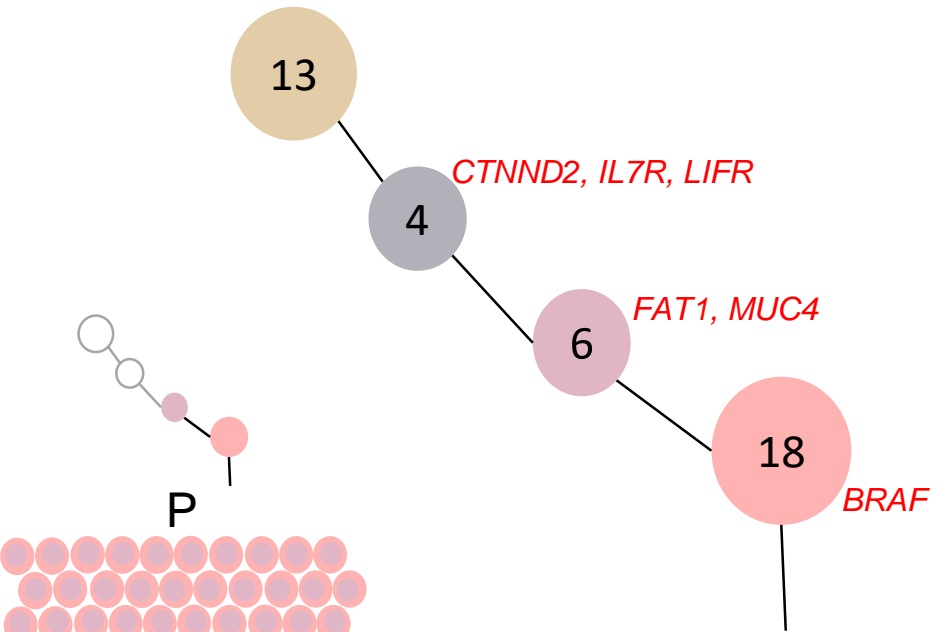
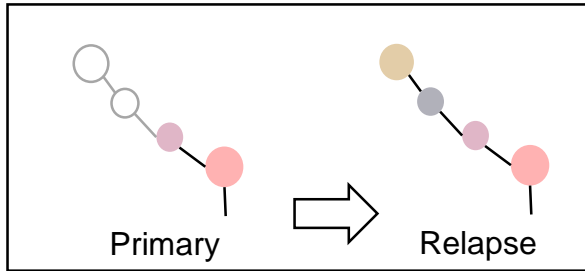
A Relapse cases

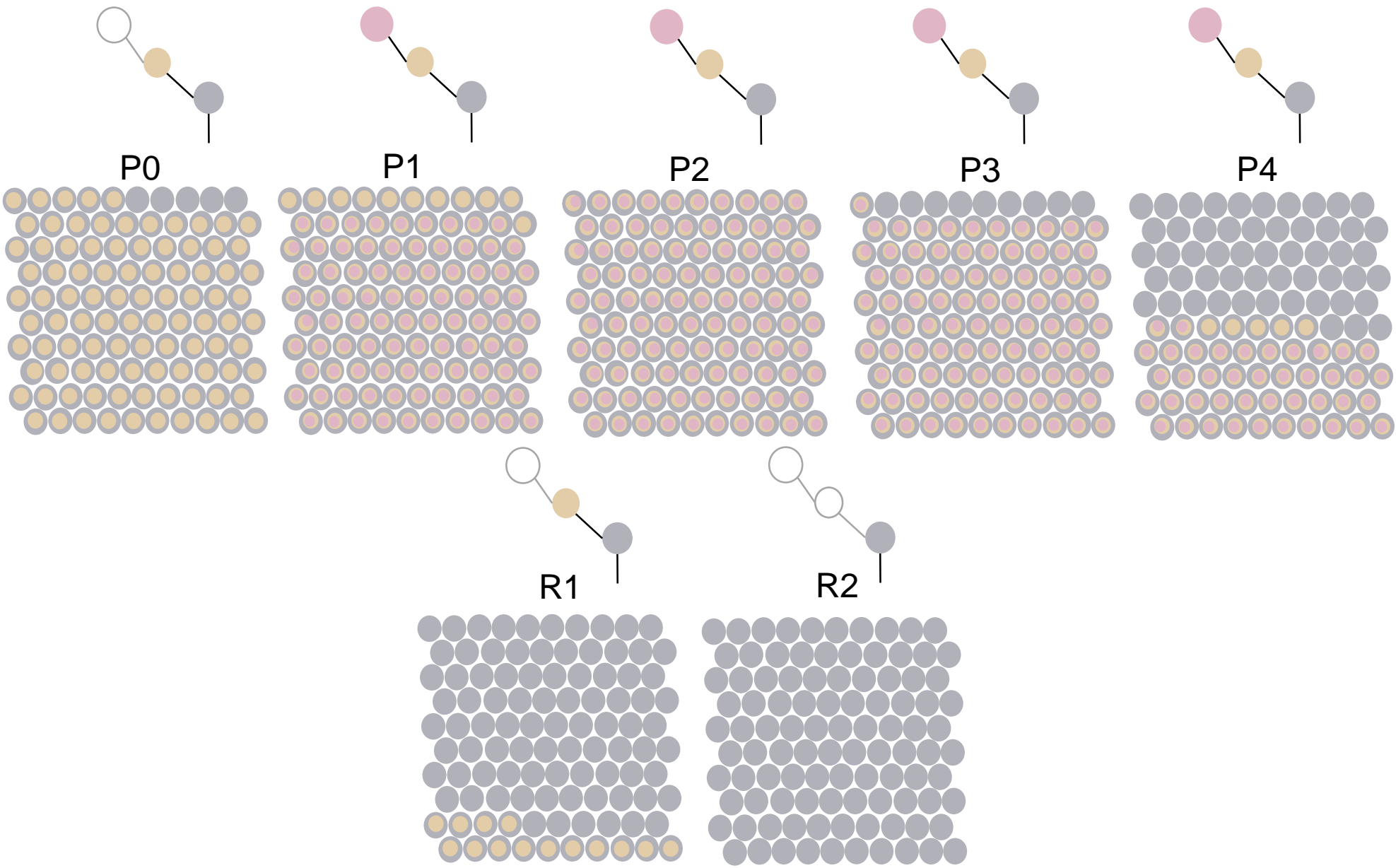
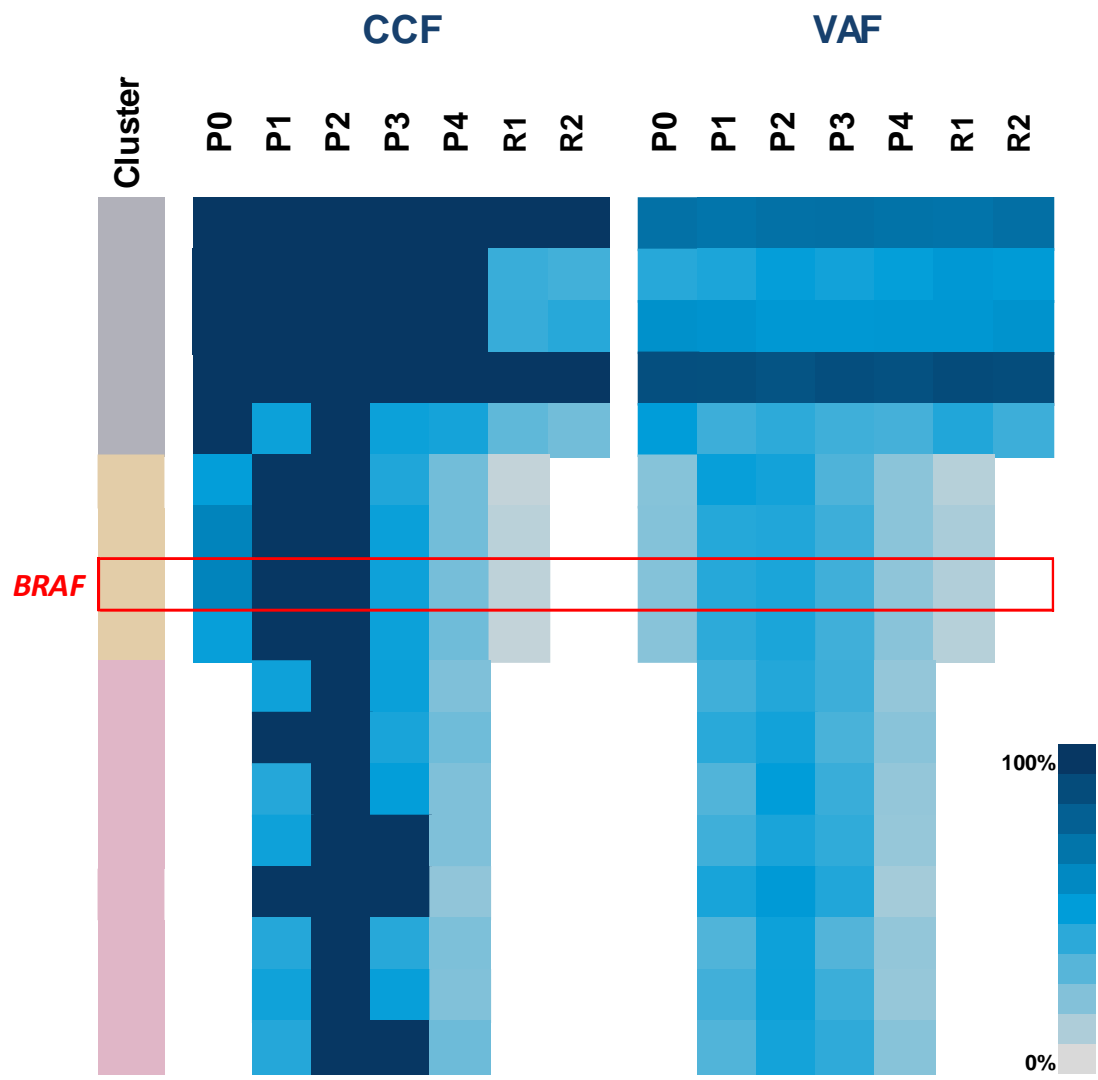
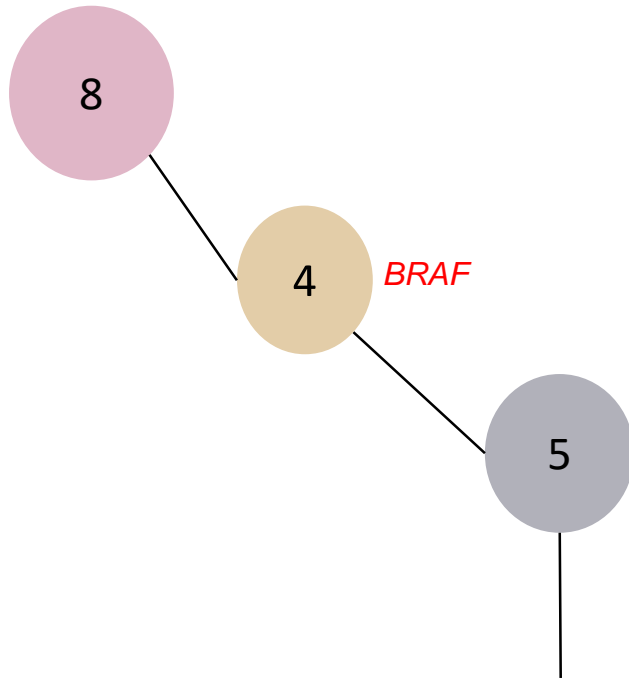
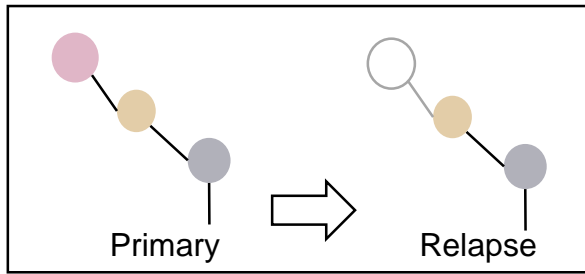
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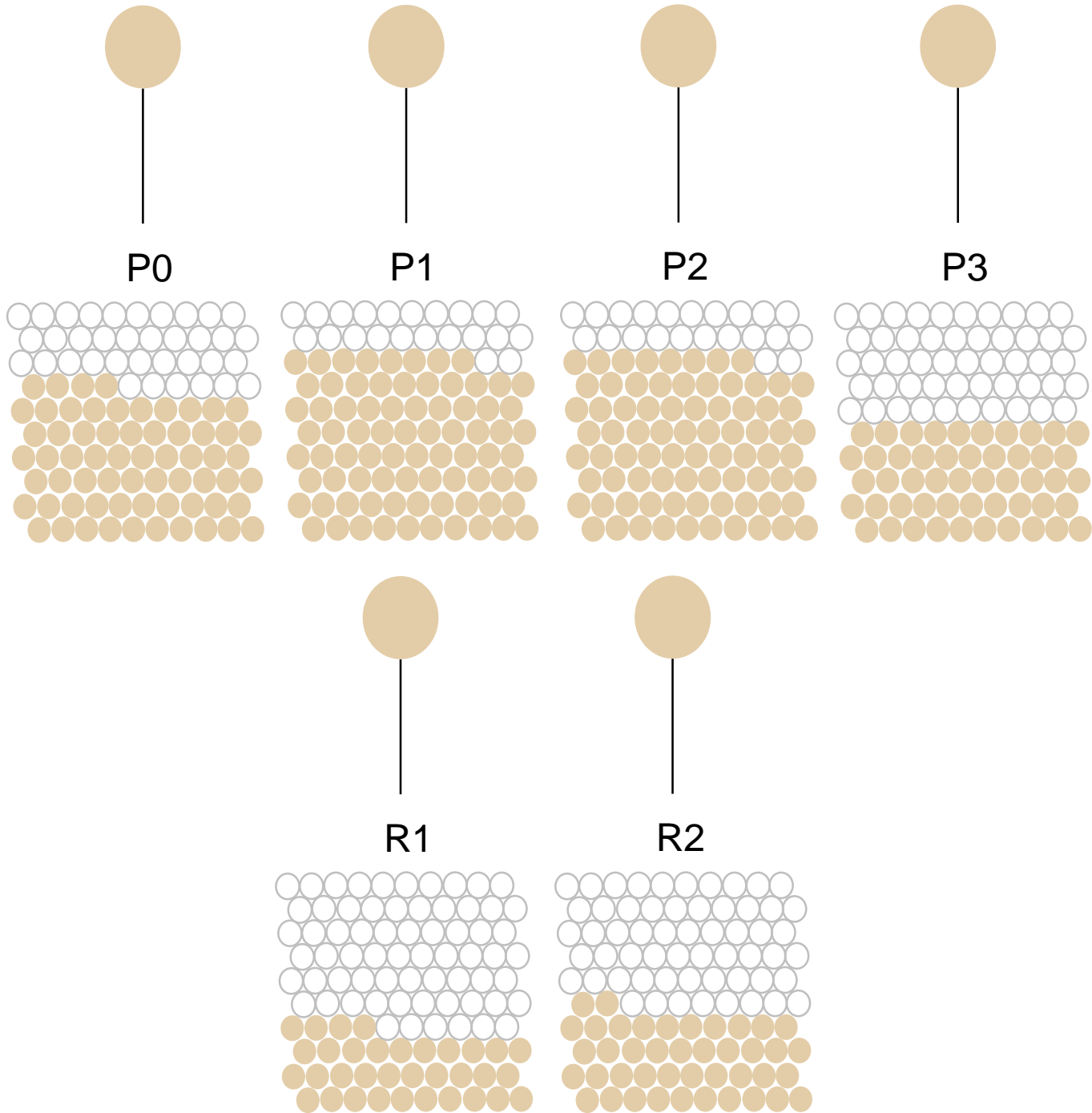
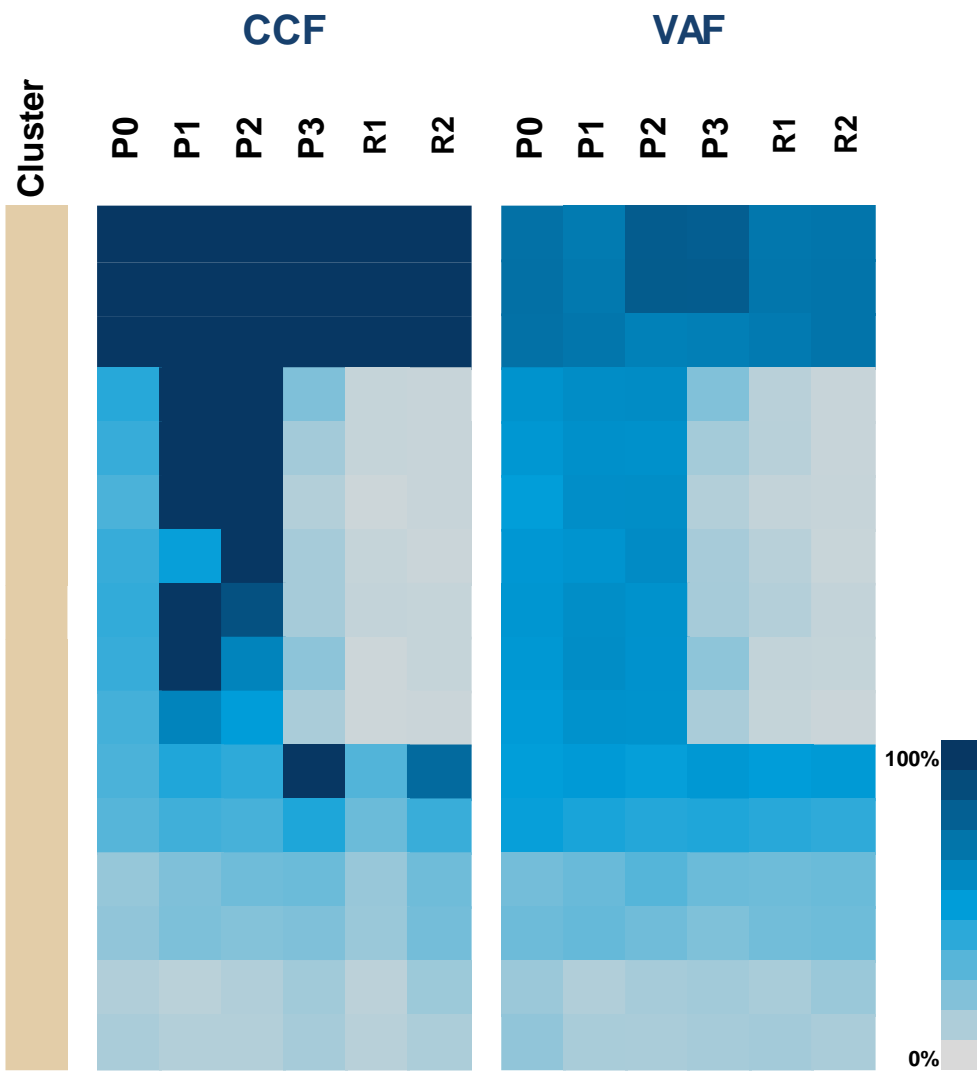
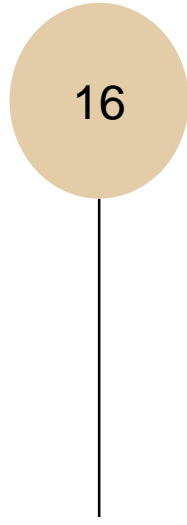
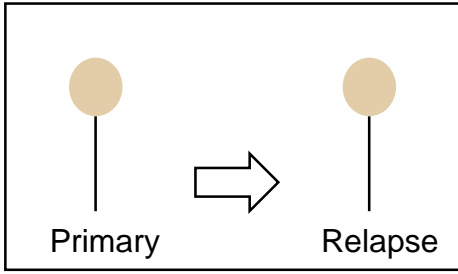


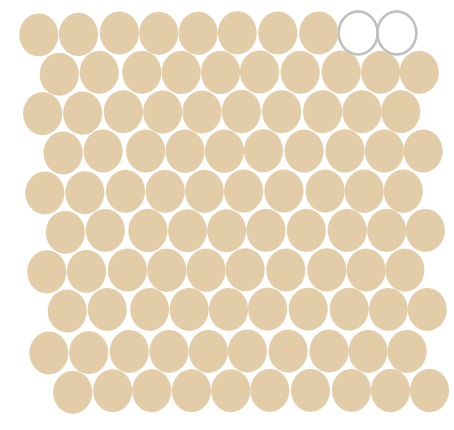
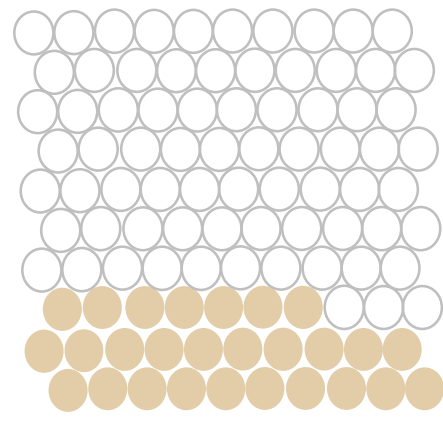
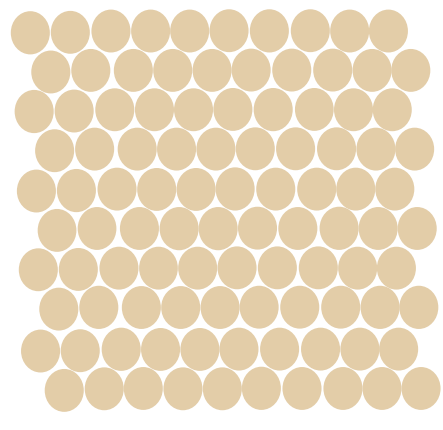
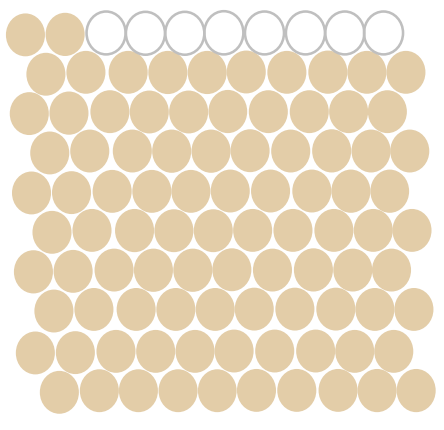
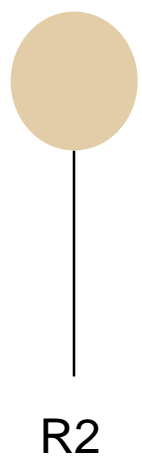
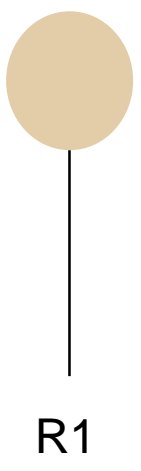
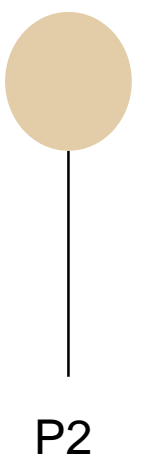
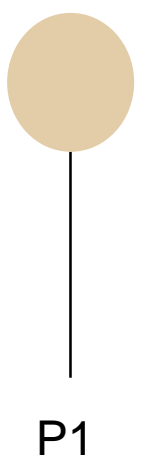
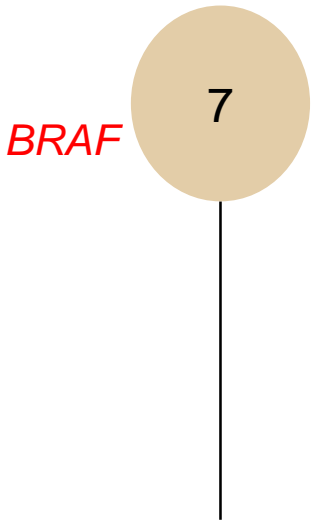
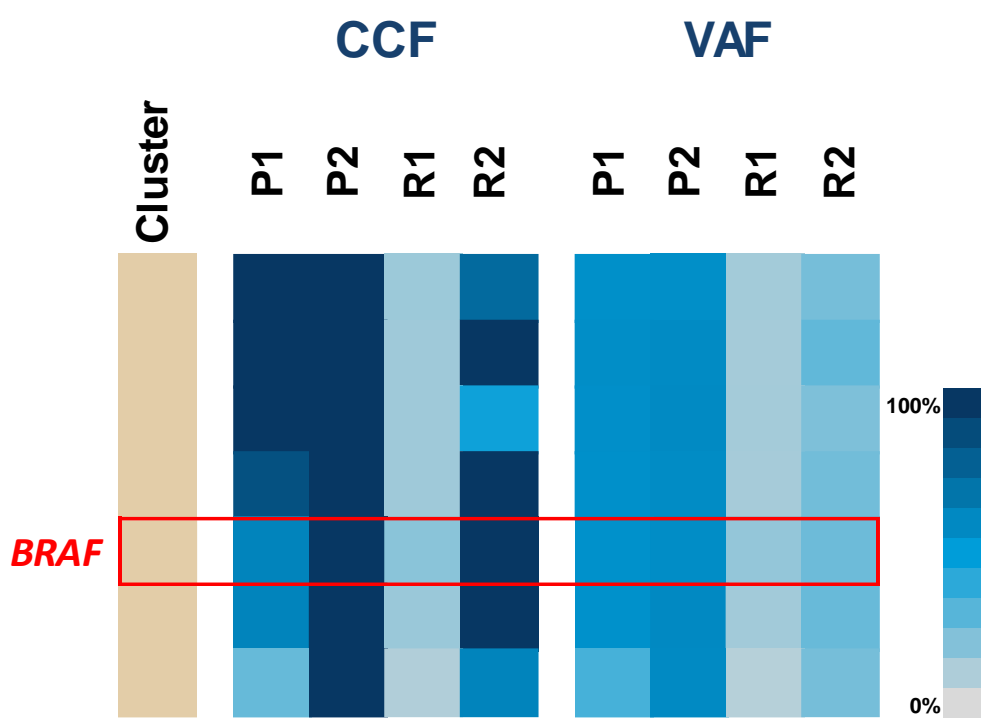
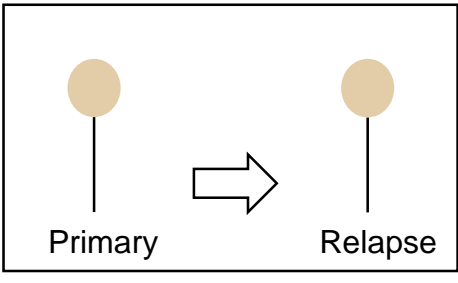


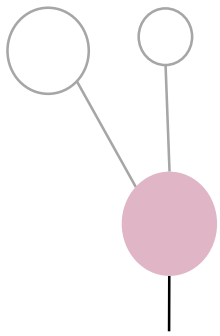
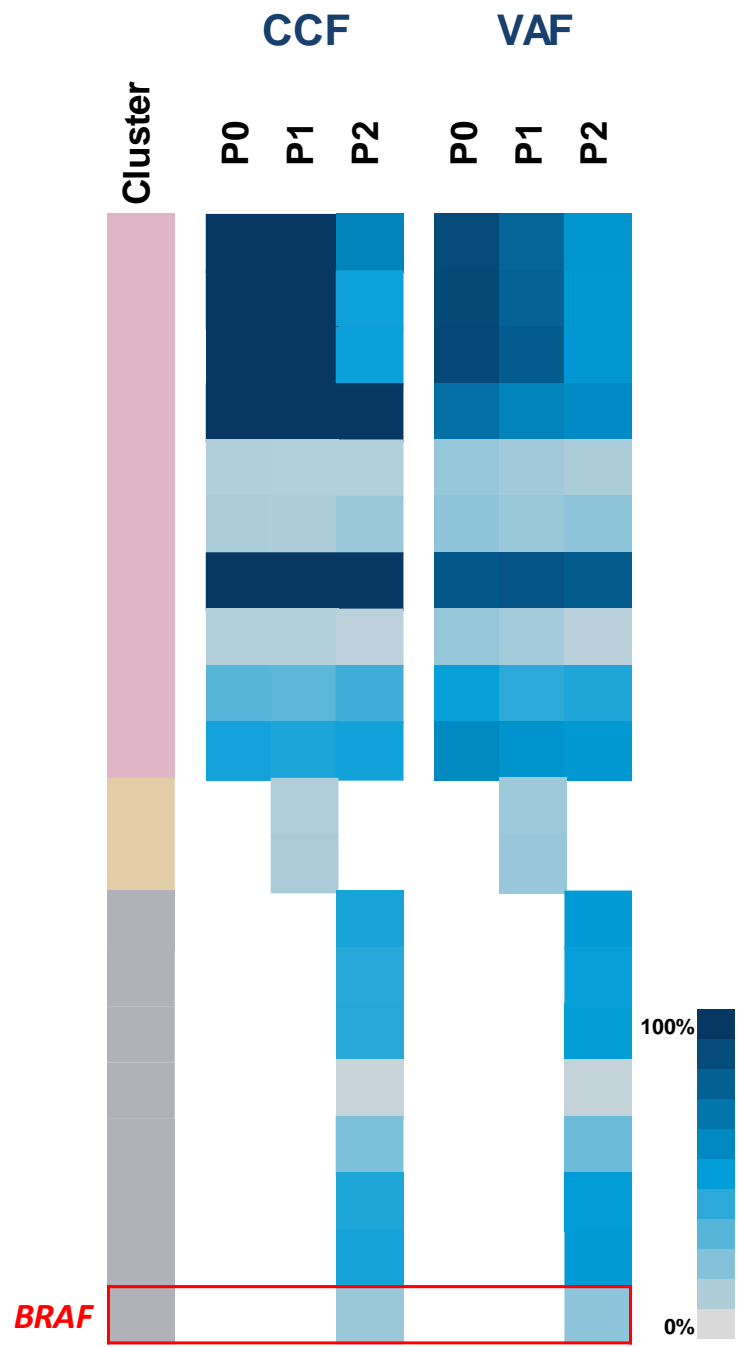
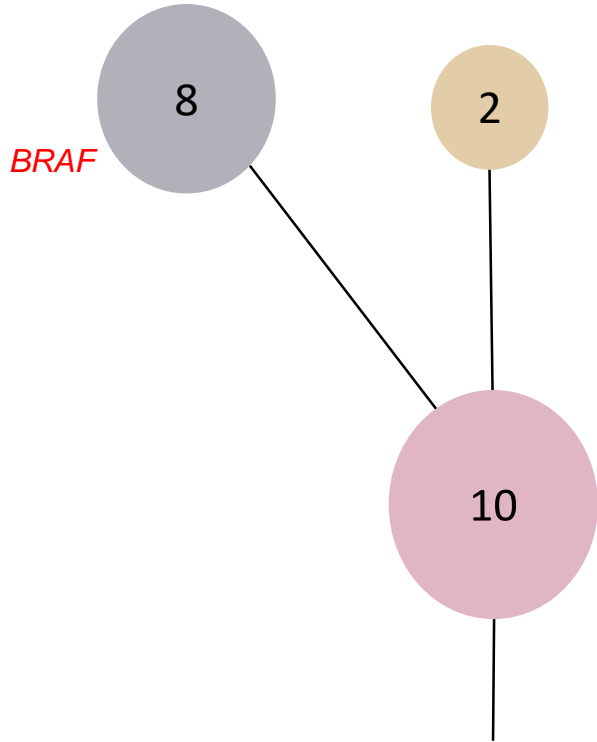
Cluster	Gene	Type
■	<i>MUC4</i>	Amp
■	<i>CTNND2</i>	Amp
■	<i>IL7R</i>	Amp
■	<i>LIFR</i>	Amp



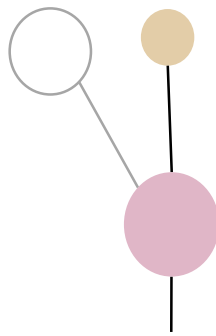




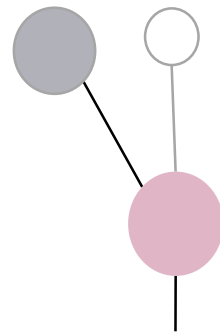




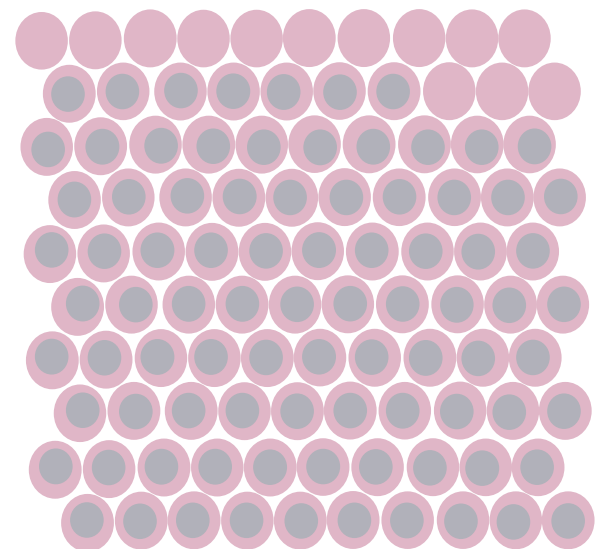
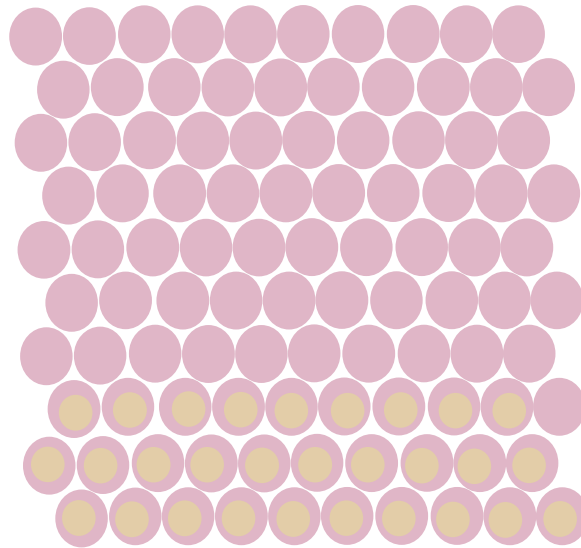
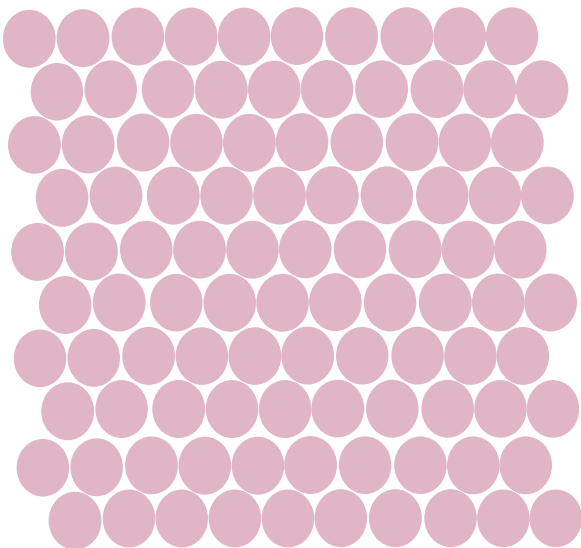
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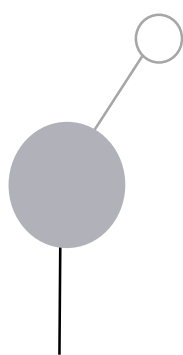
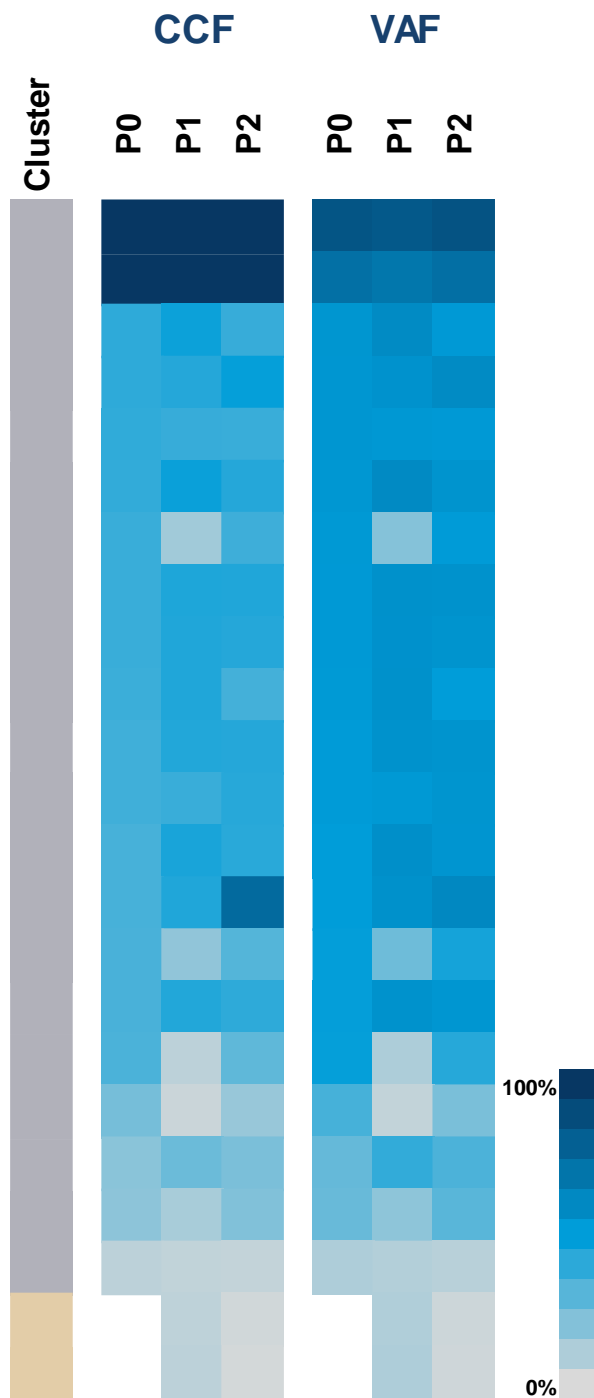
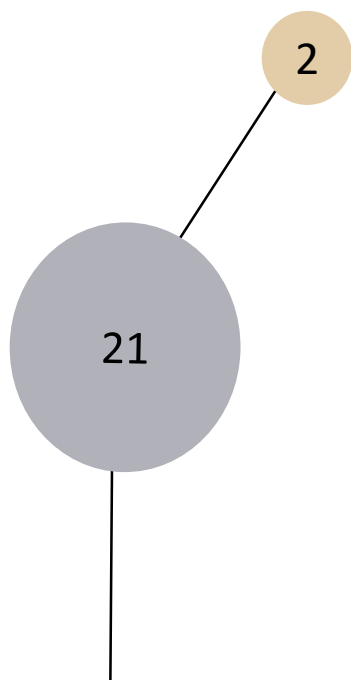


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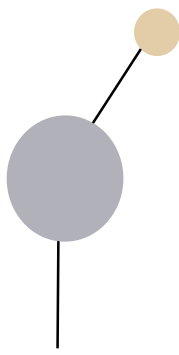


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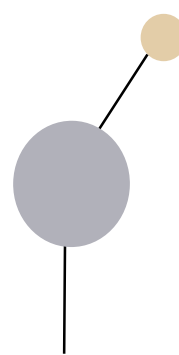




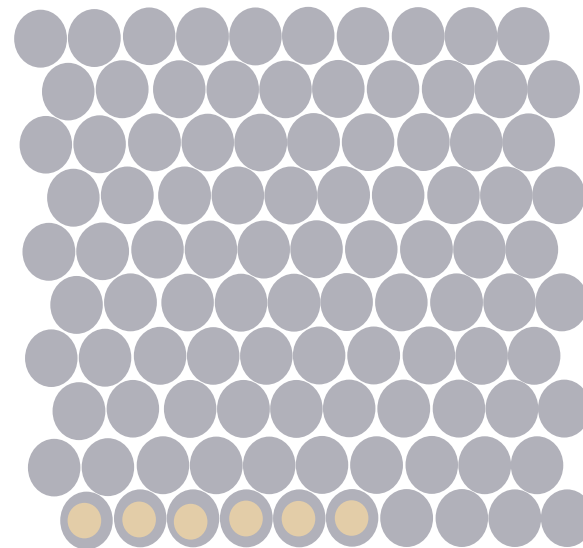
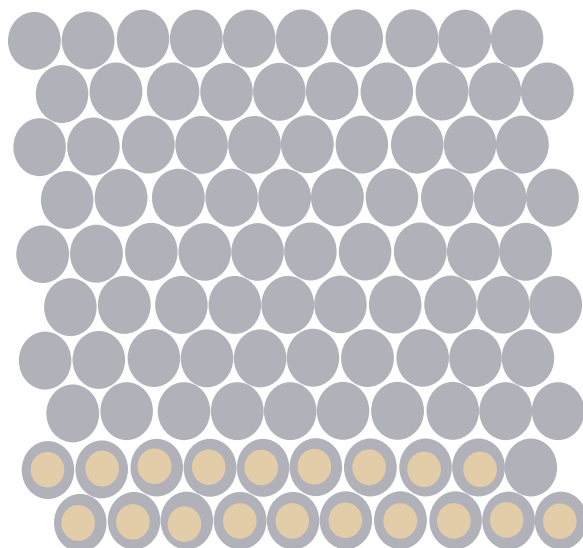
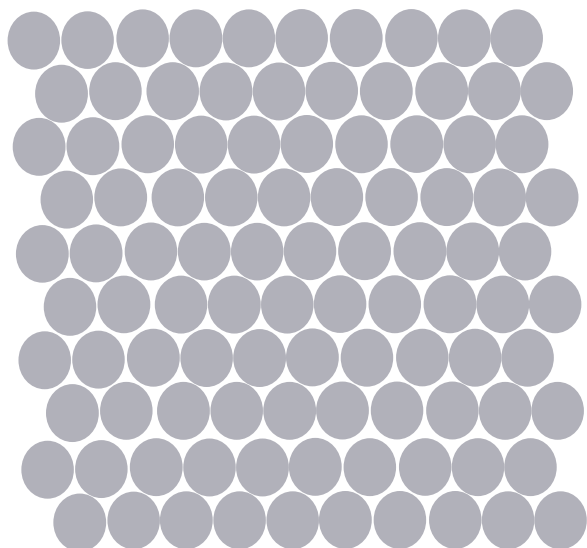
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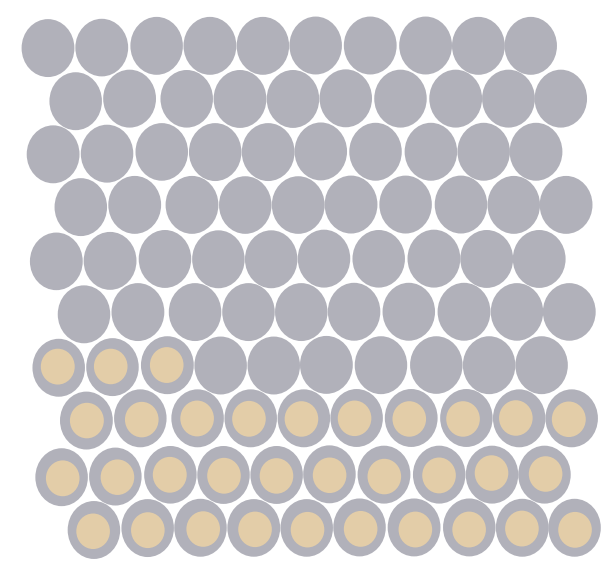
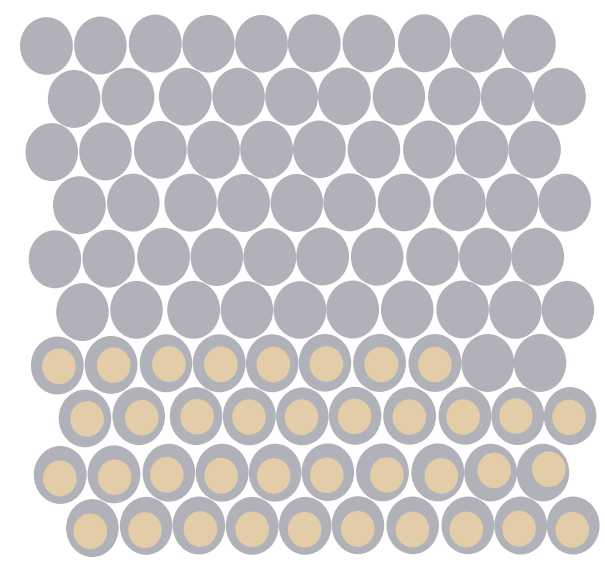
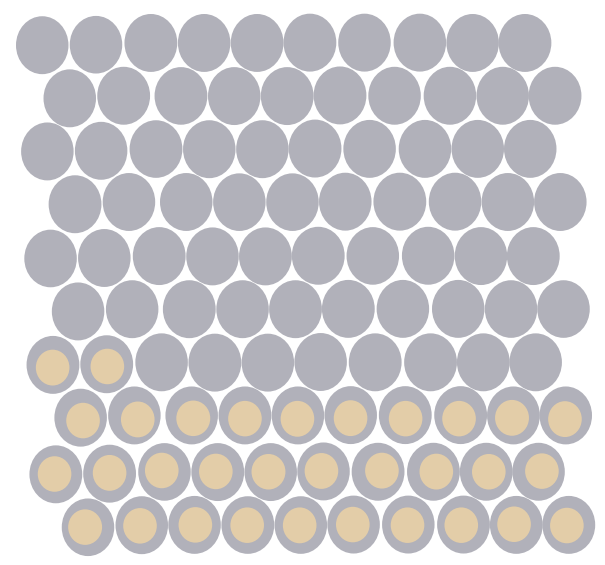
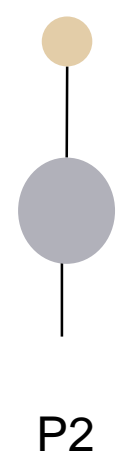
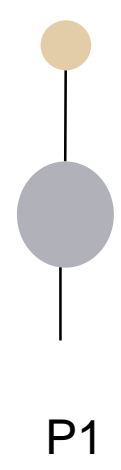
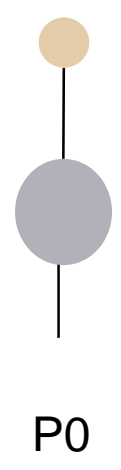
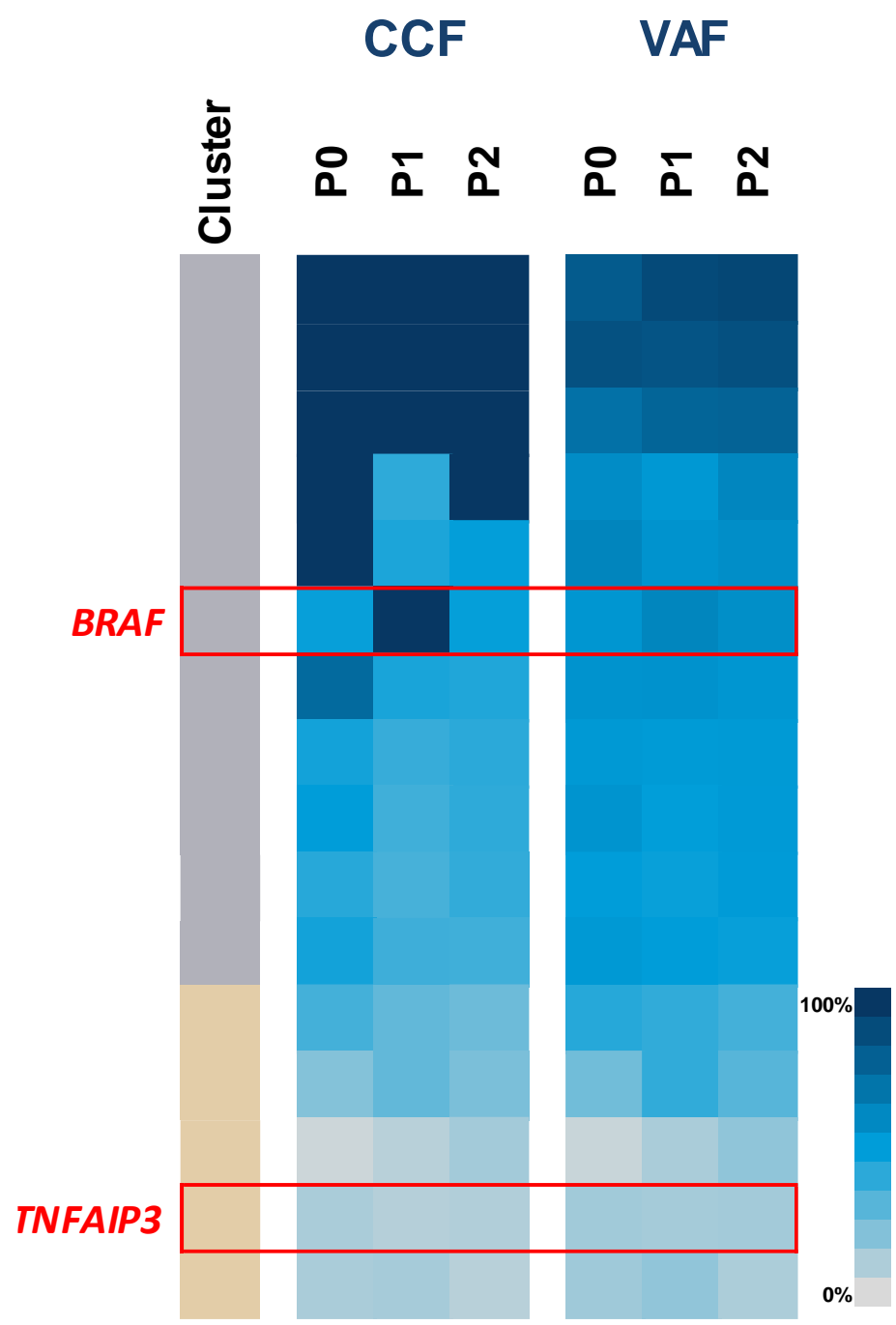
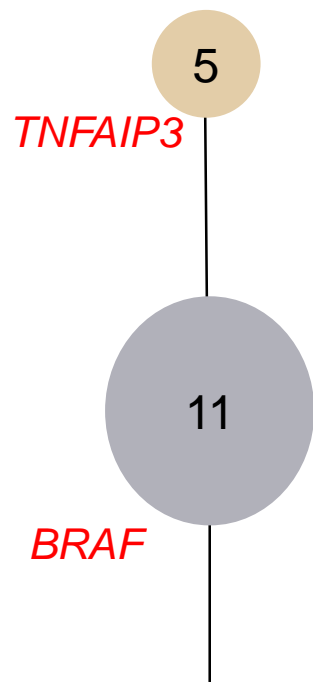


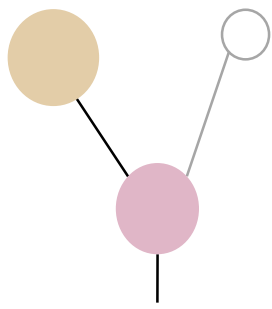
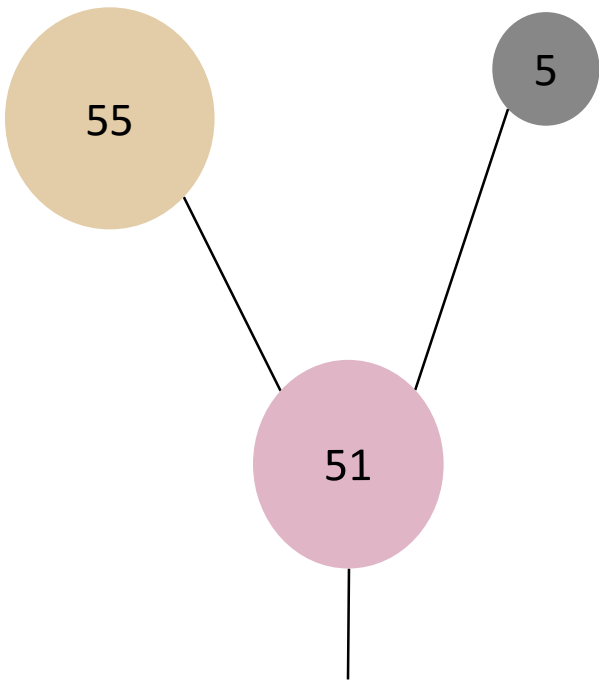
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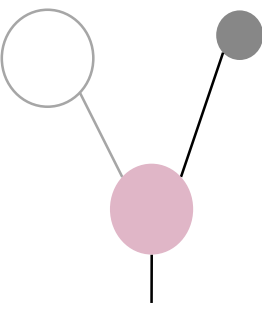
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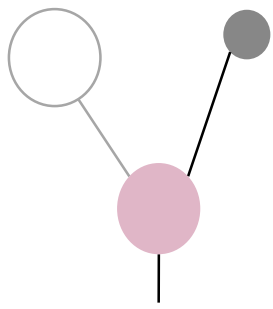




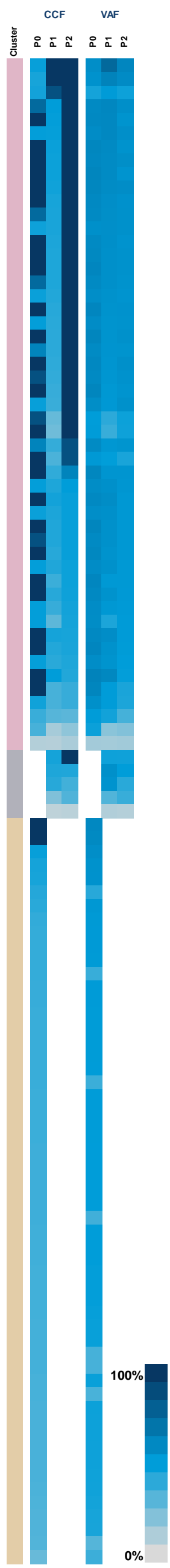
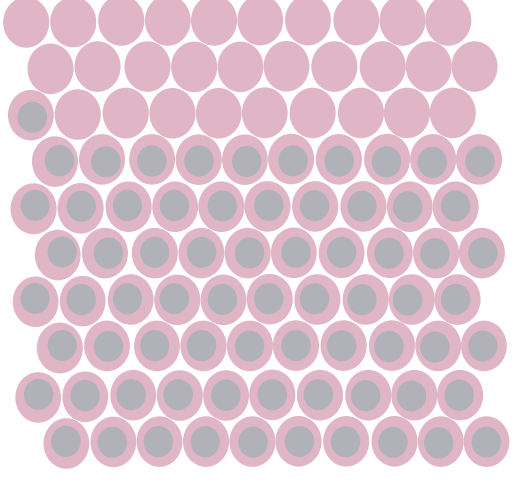
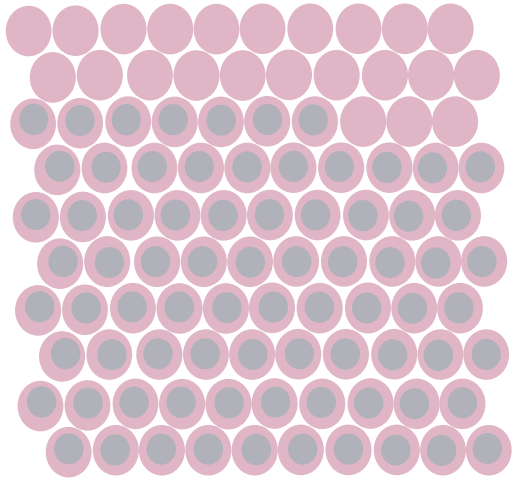
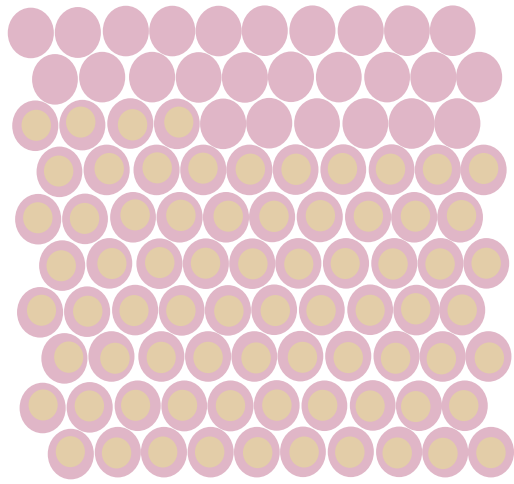
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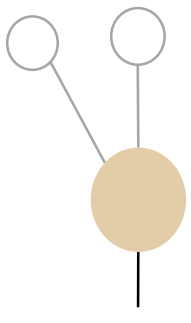
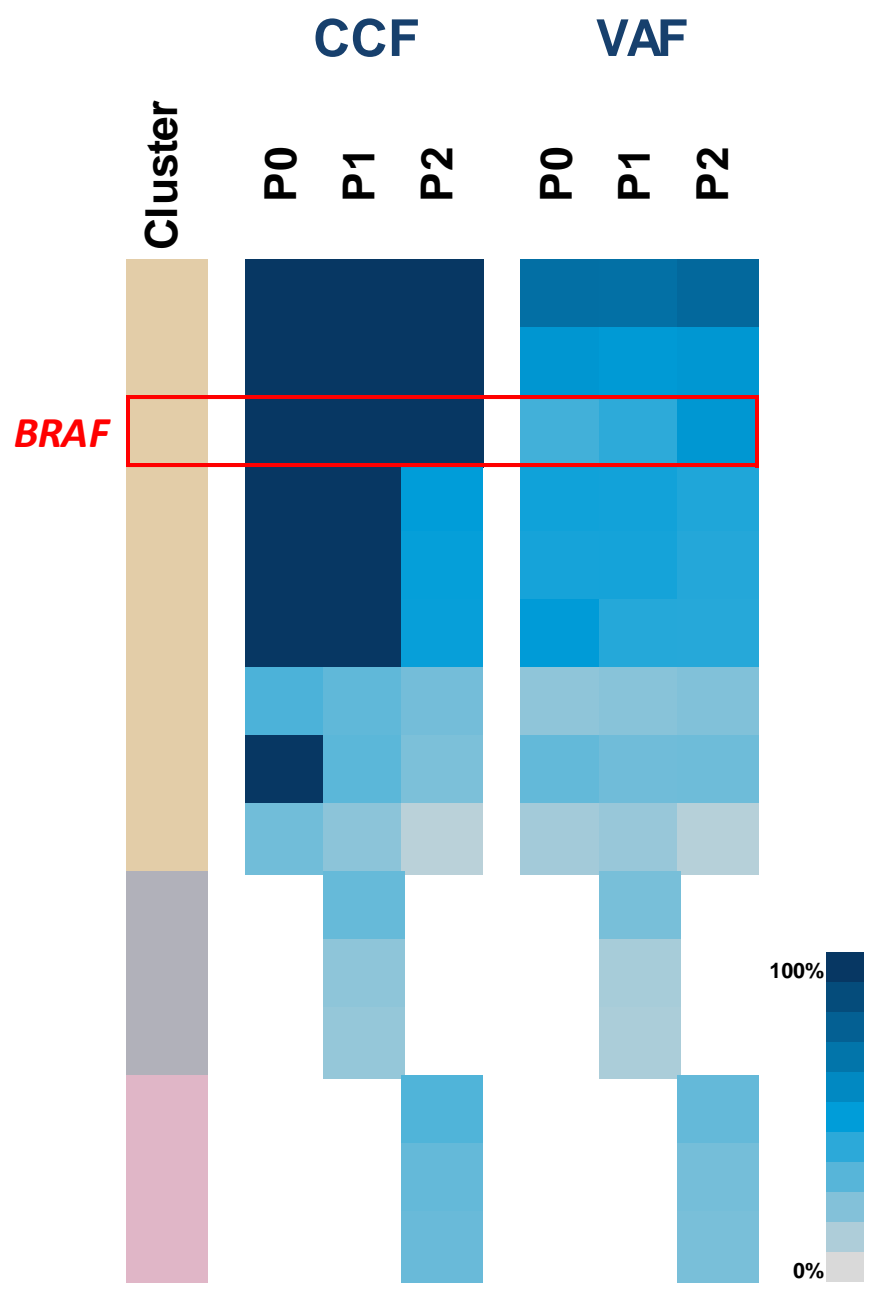
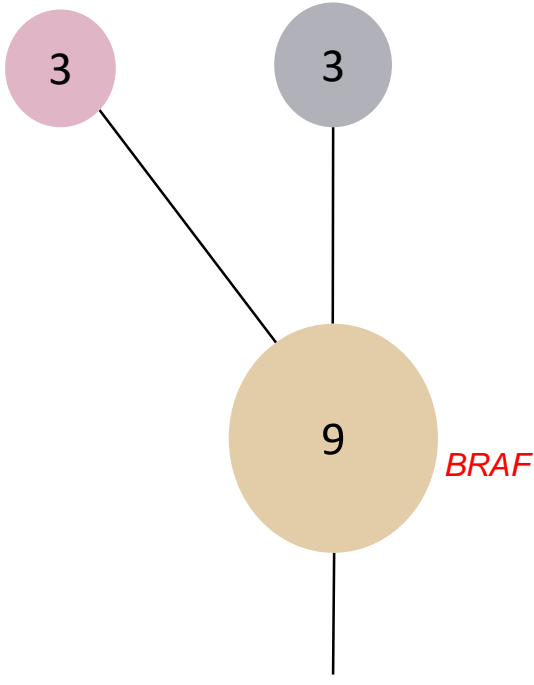


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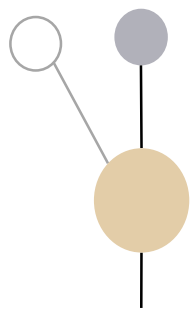


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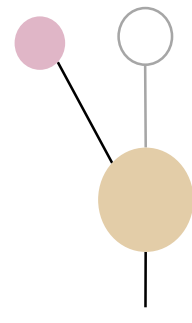




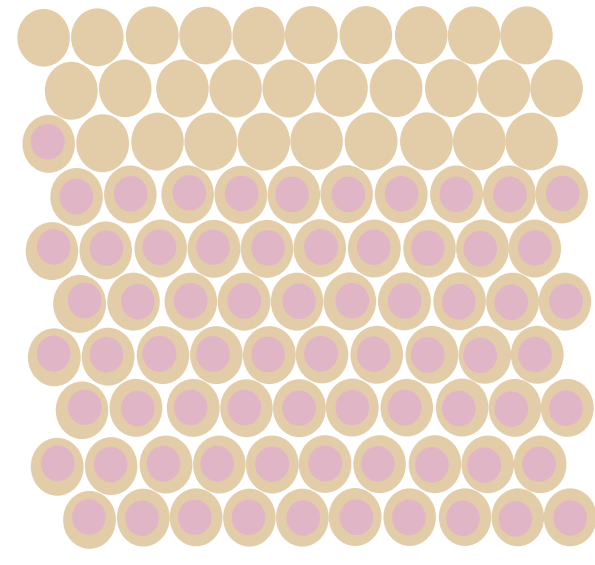
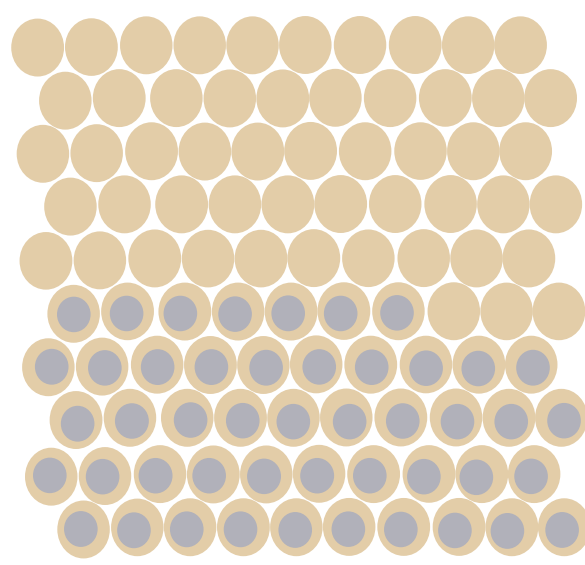
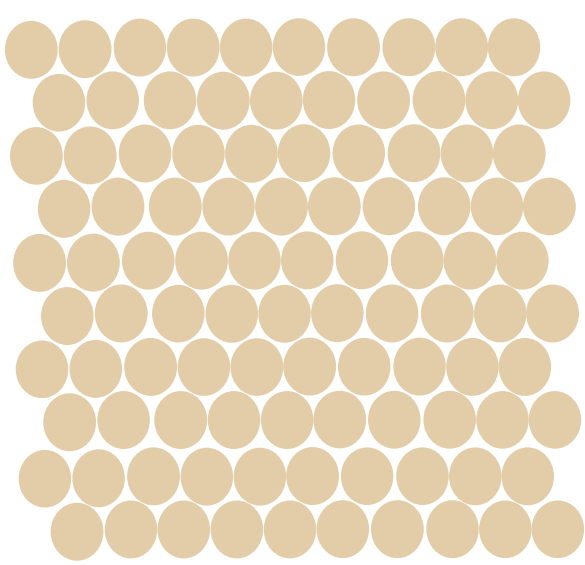
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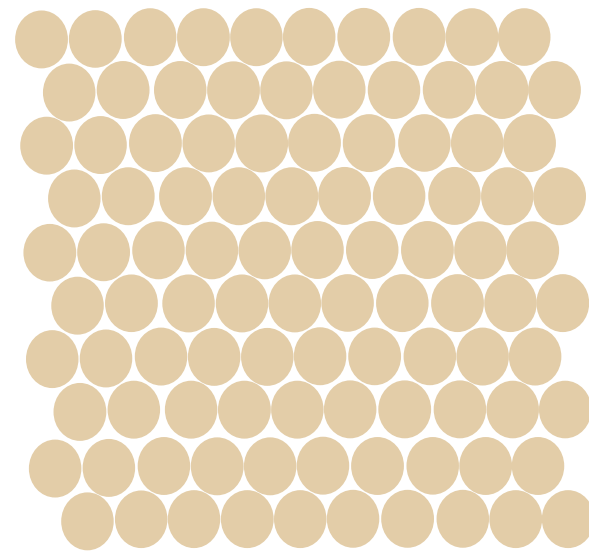
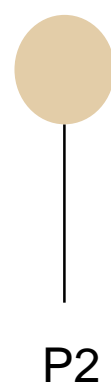
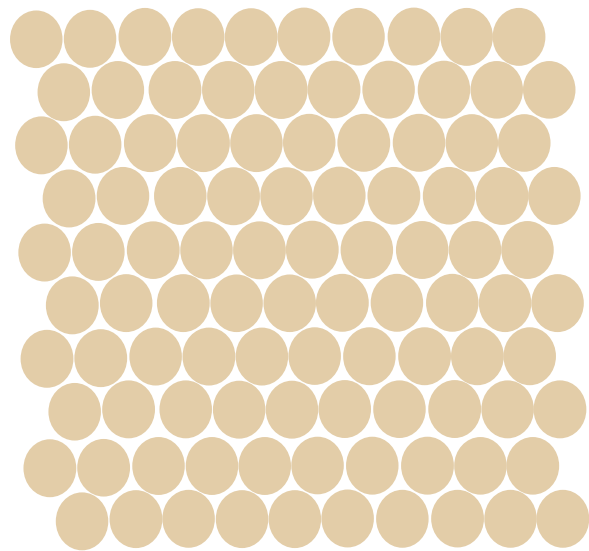
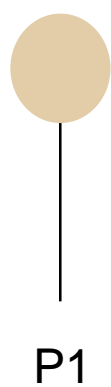
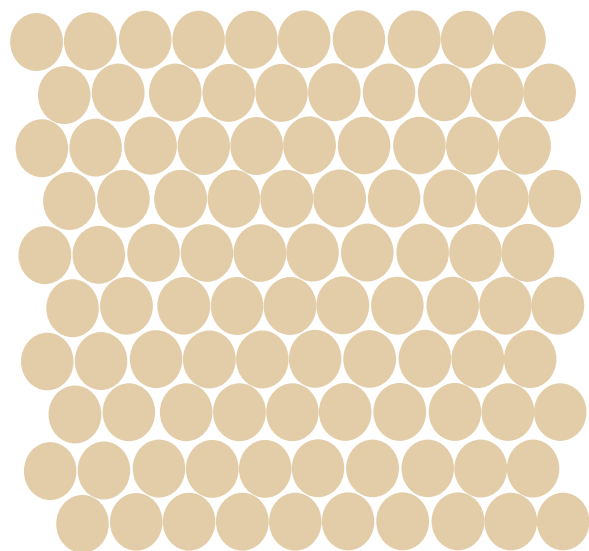
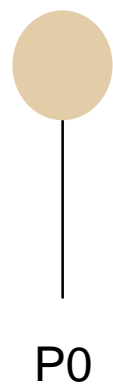
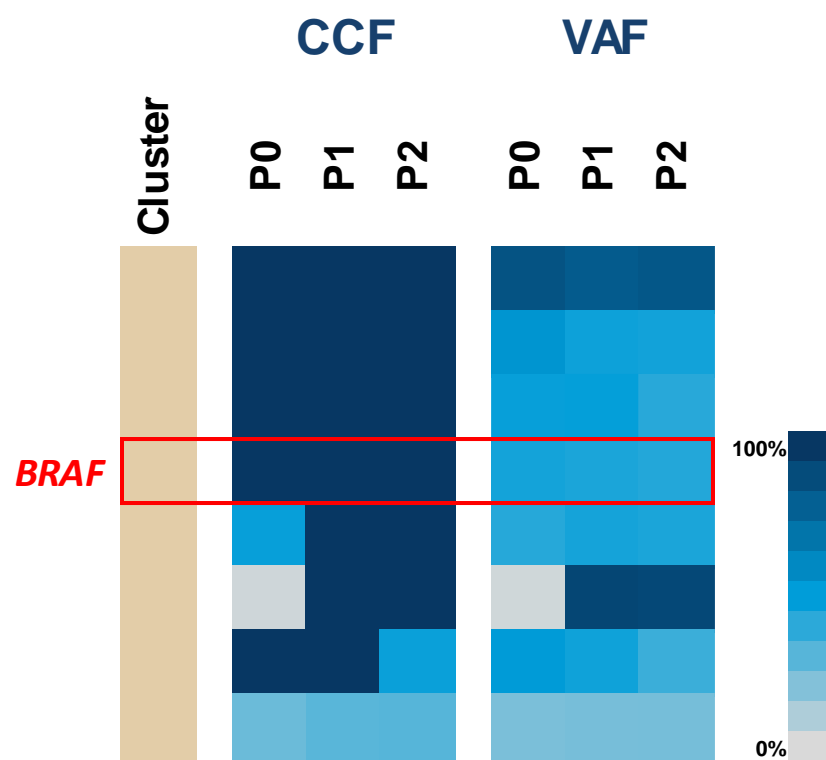
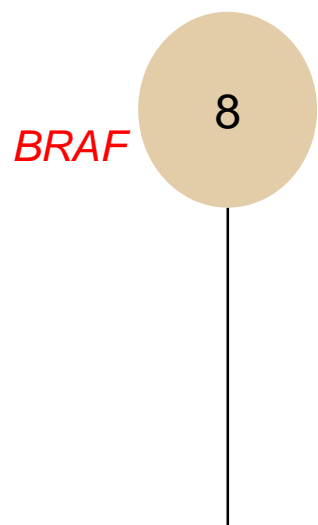


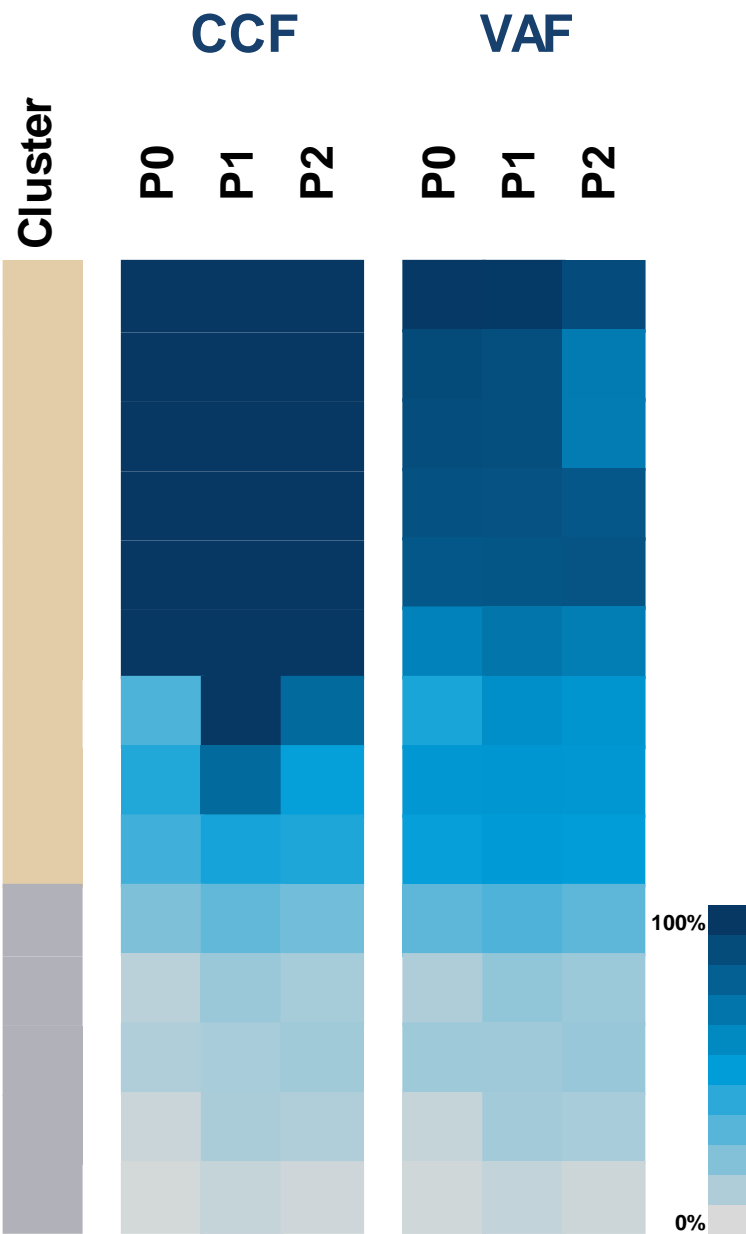
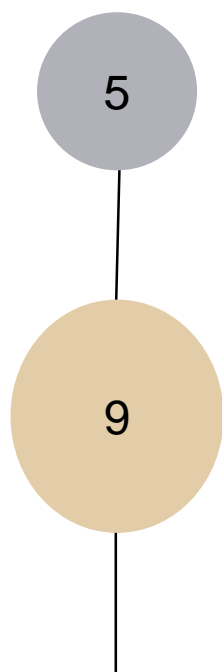
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P2







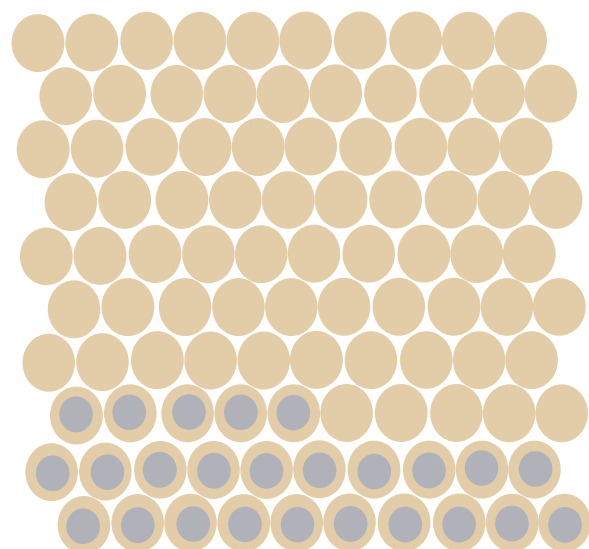
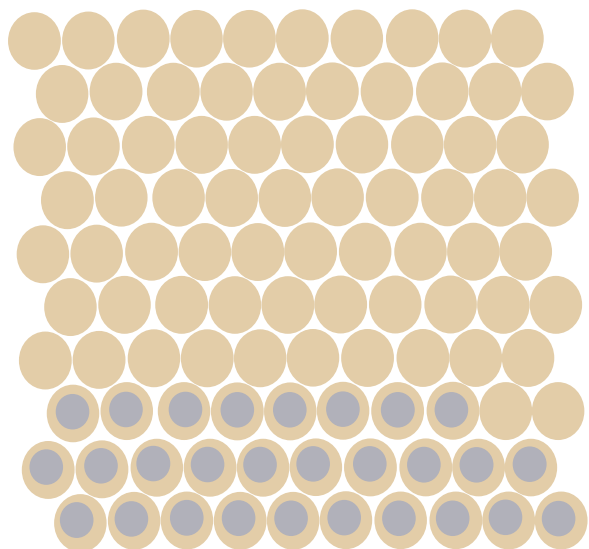
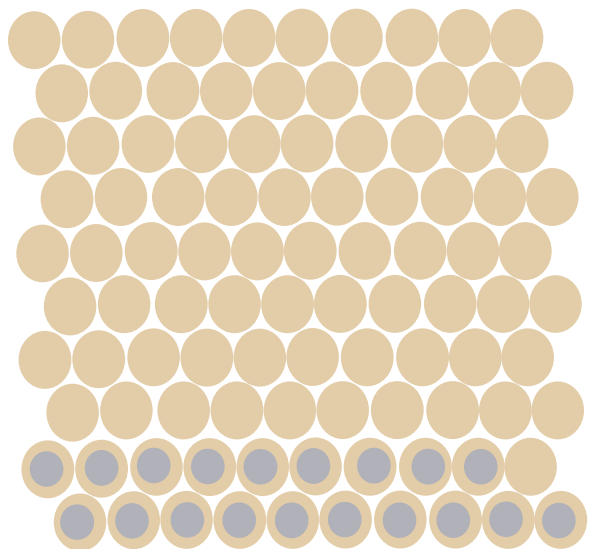
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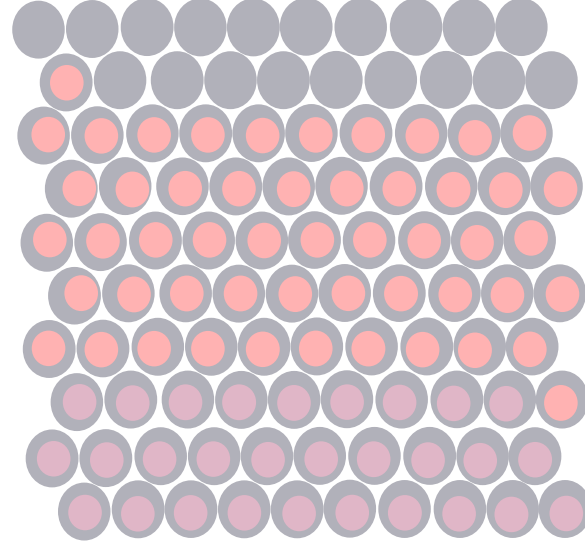
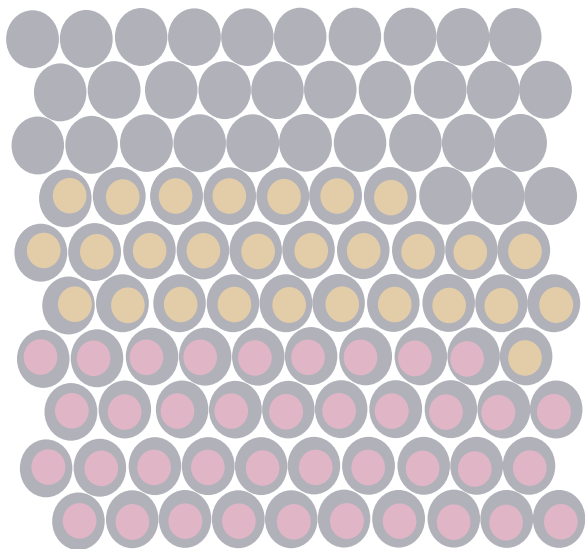
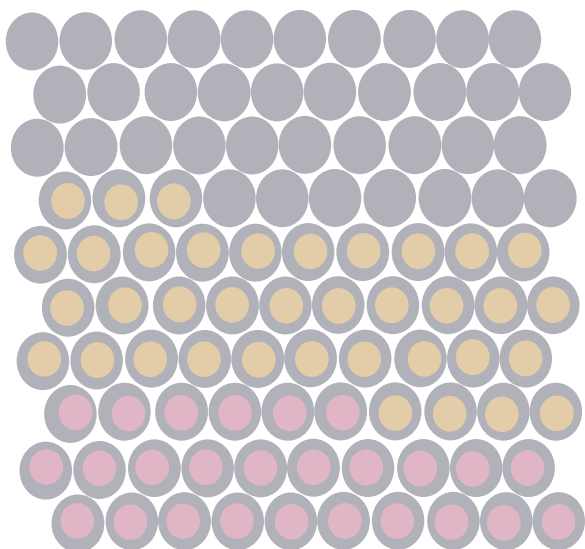
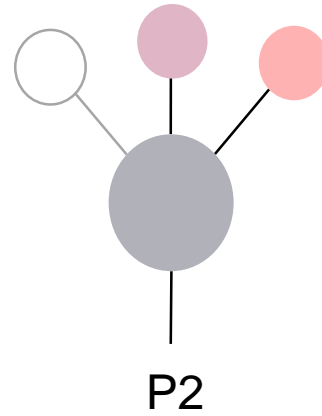
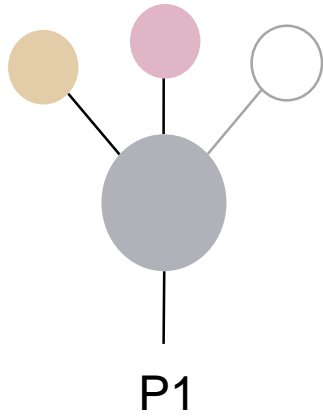
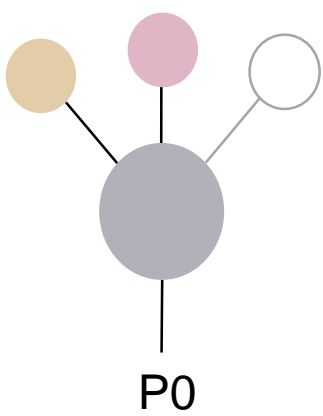
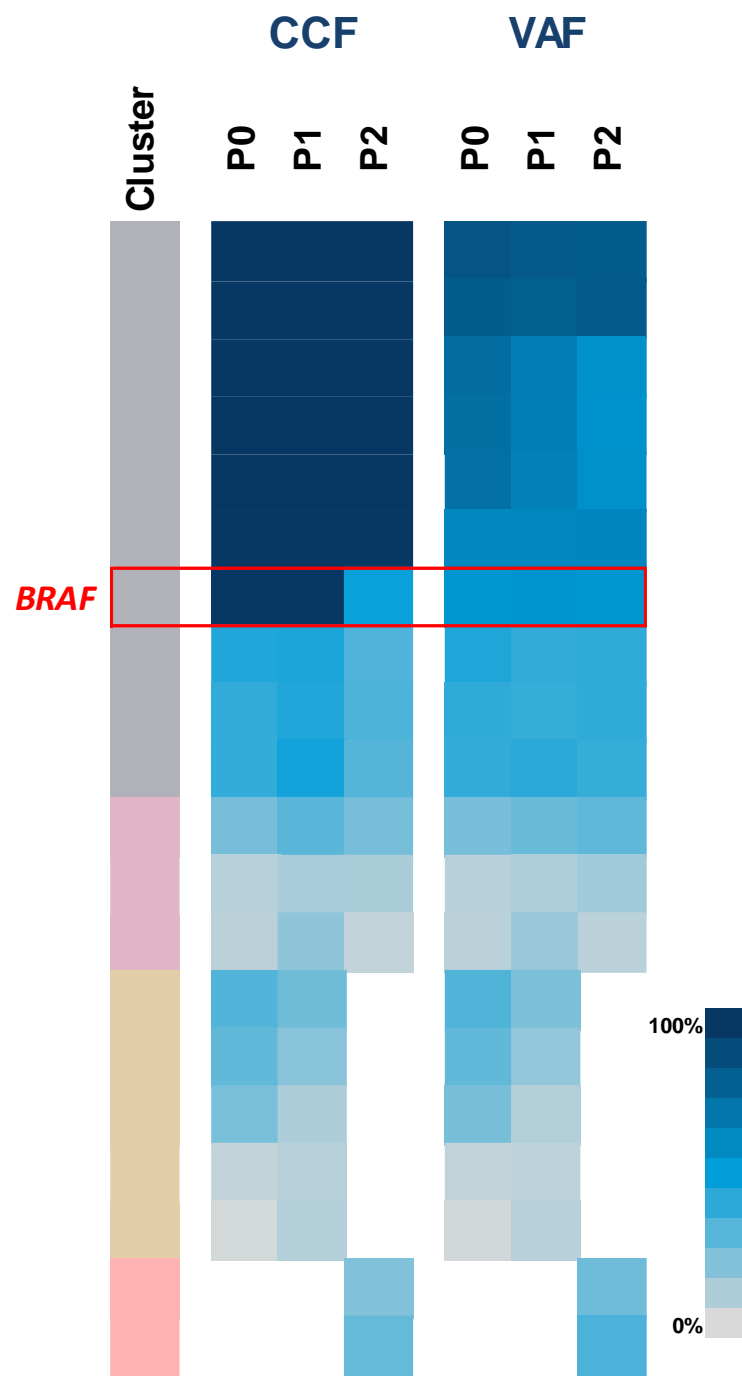
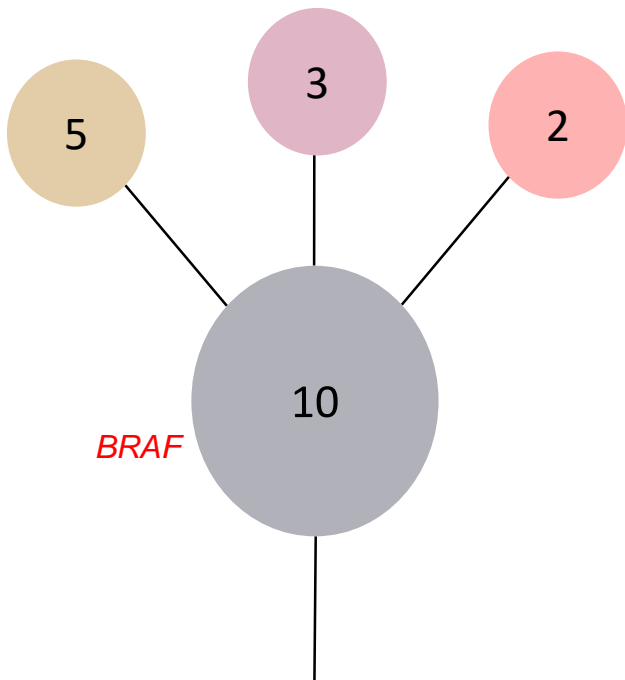


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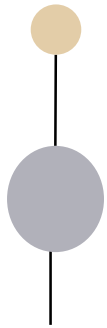
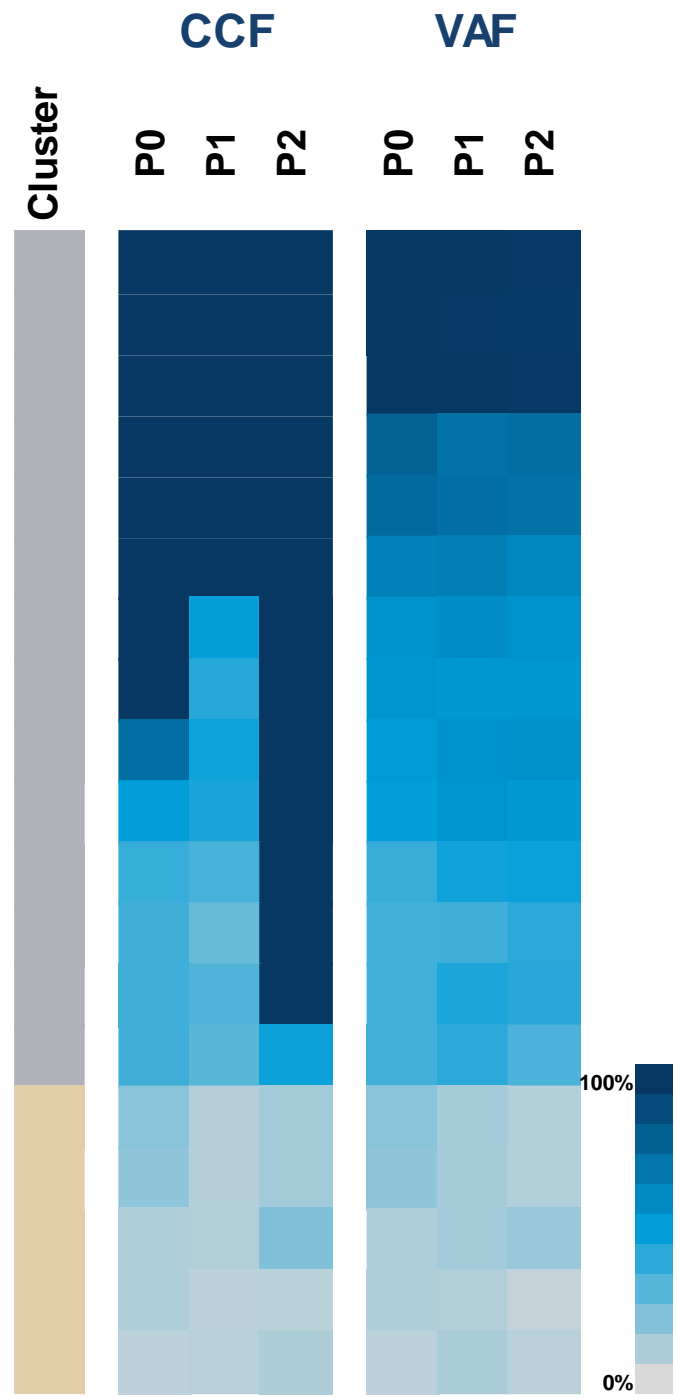
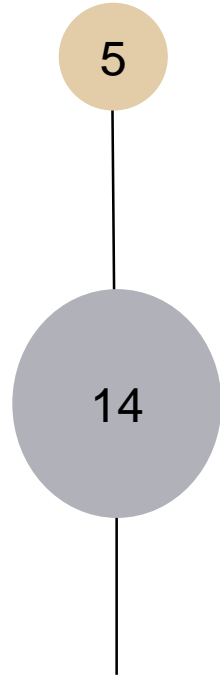
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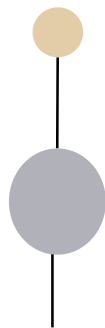


B Non-relapse cases

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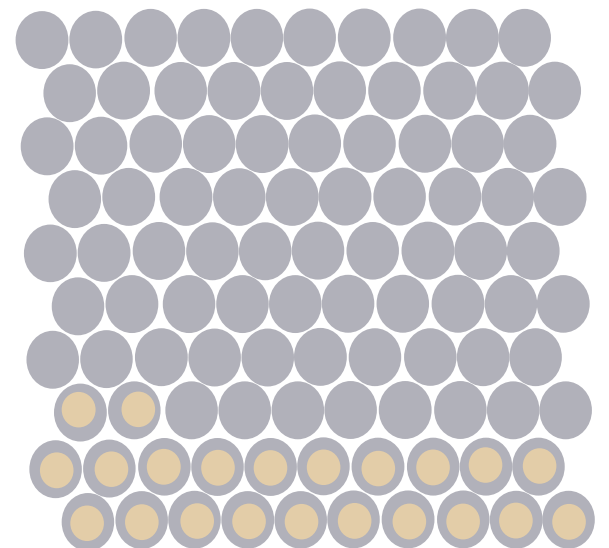
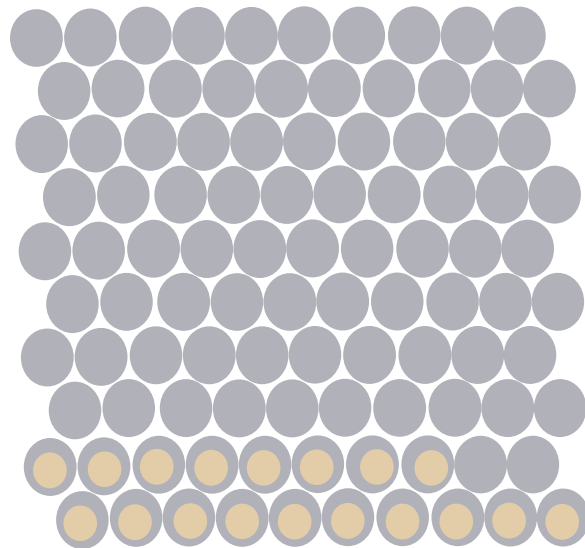
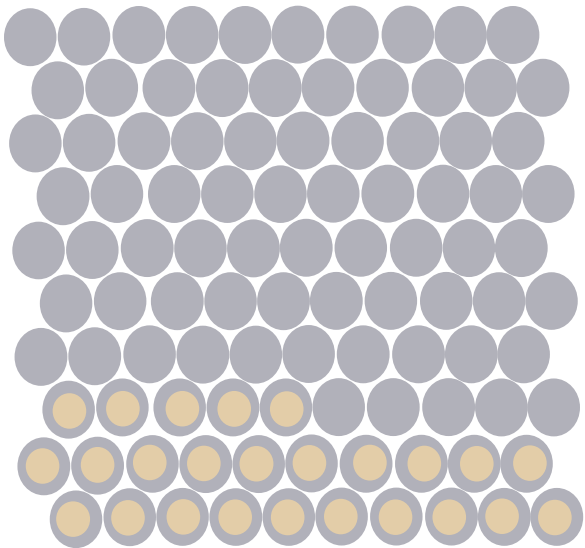
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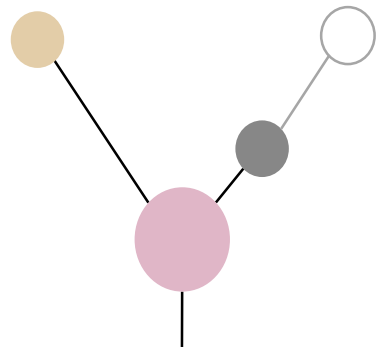
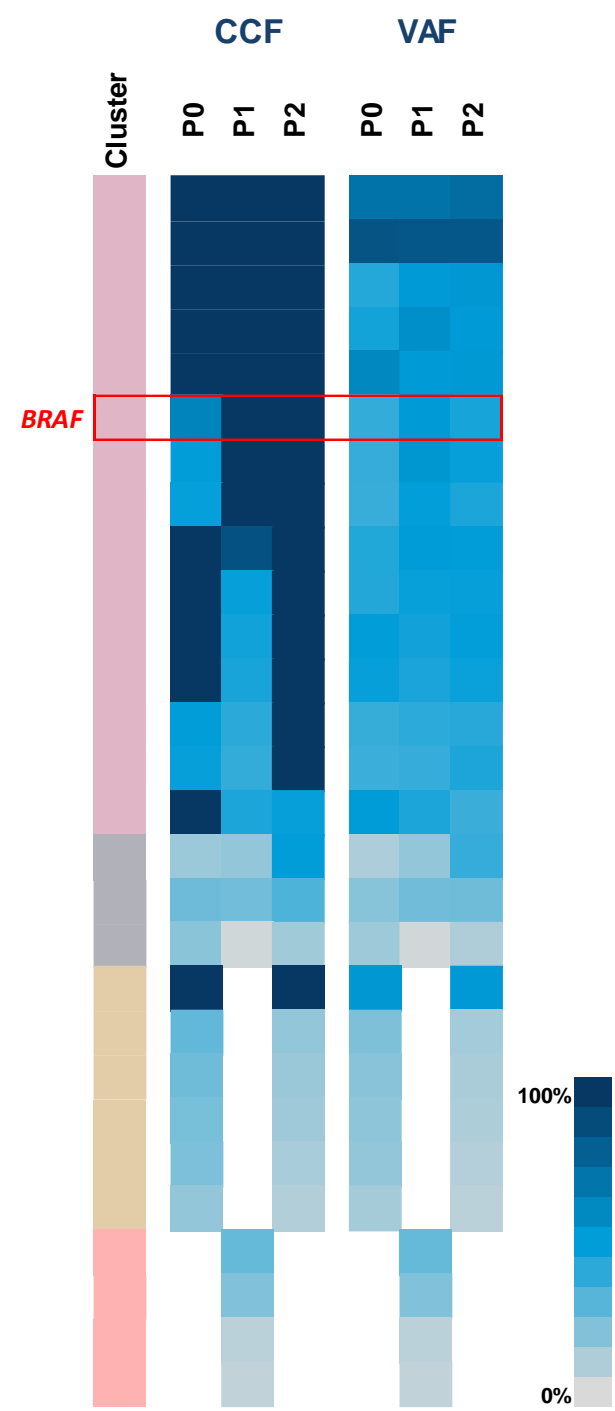
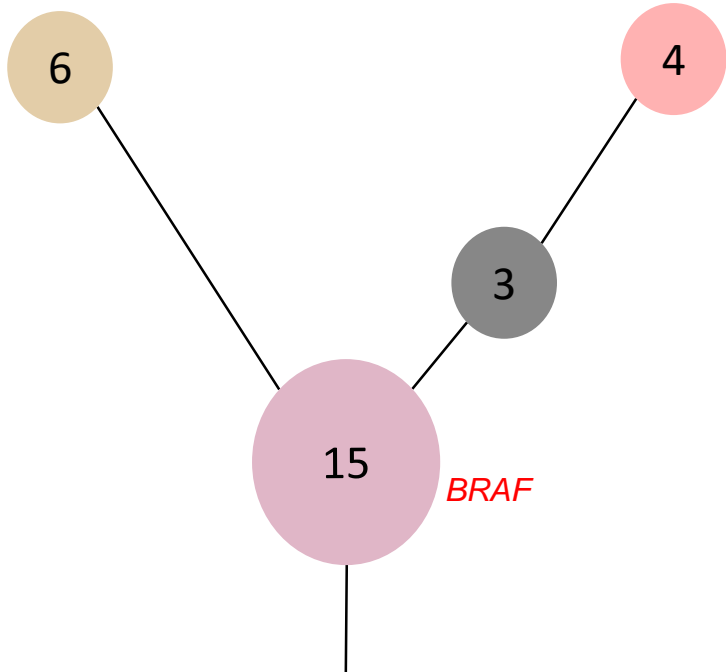


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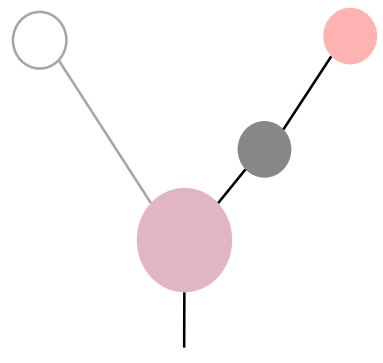


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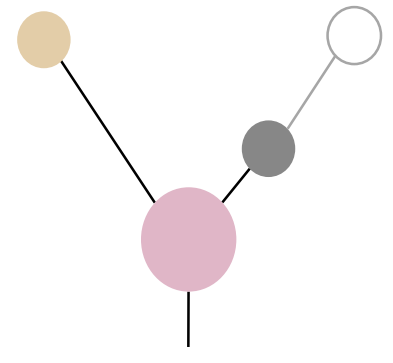




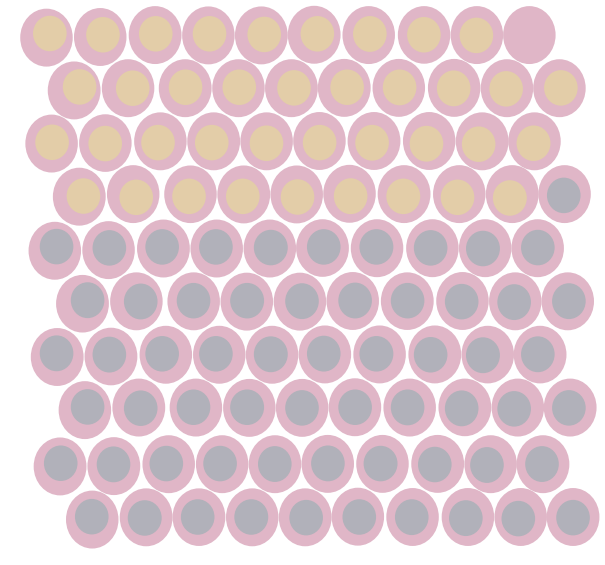
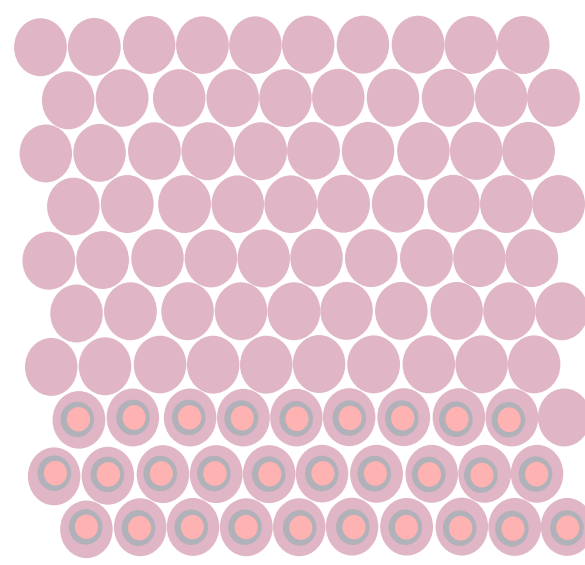
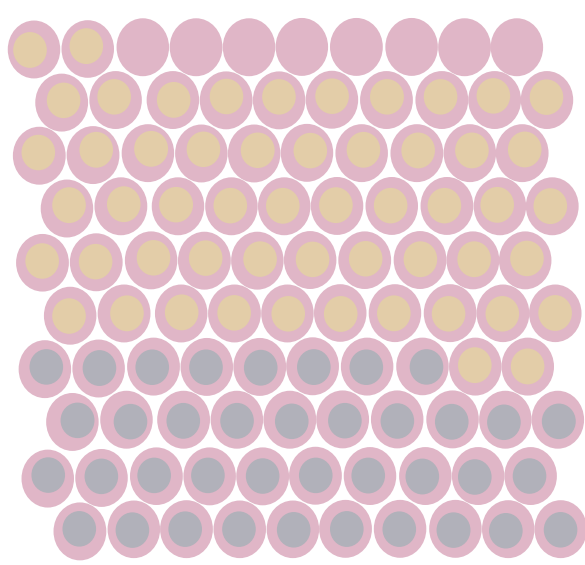
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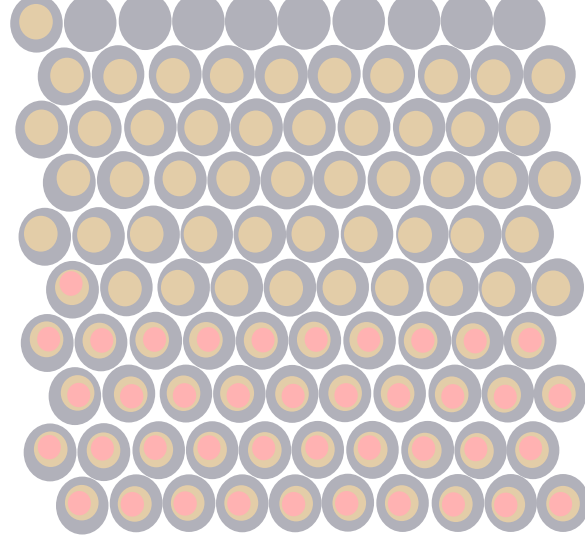
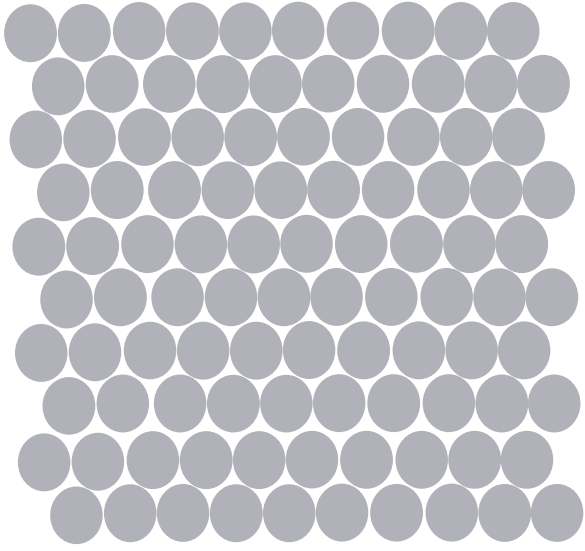
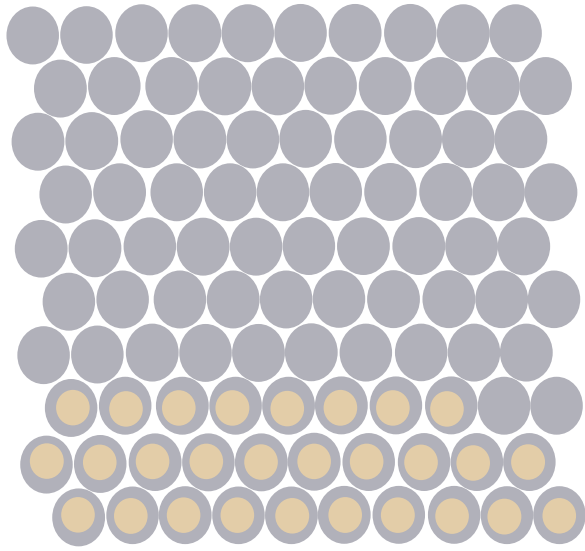
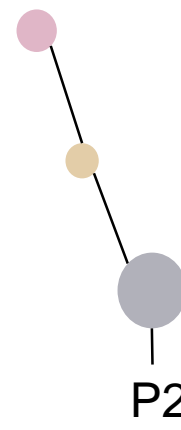
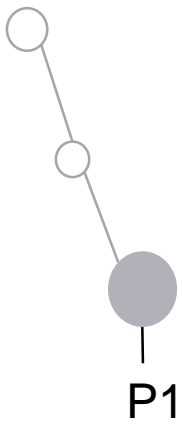
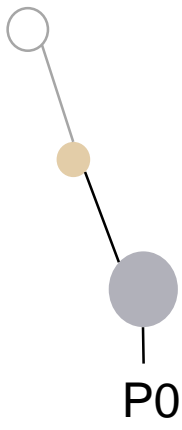
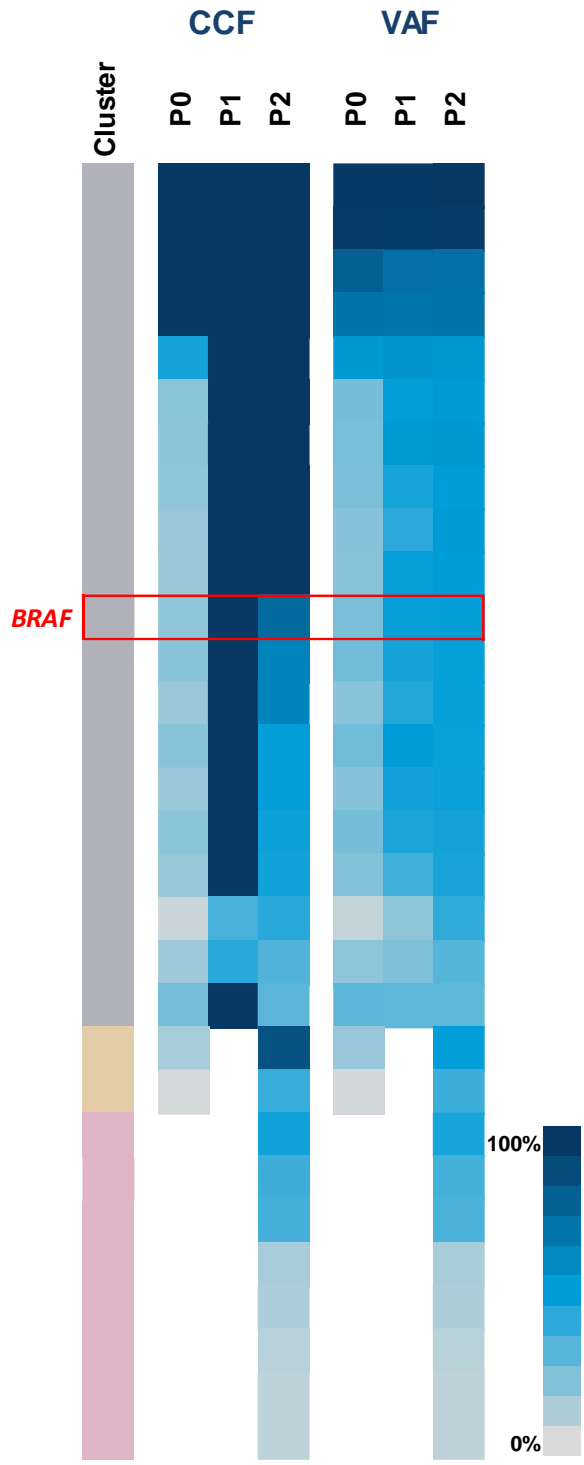
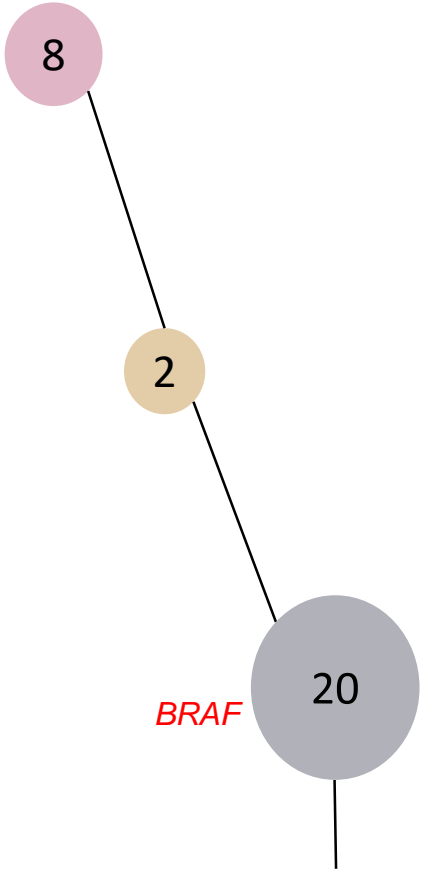


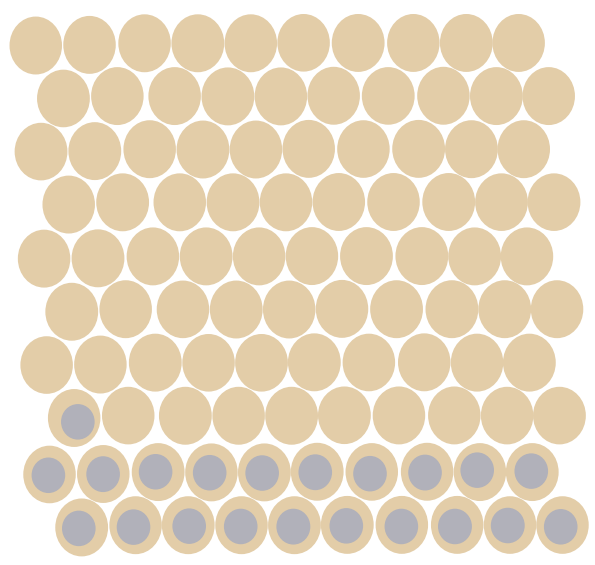
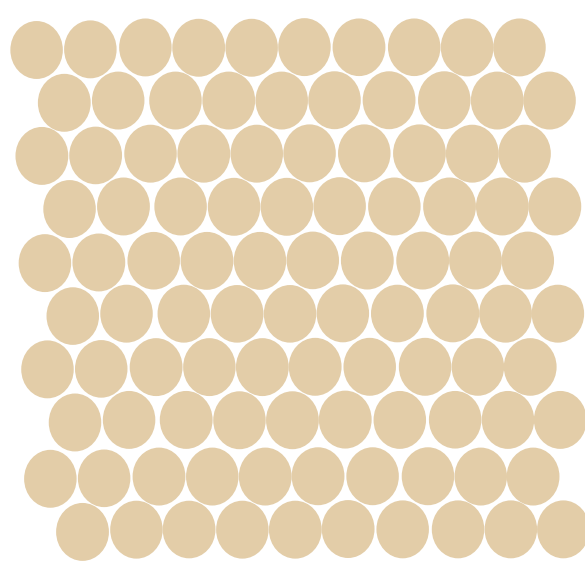
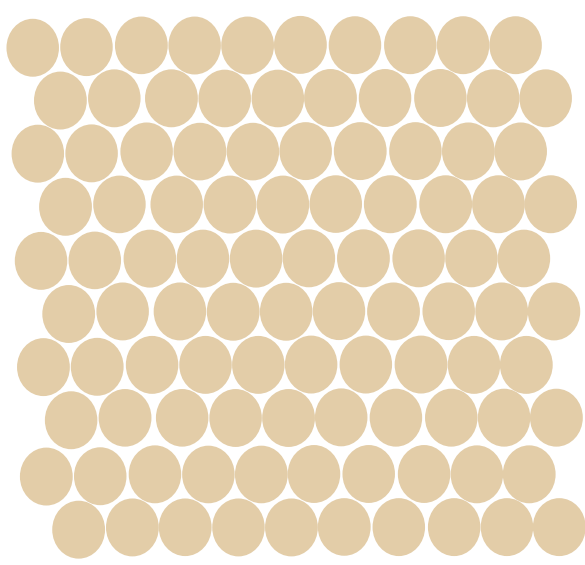
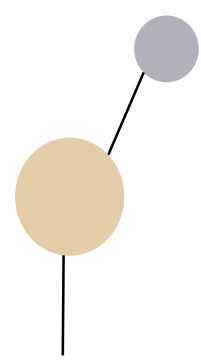
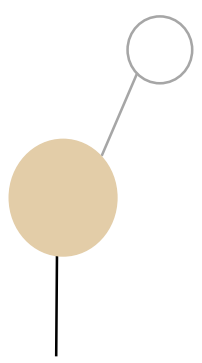
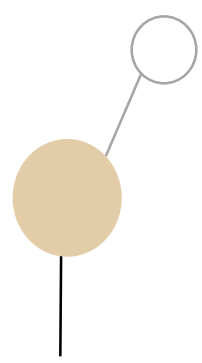
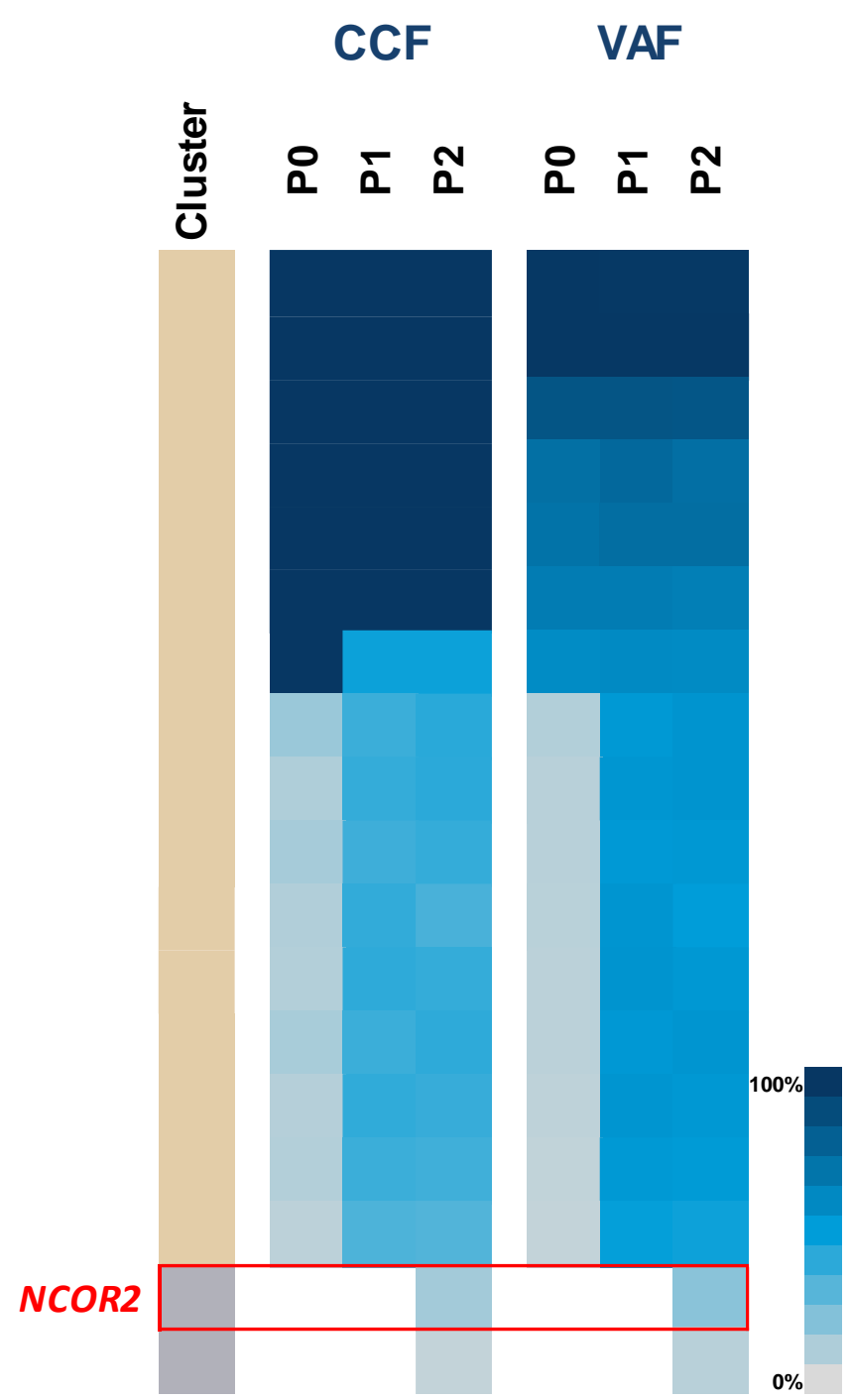
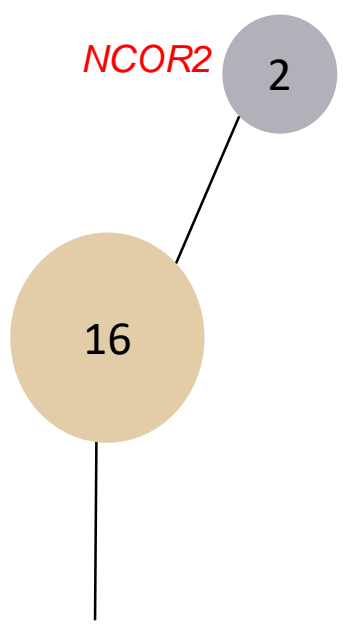
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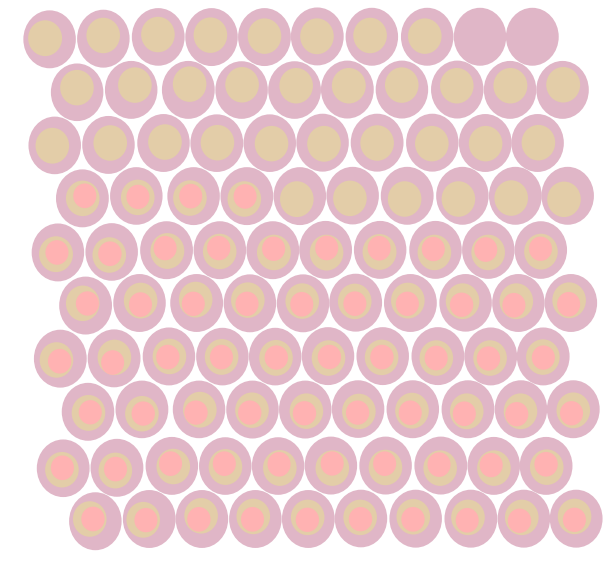
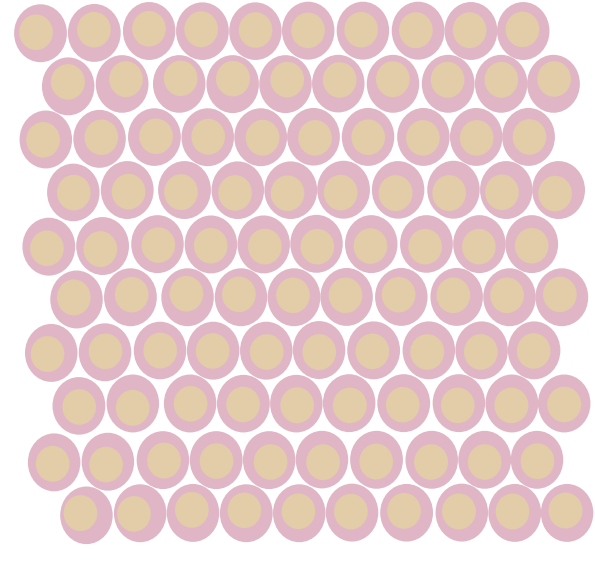
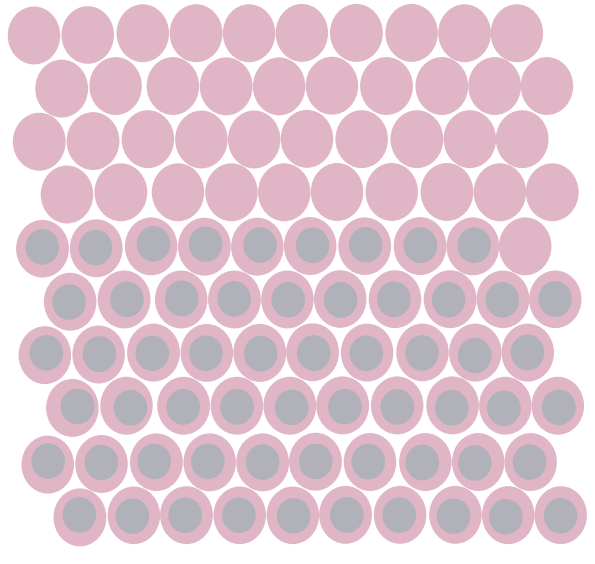
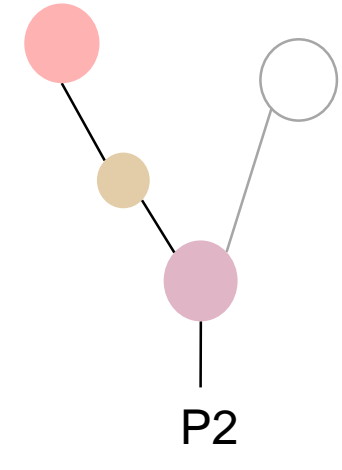
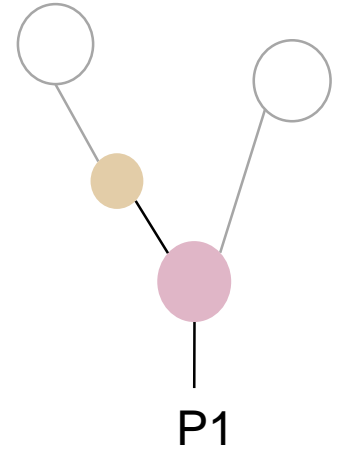
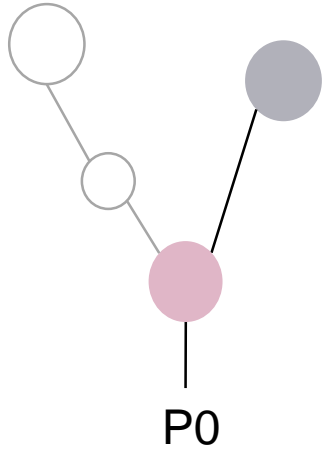
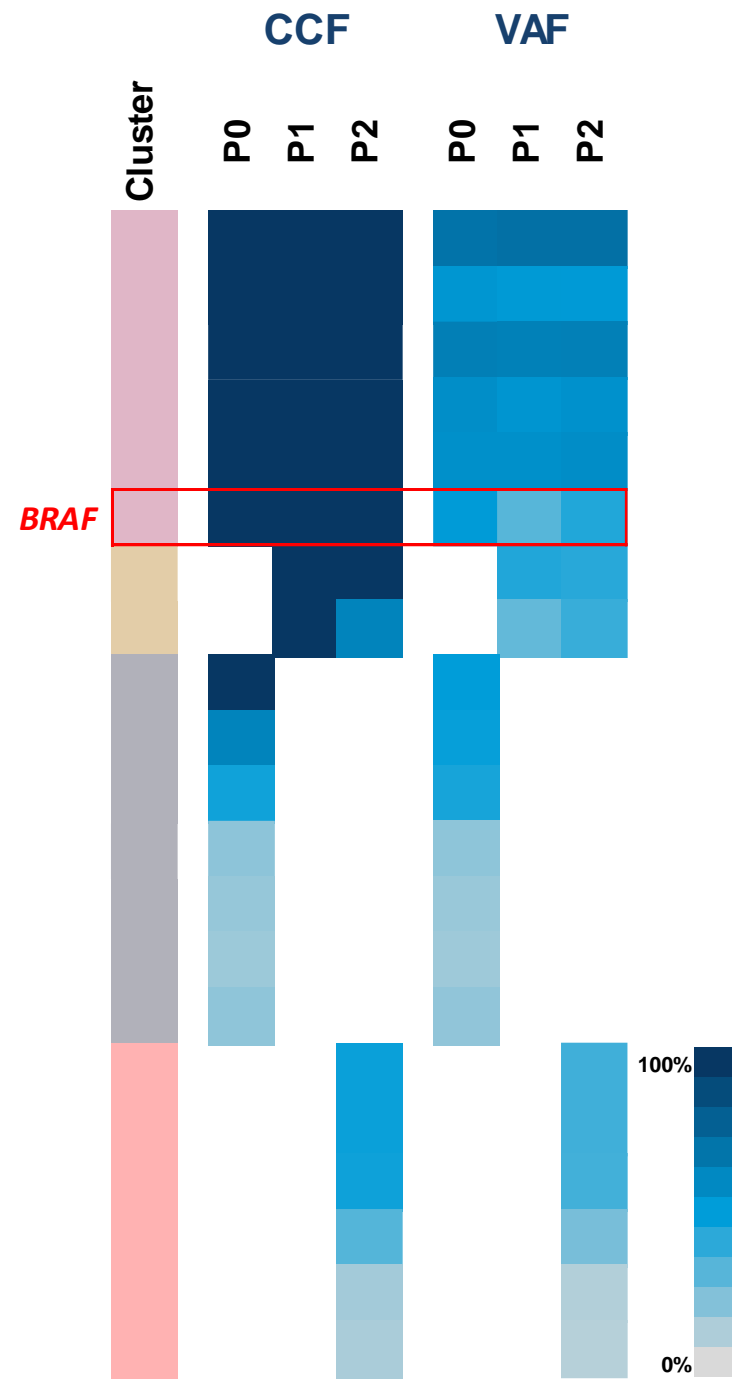
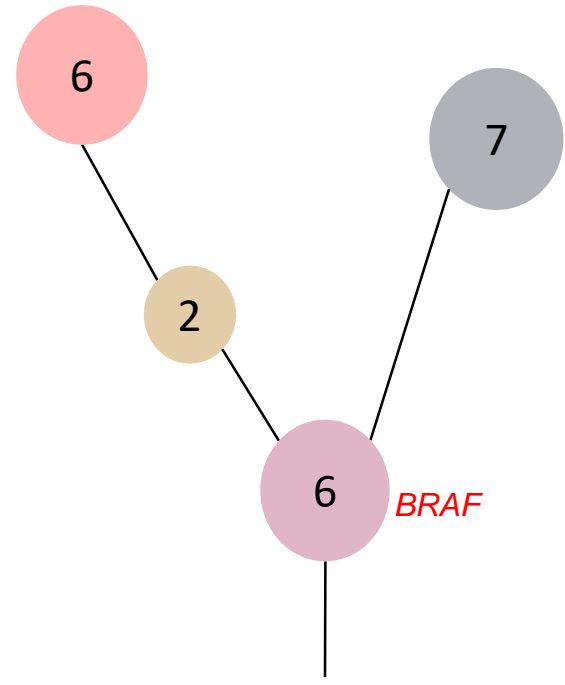


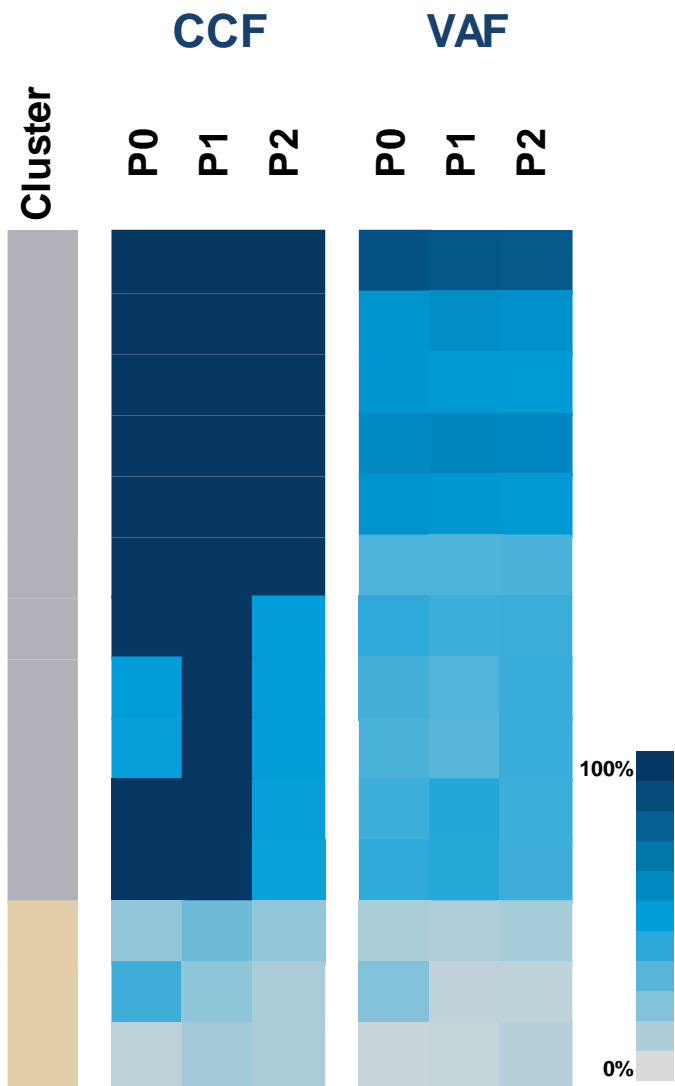
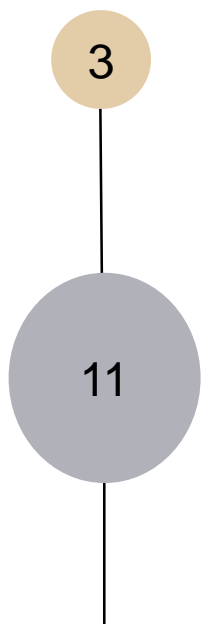
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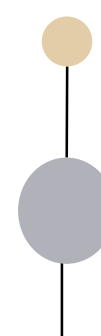




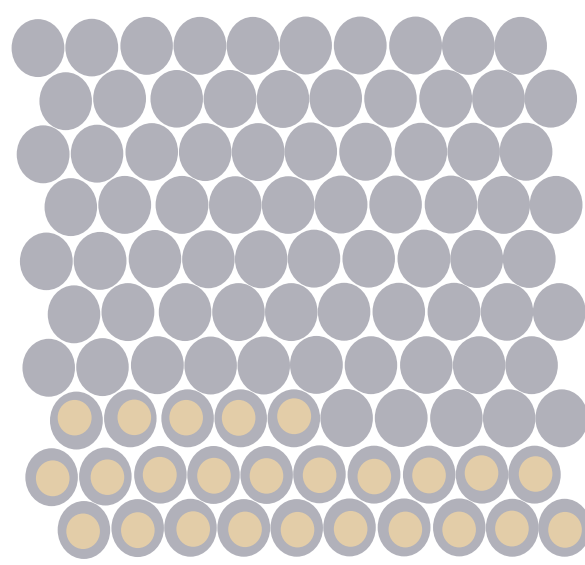
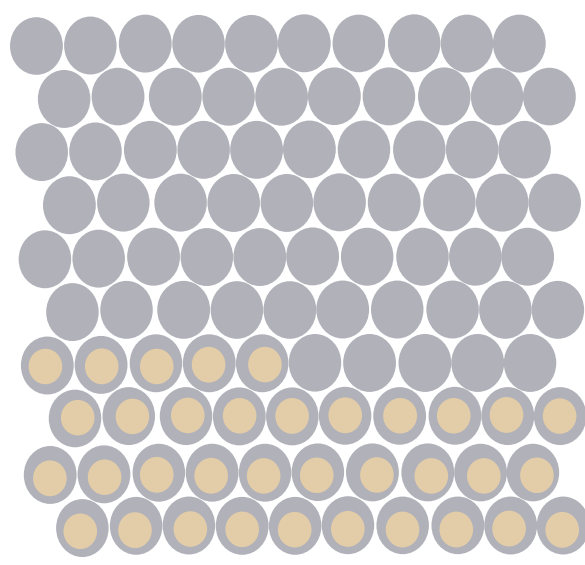
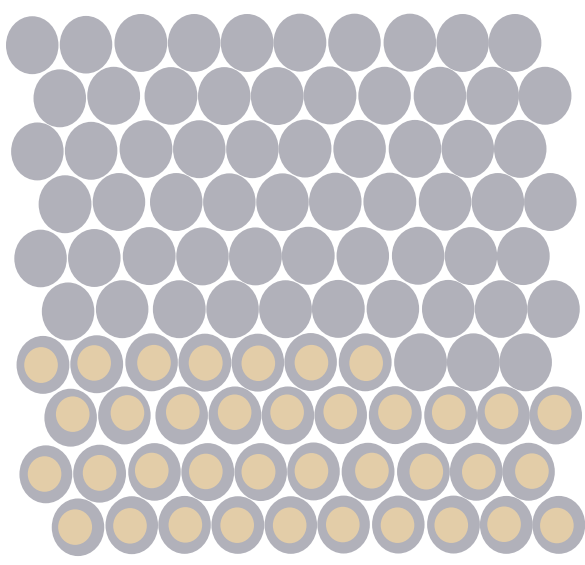
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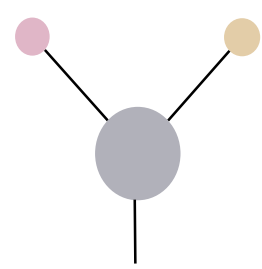
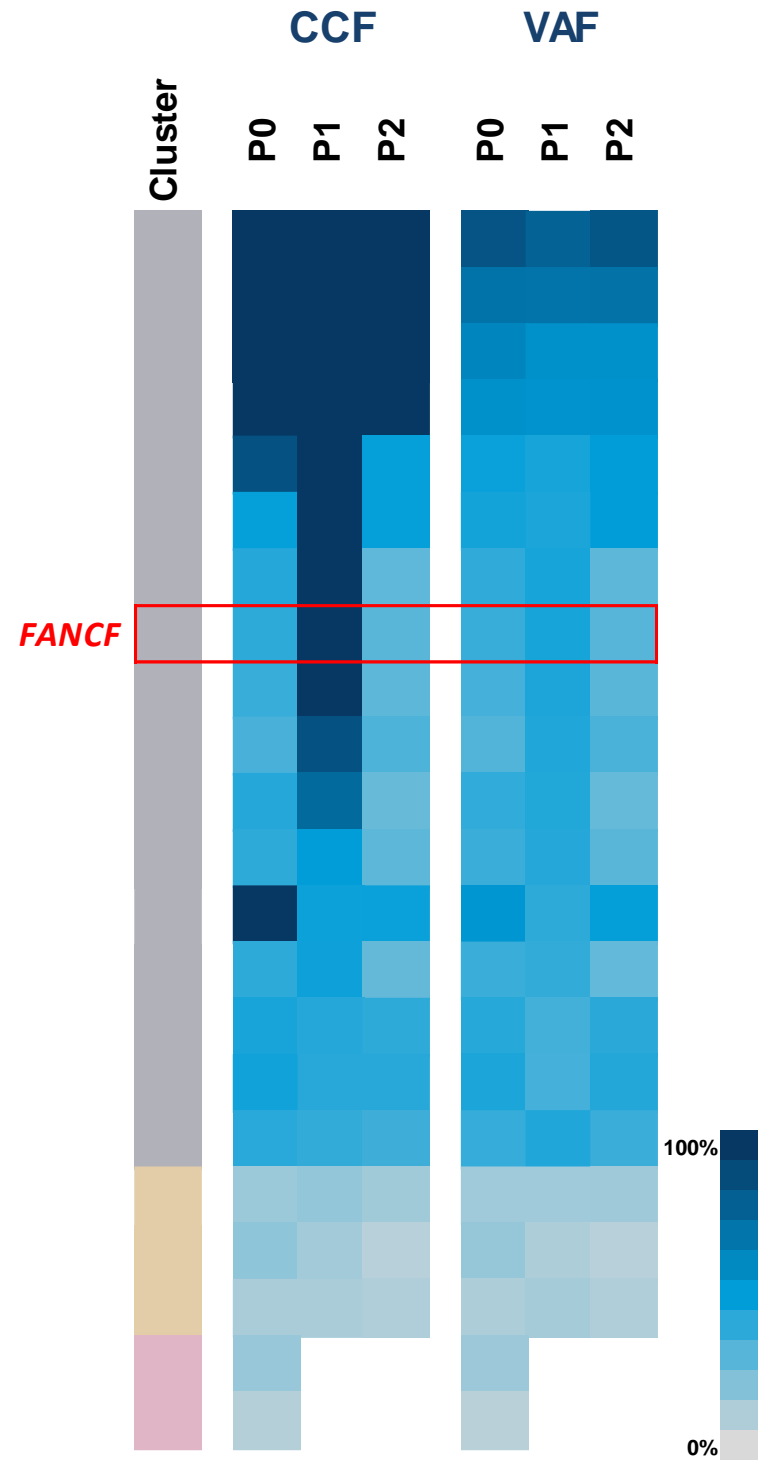
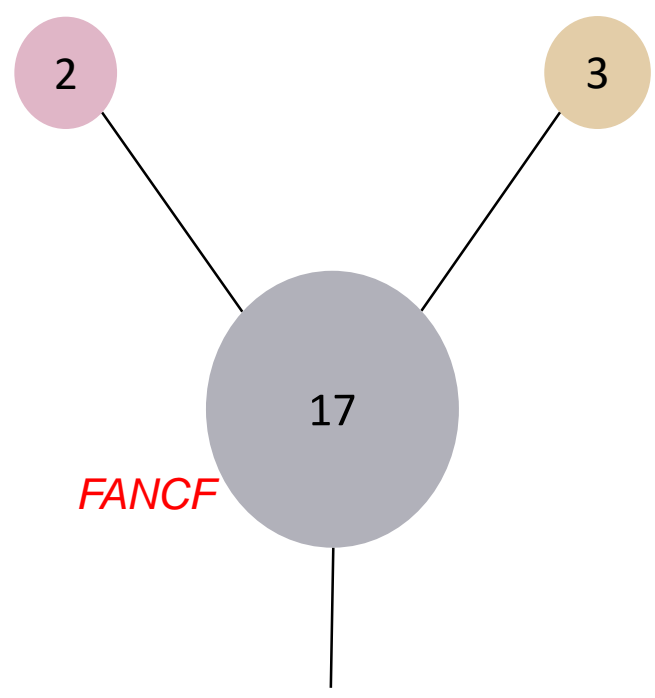


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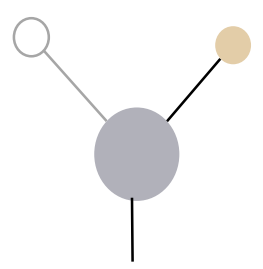


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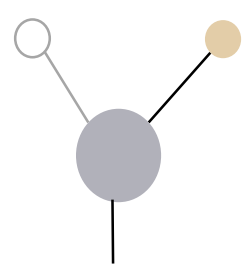




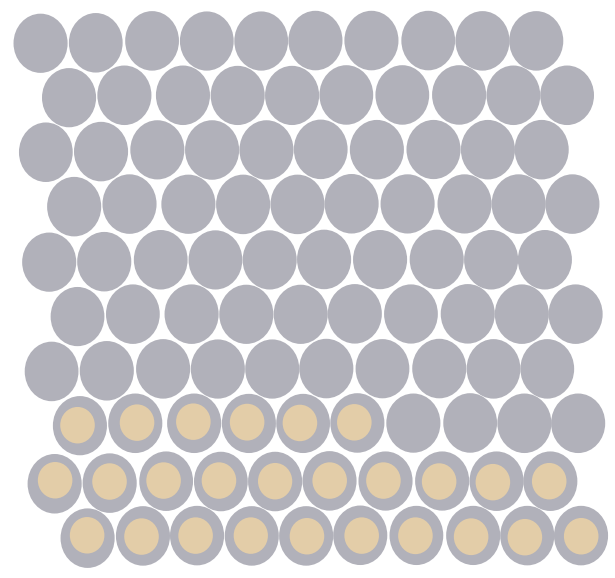
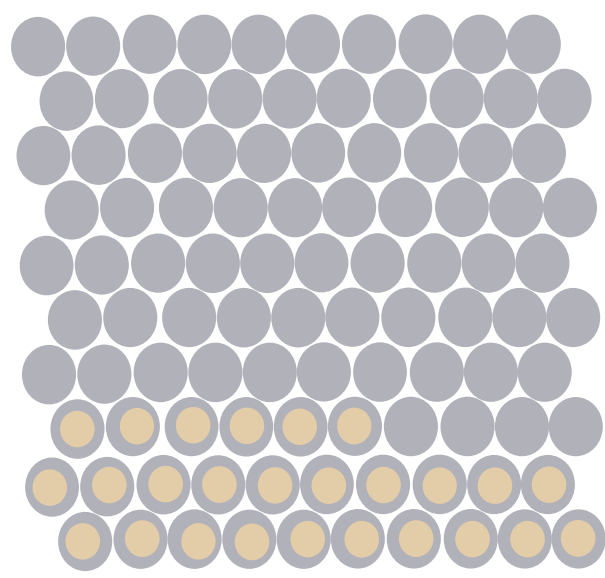
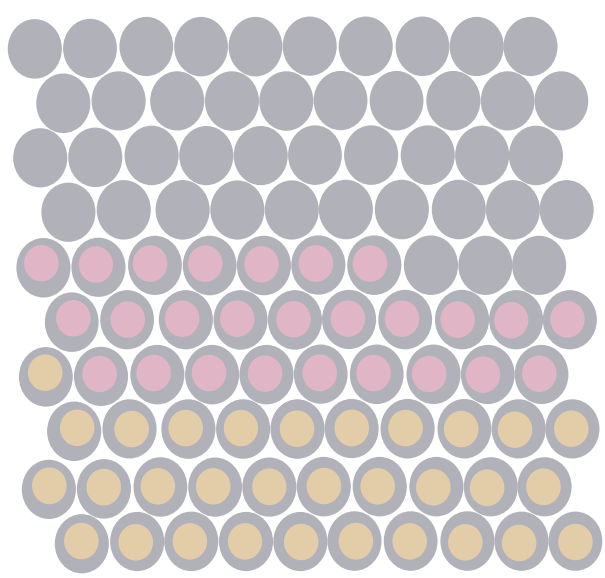
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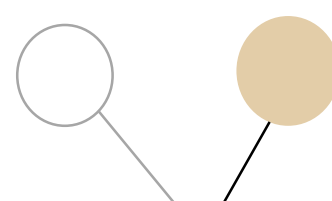
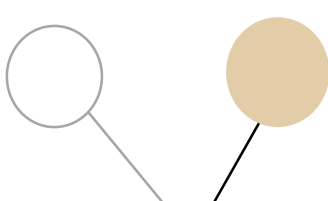
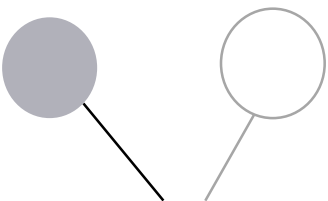
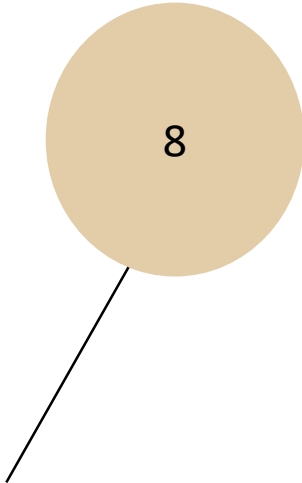
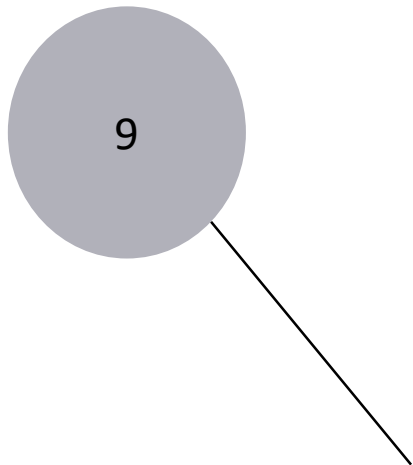


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P2

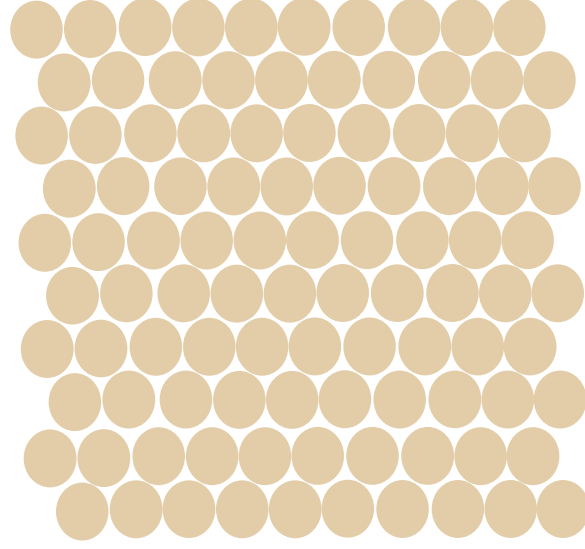
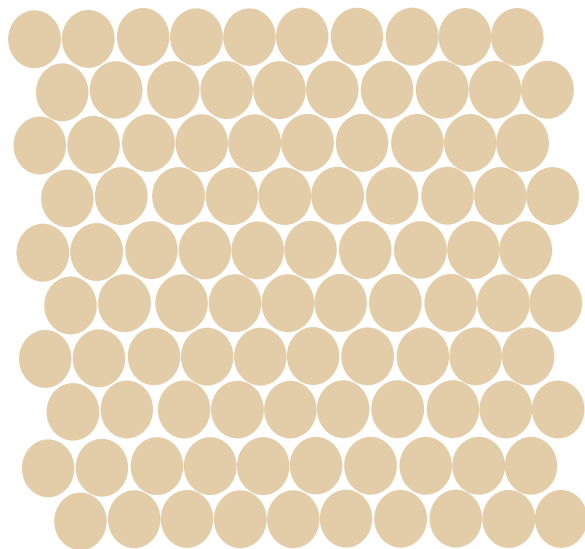
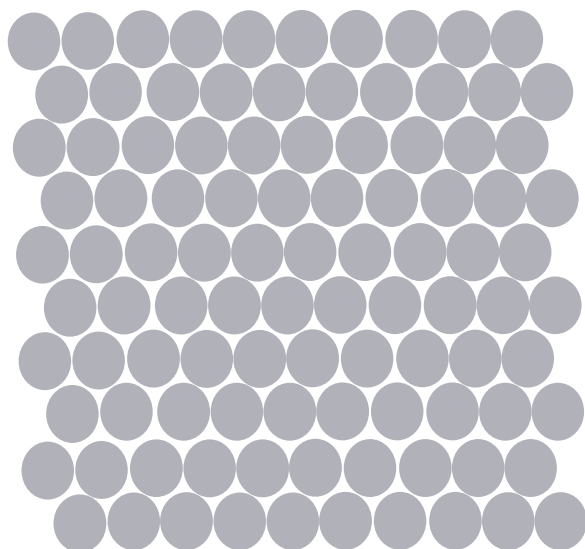


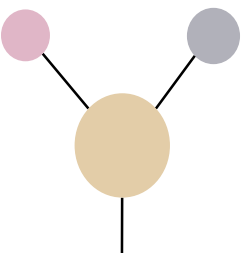
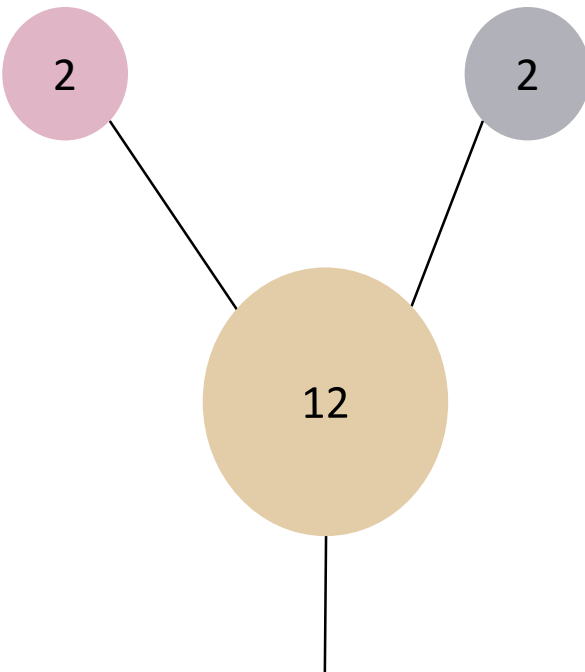


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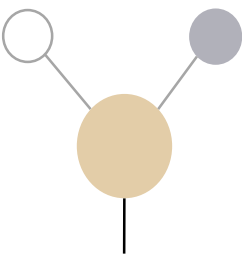
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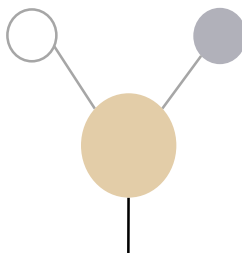




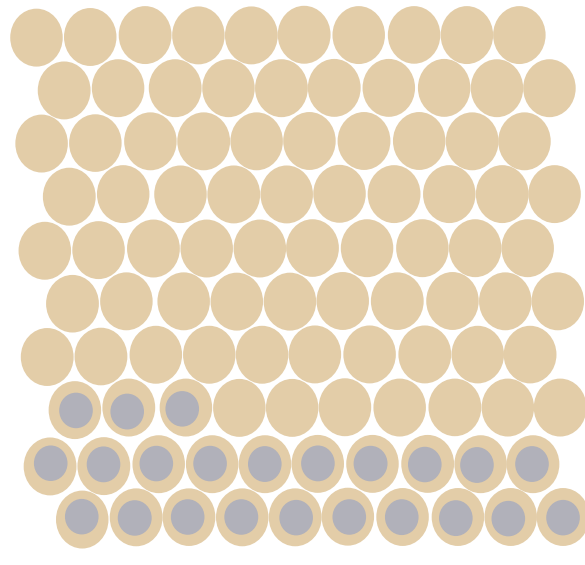
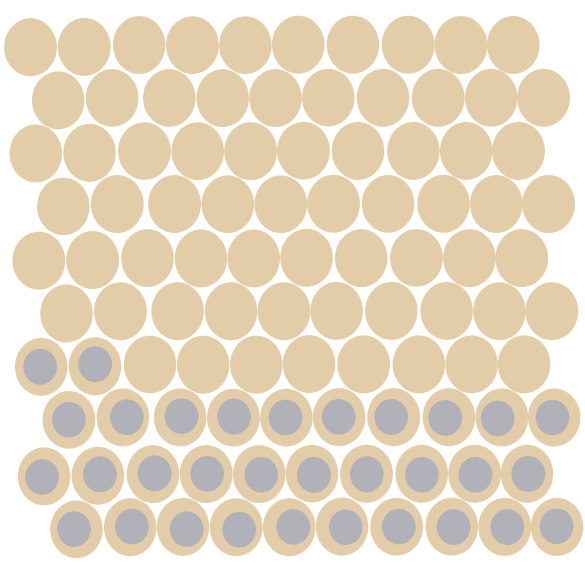
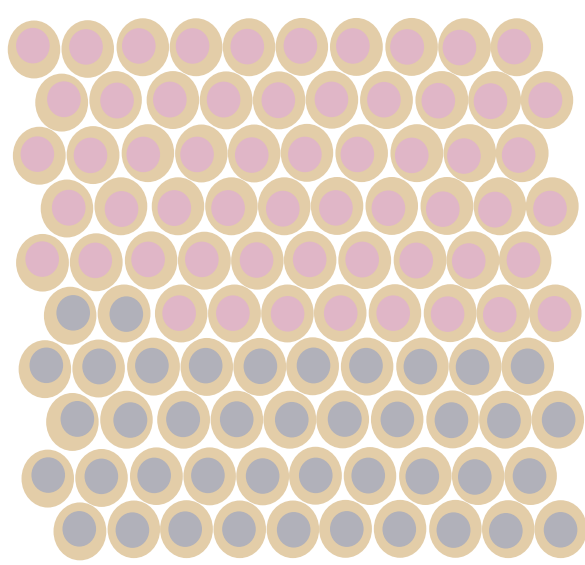
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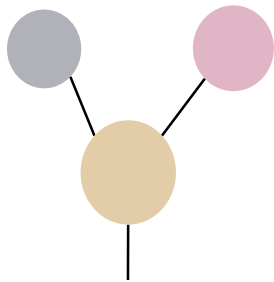
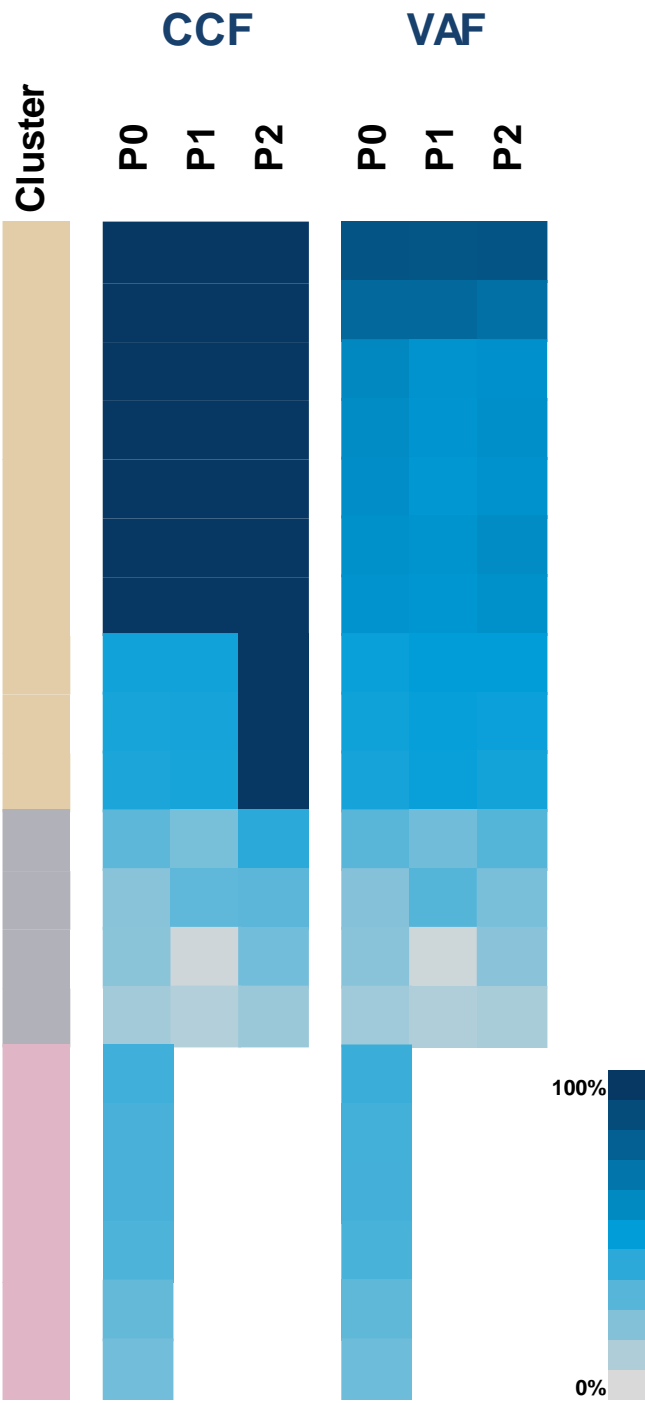
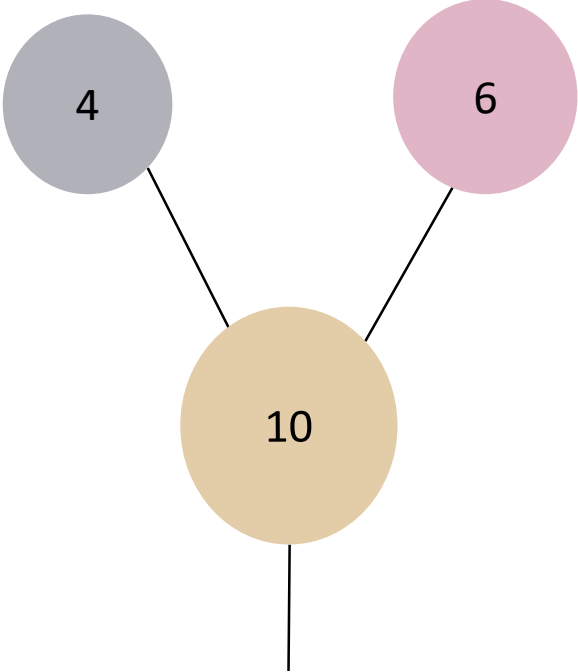


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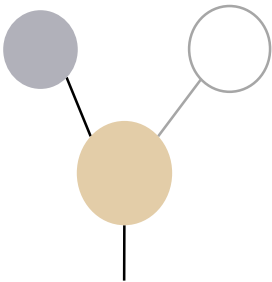


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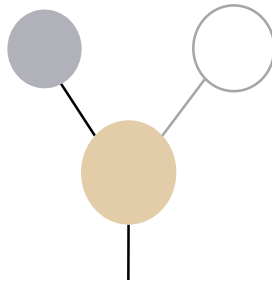




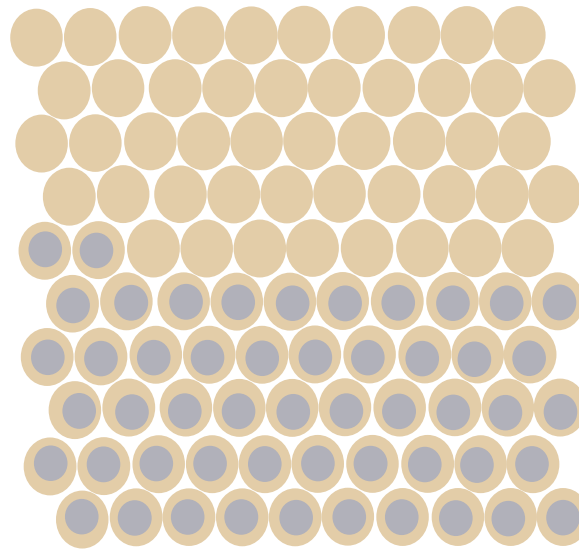
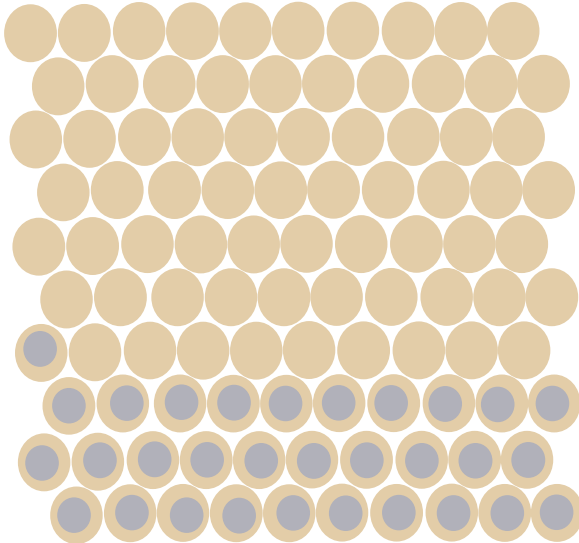
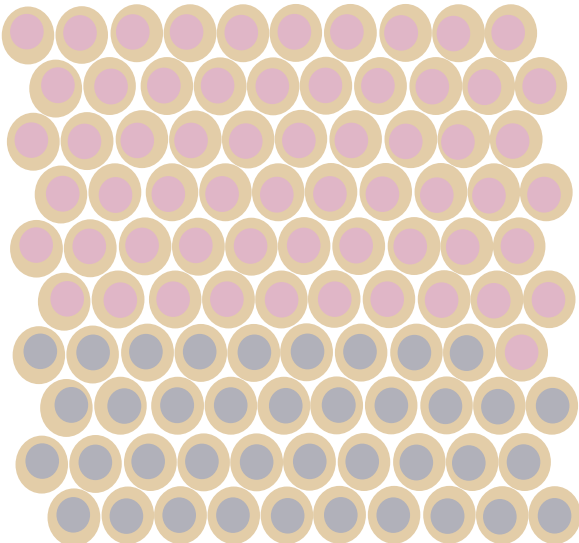
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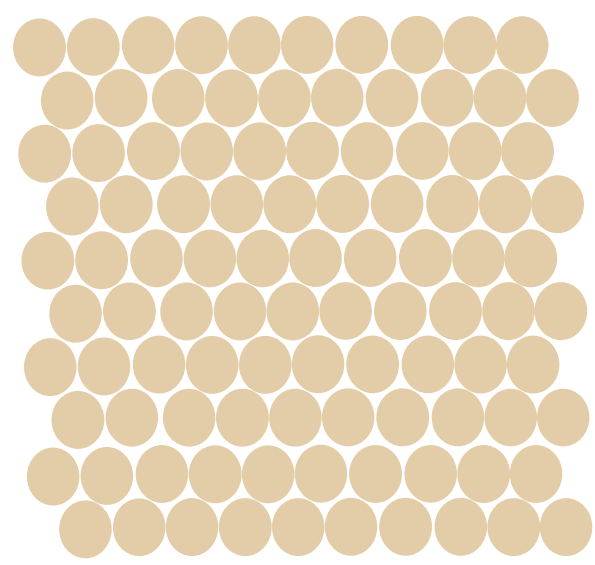
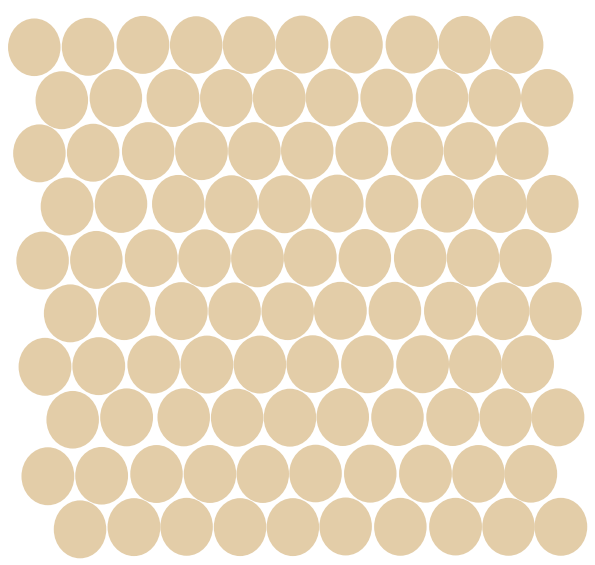
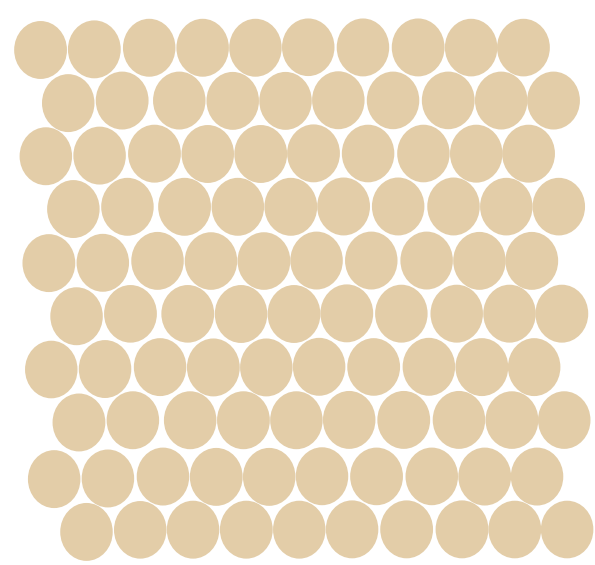
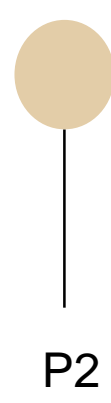
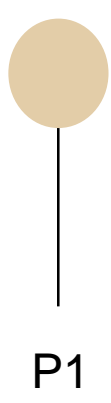
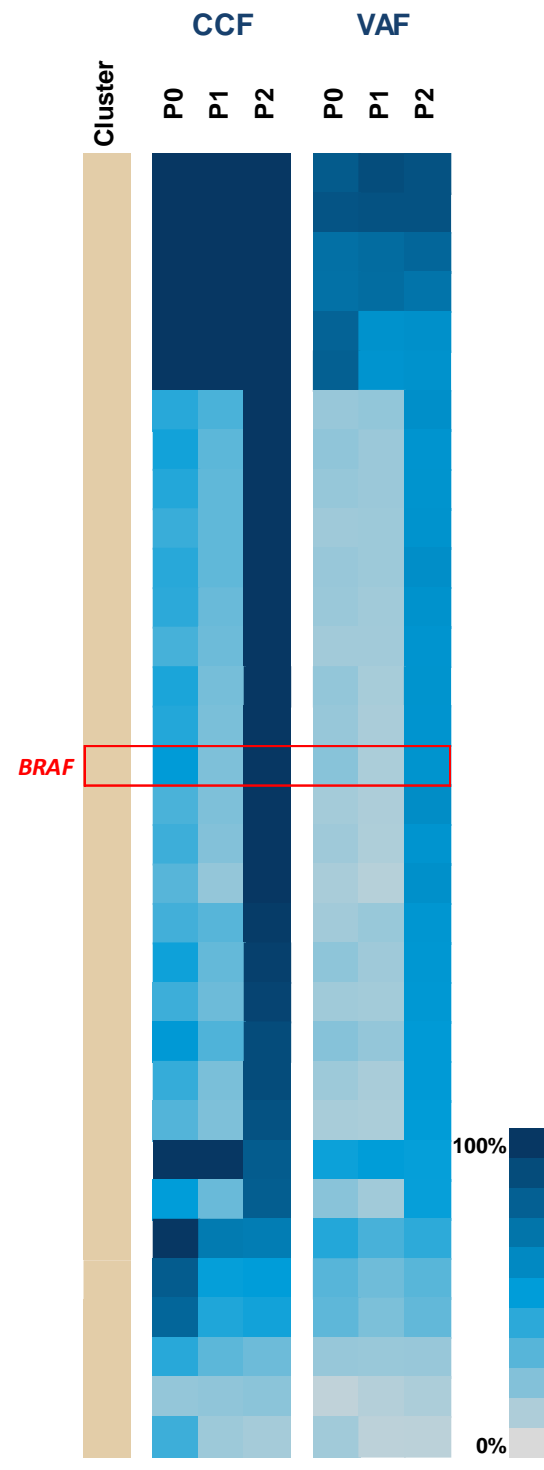
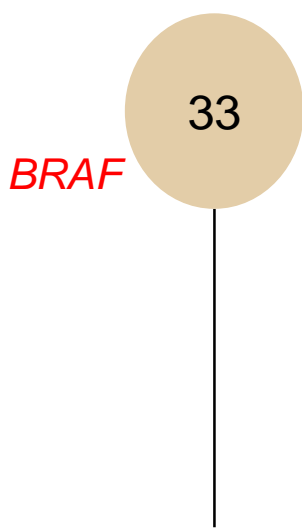


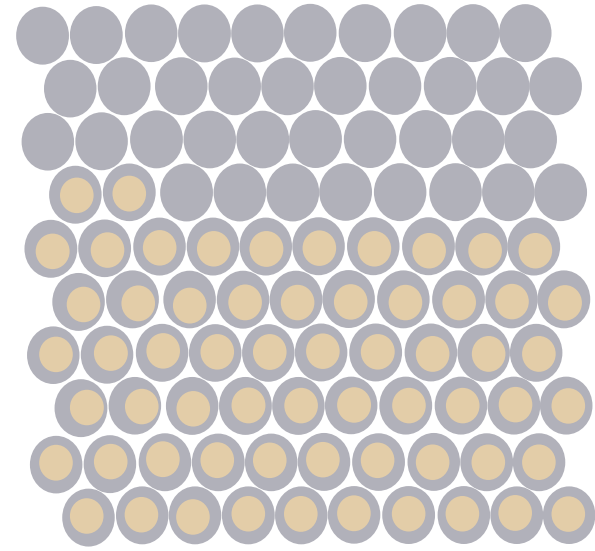
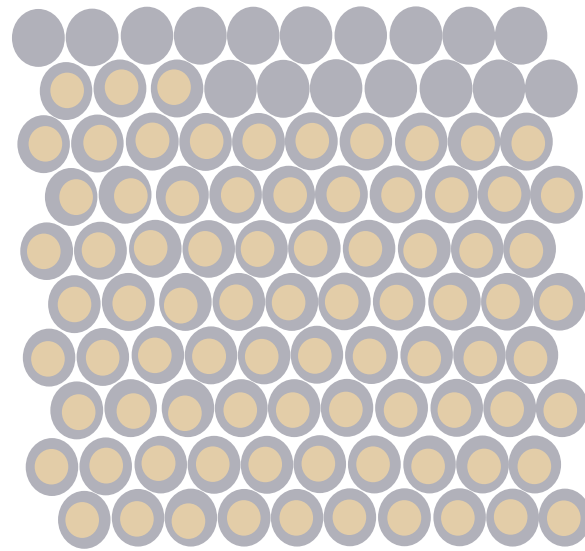
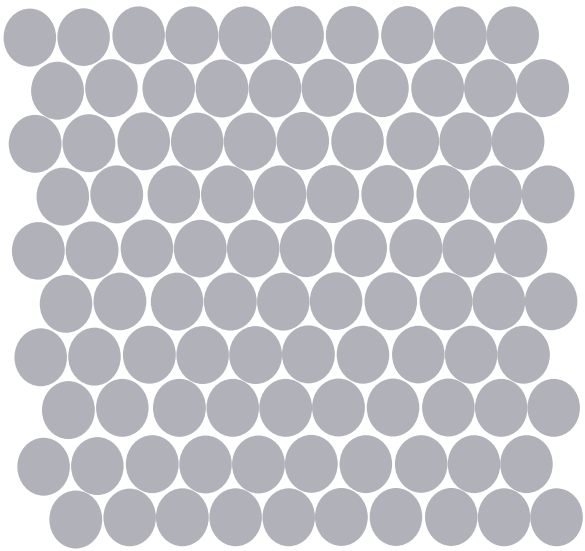
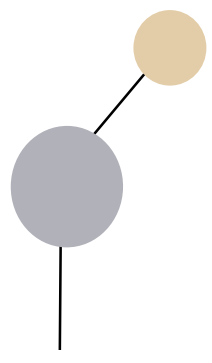
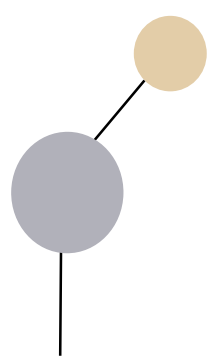
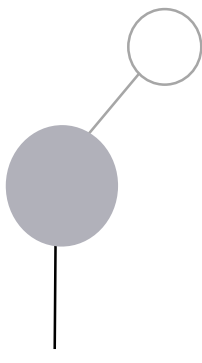
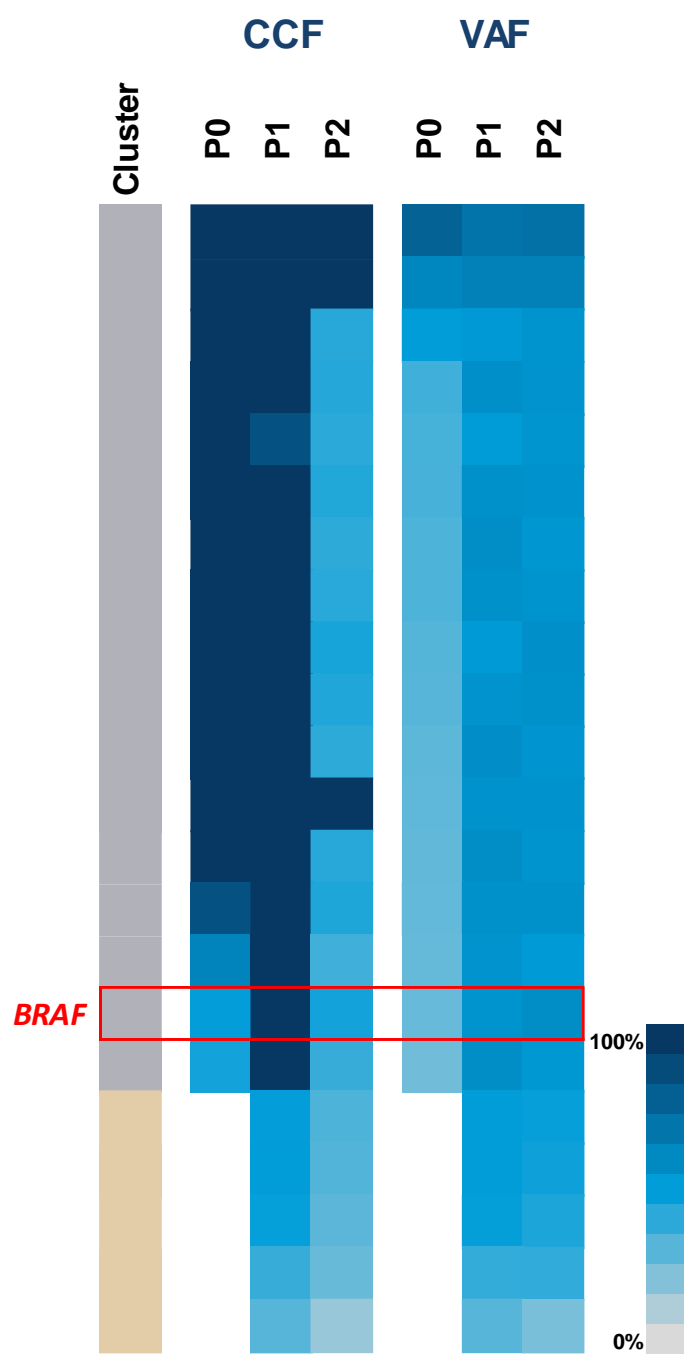
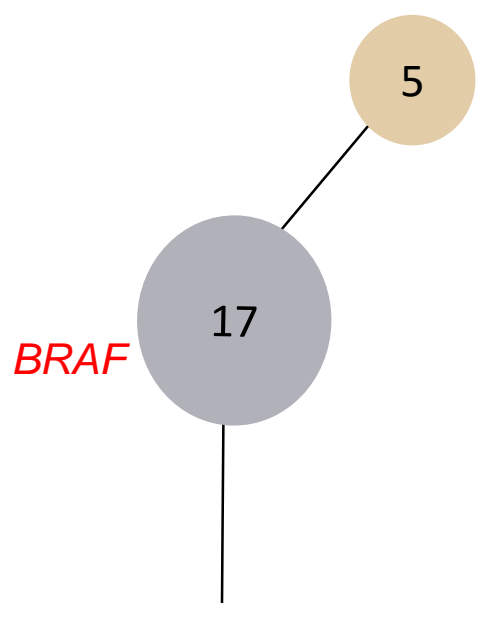
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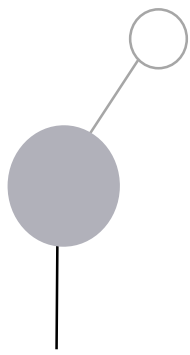
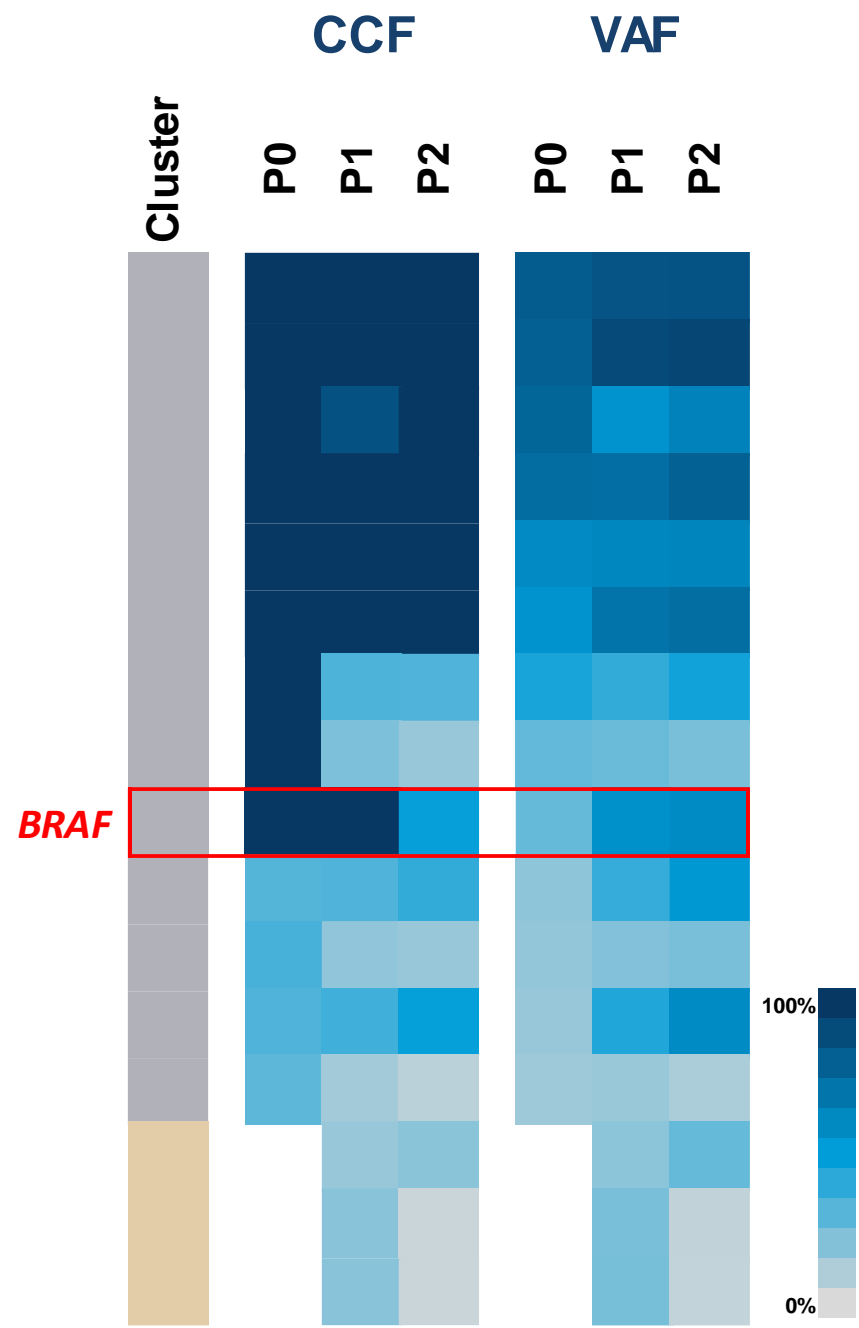
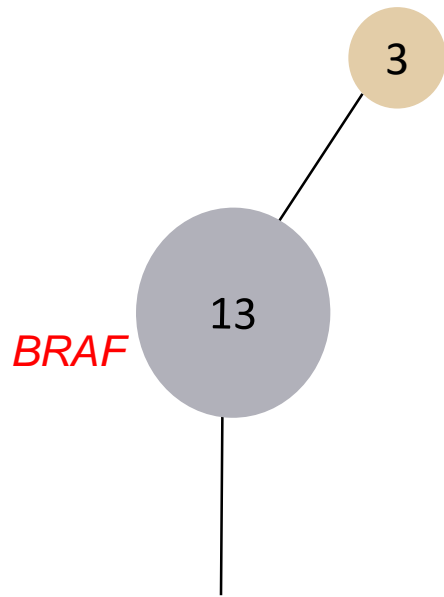


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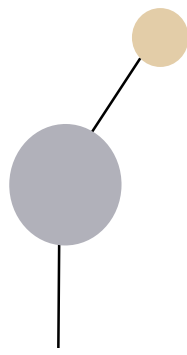




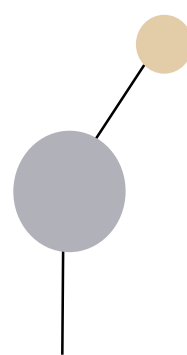




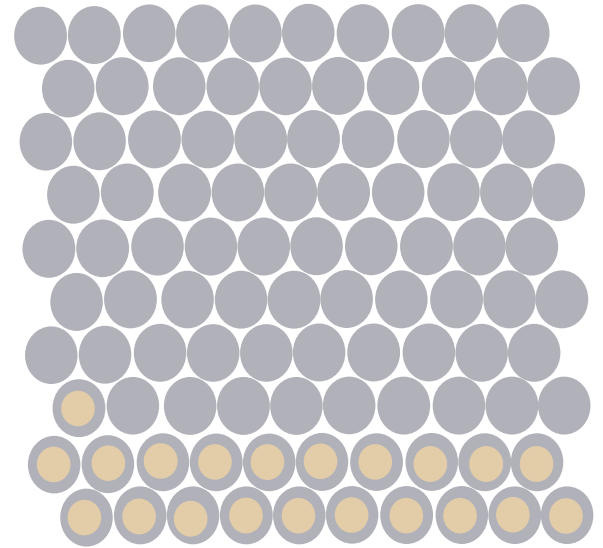
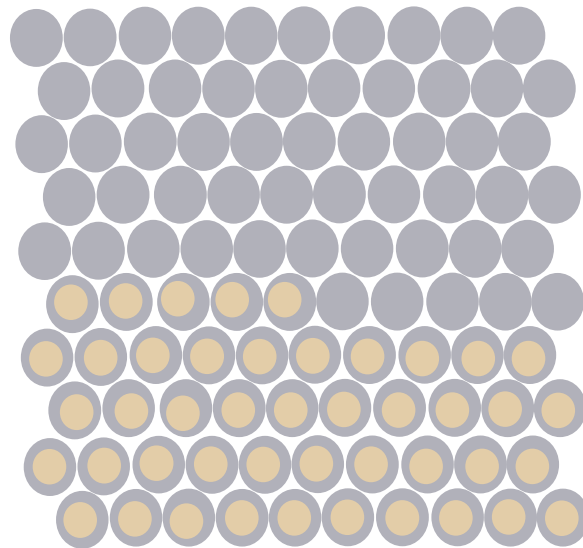
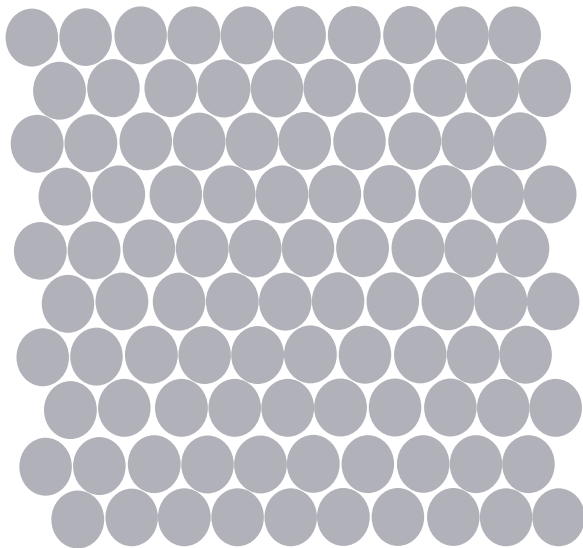
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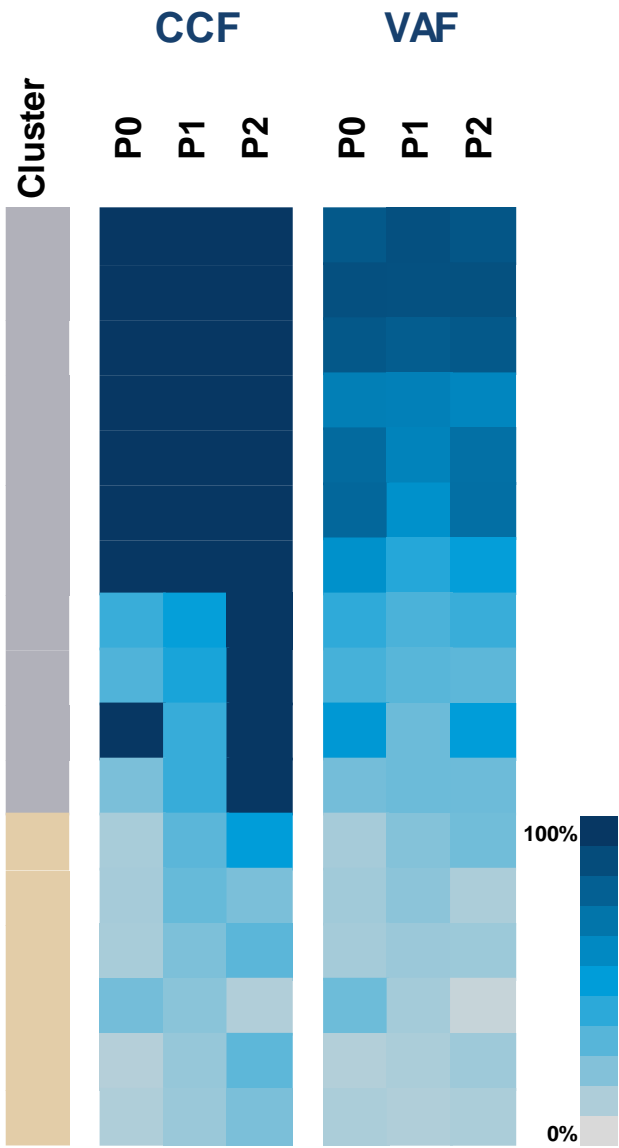
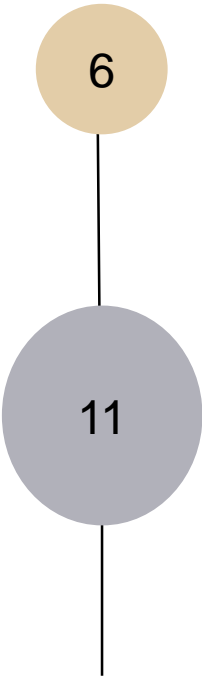


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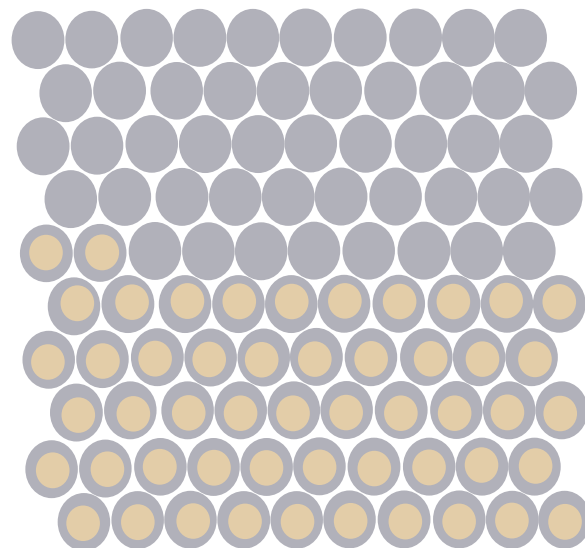
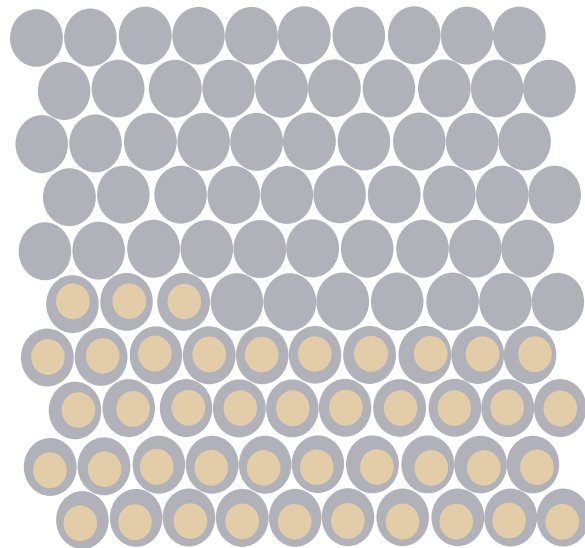
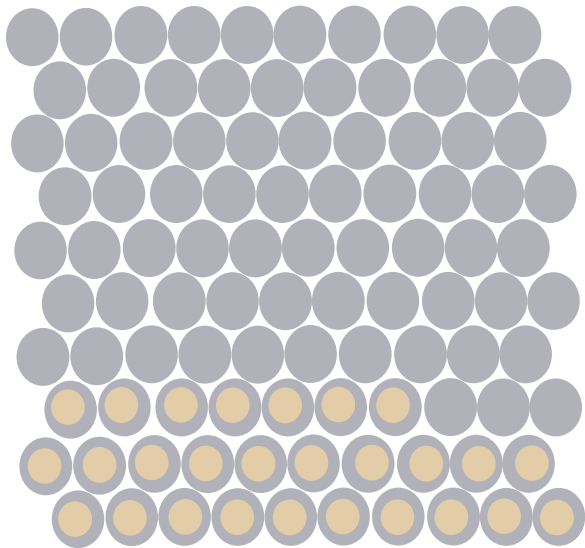
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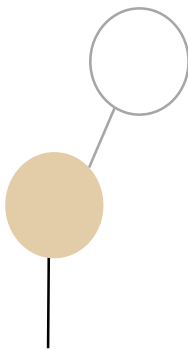
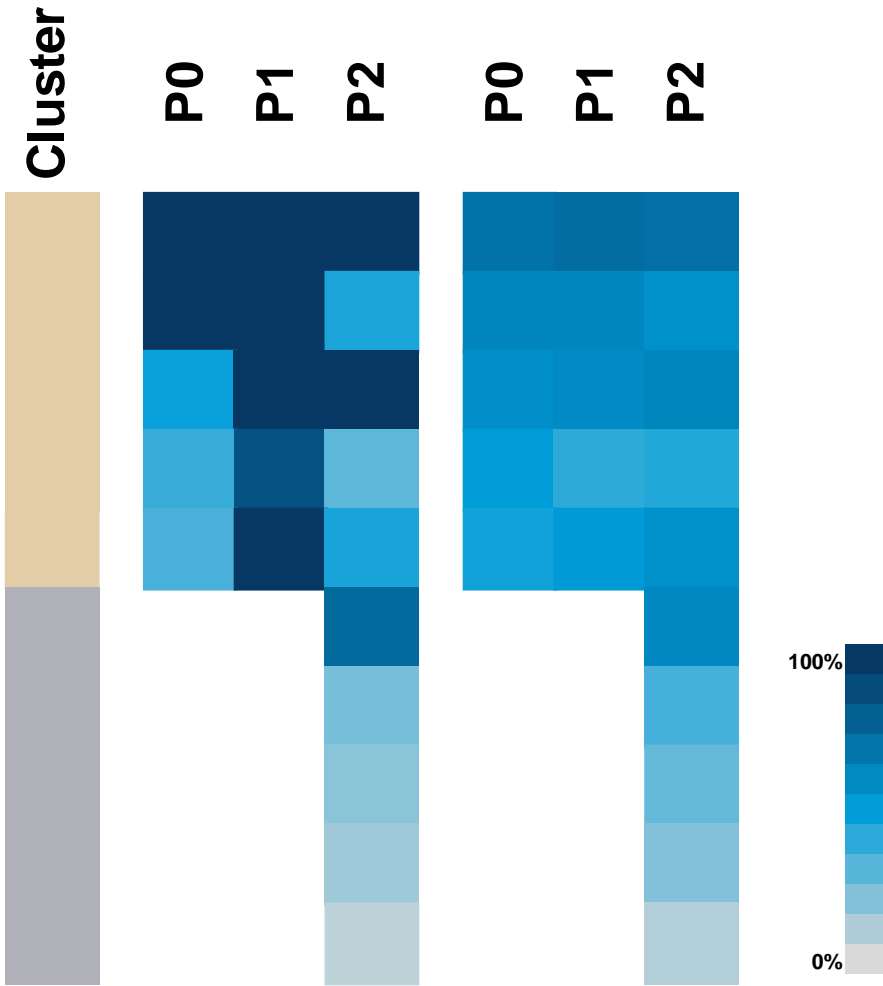
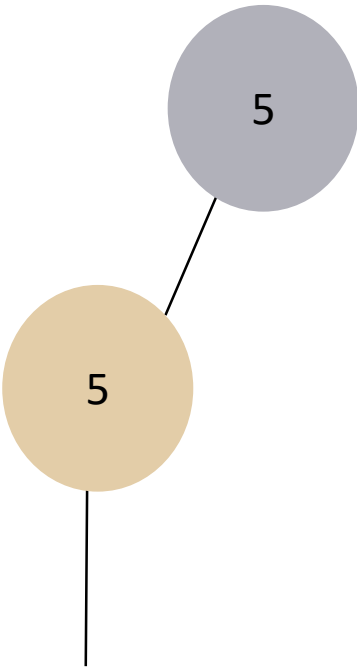


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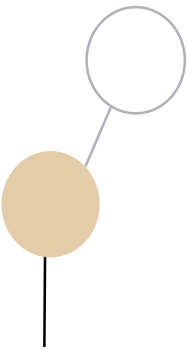


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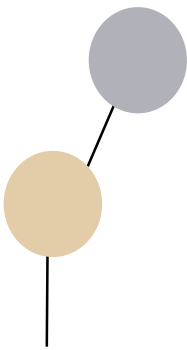
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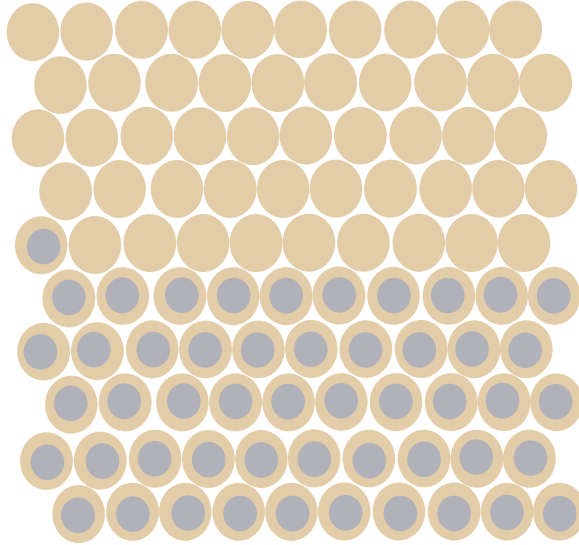
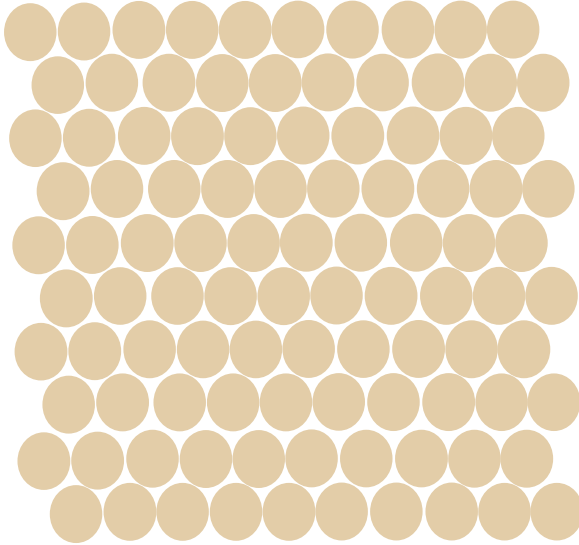
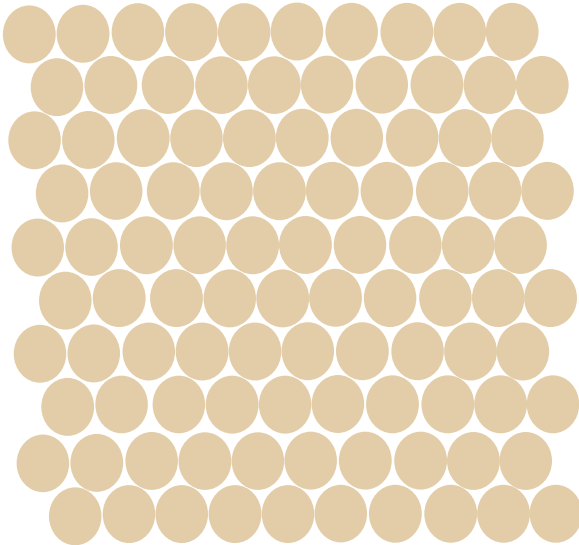
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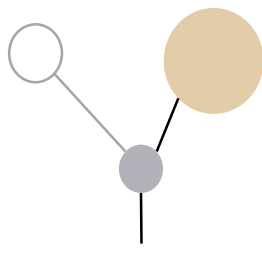
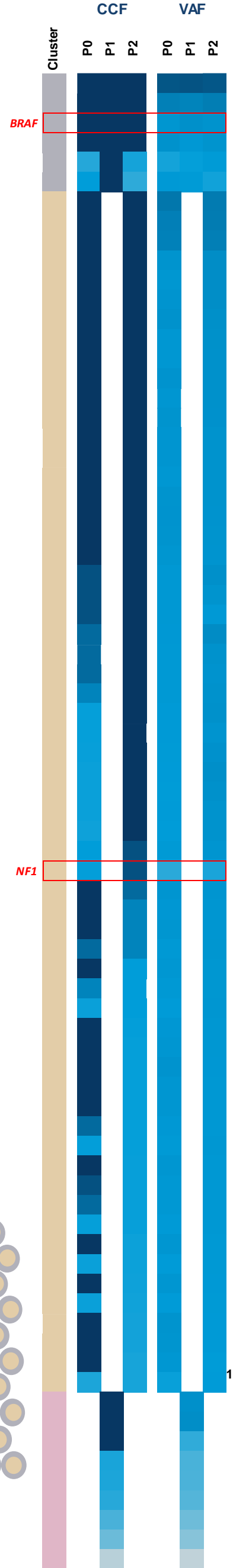
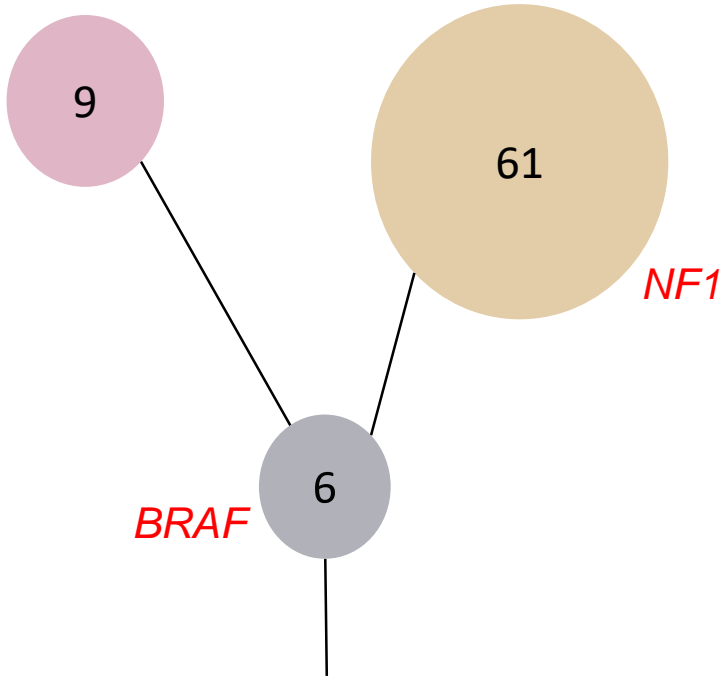


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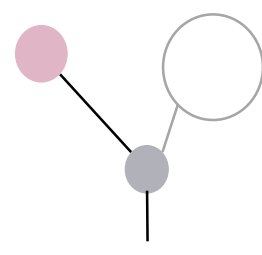


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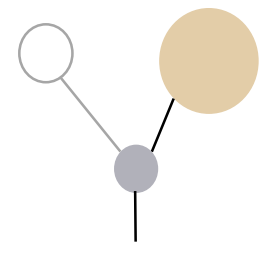




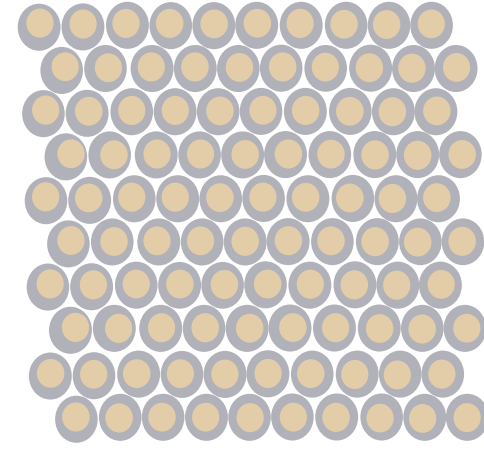
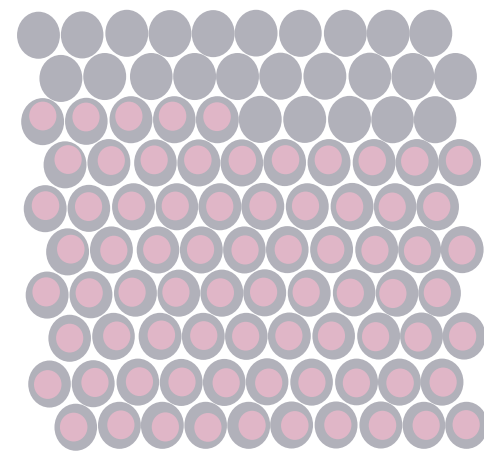
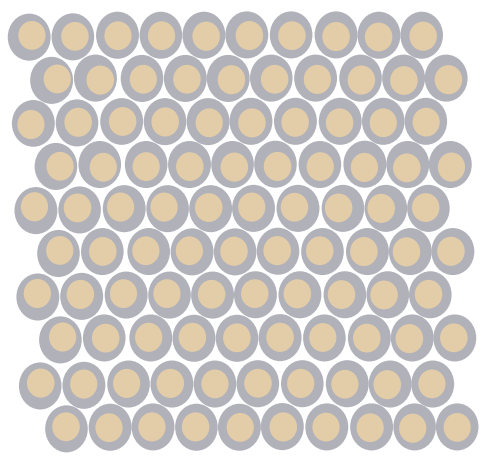
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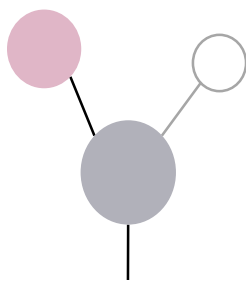
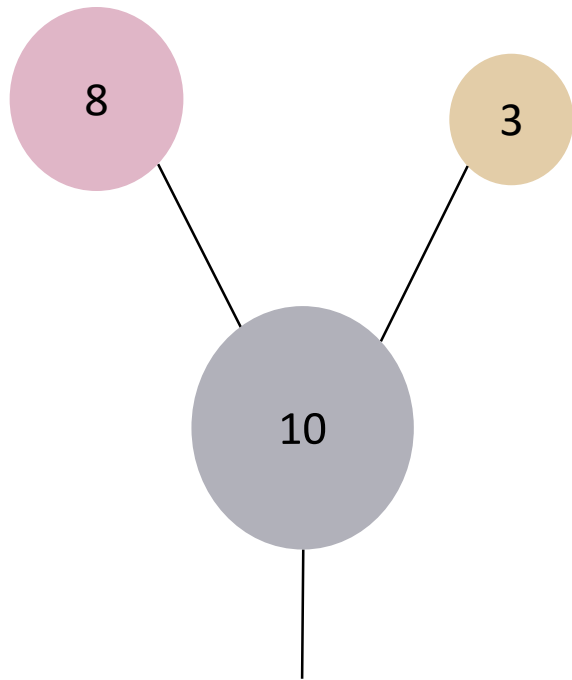


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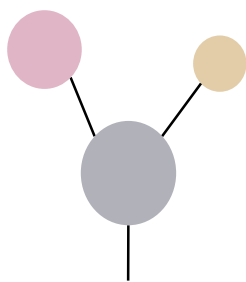


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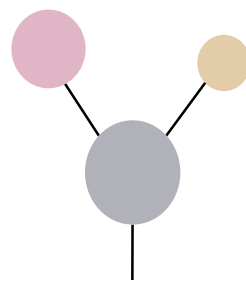




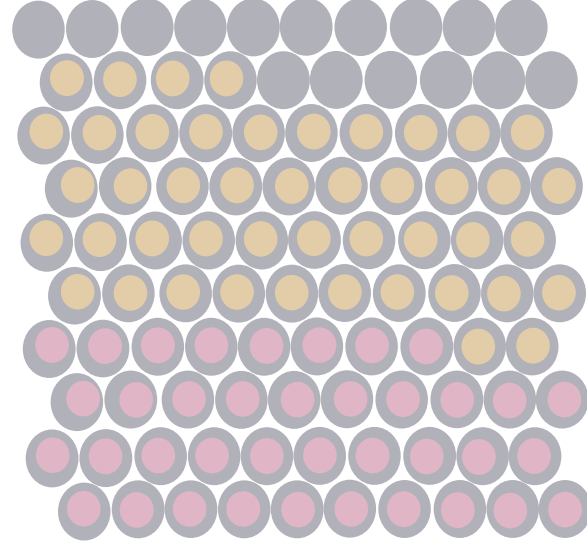
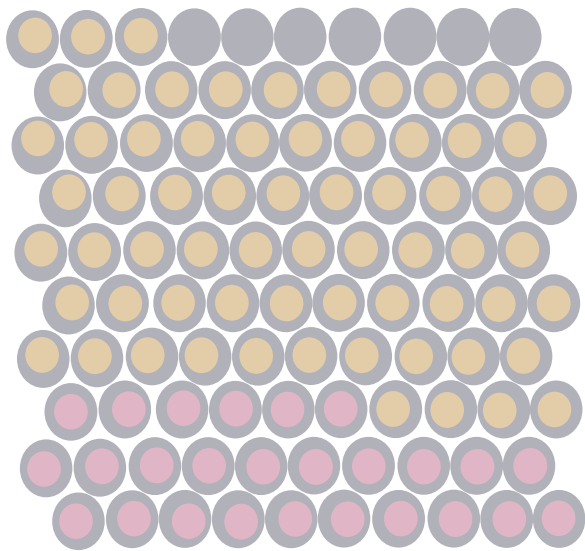
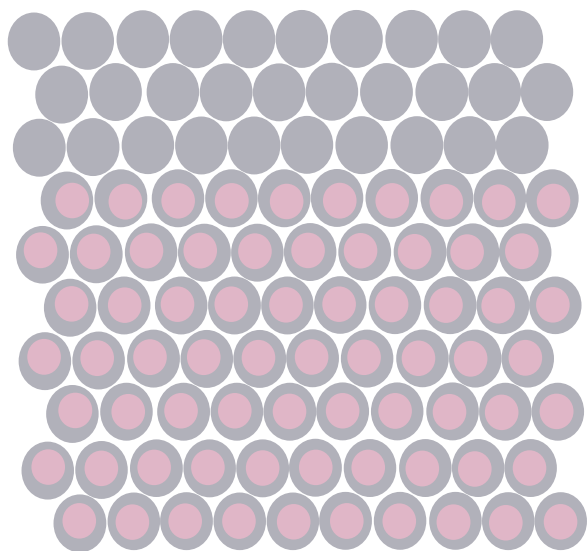
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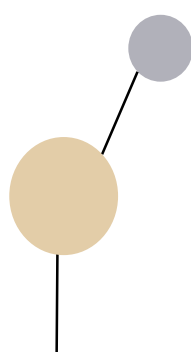
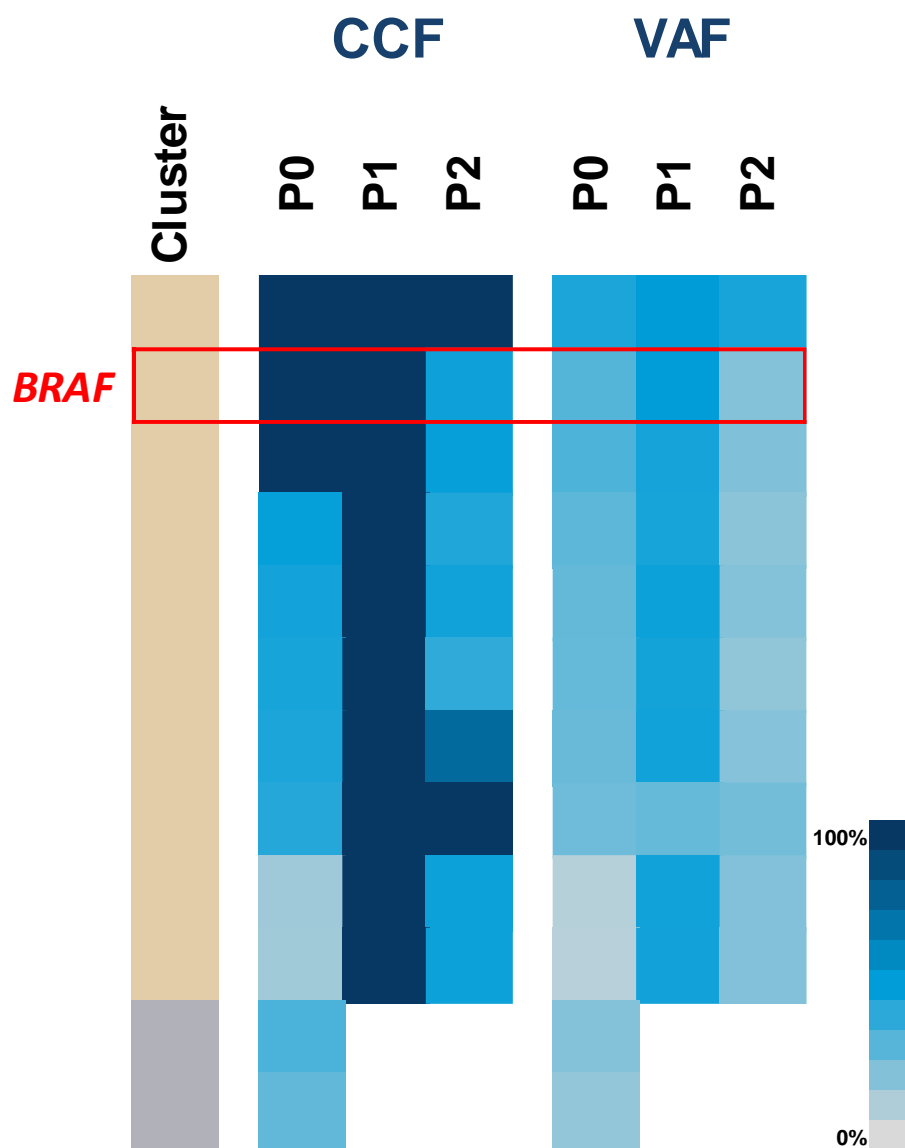
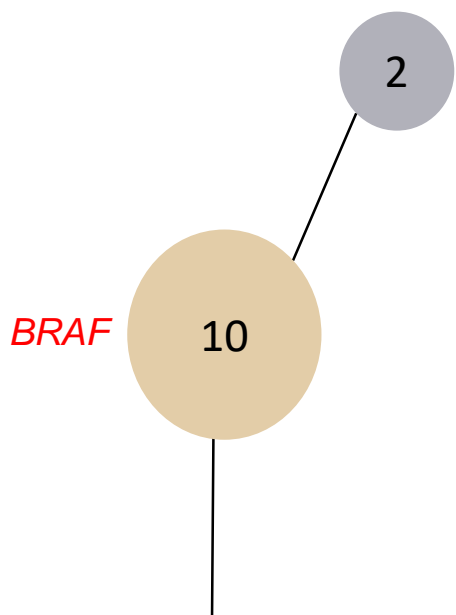


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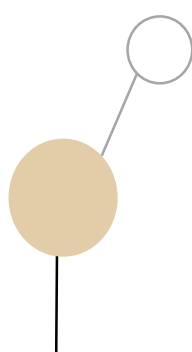


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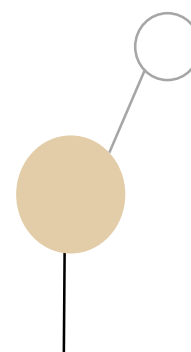




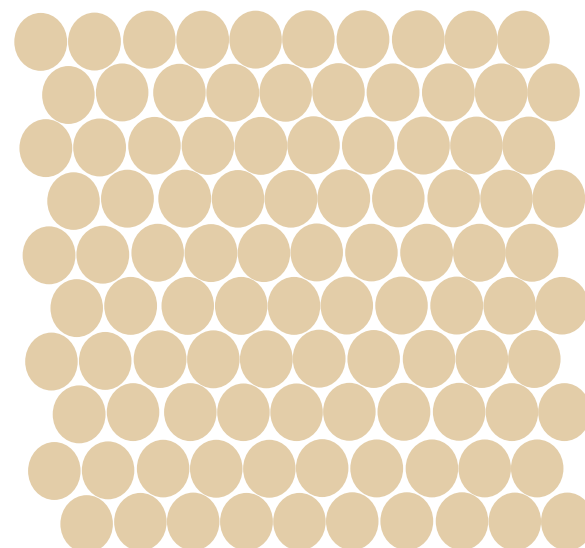
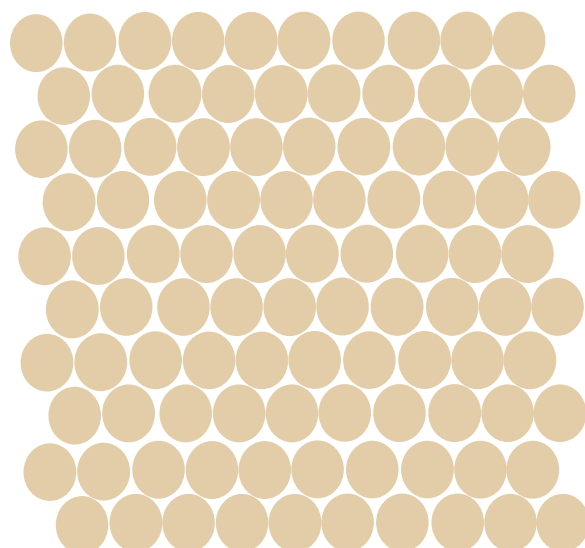
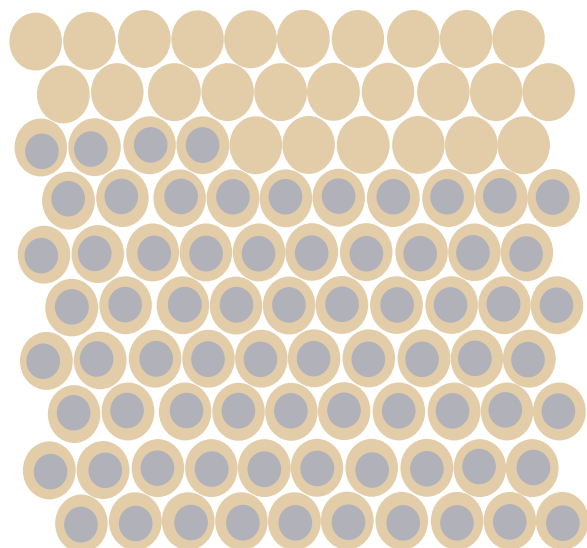
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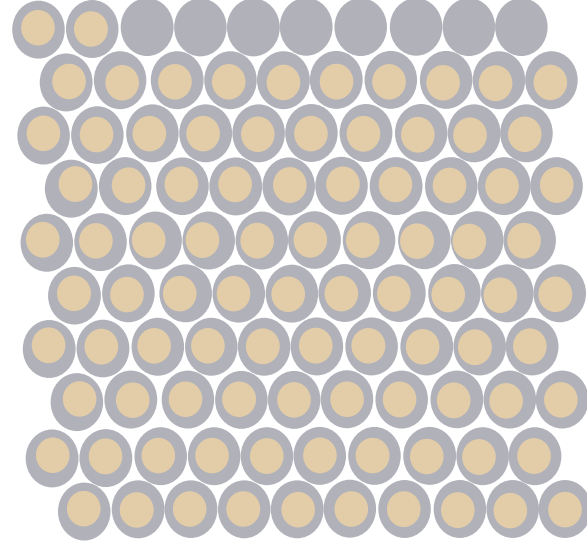
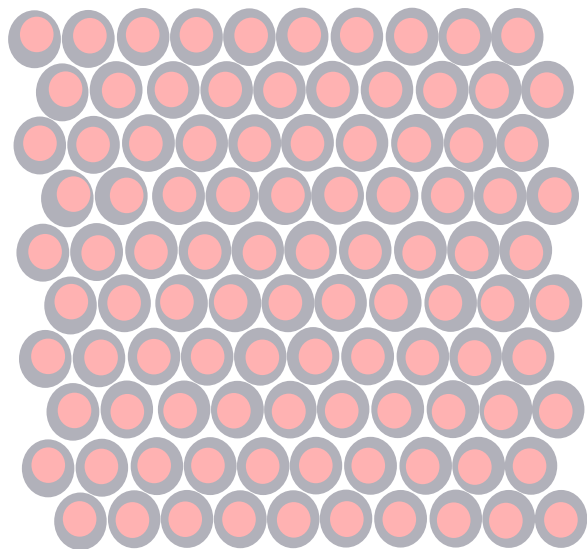
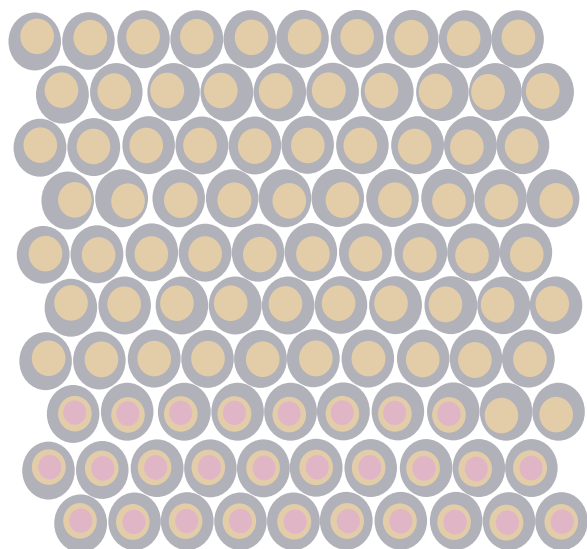
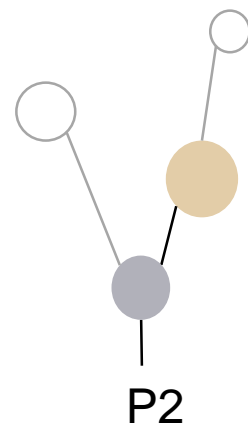
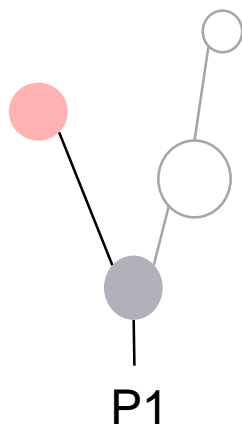
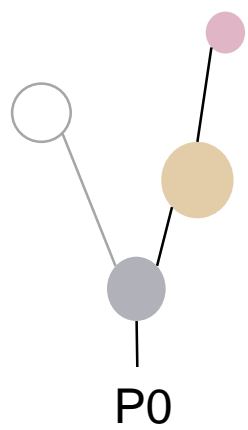
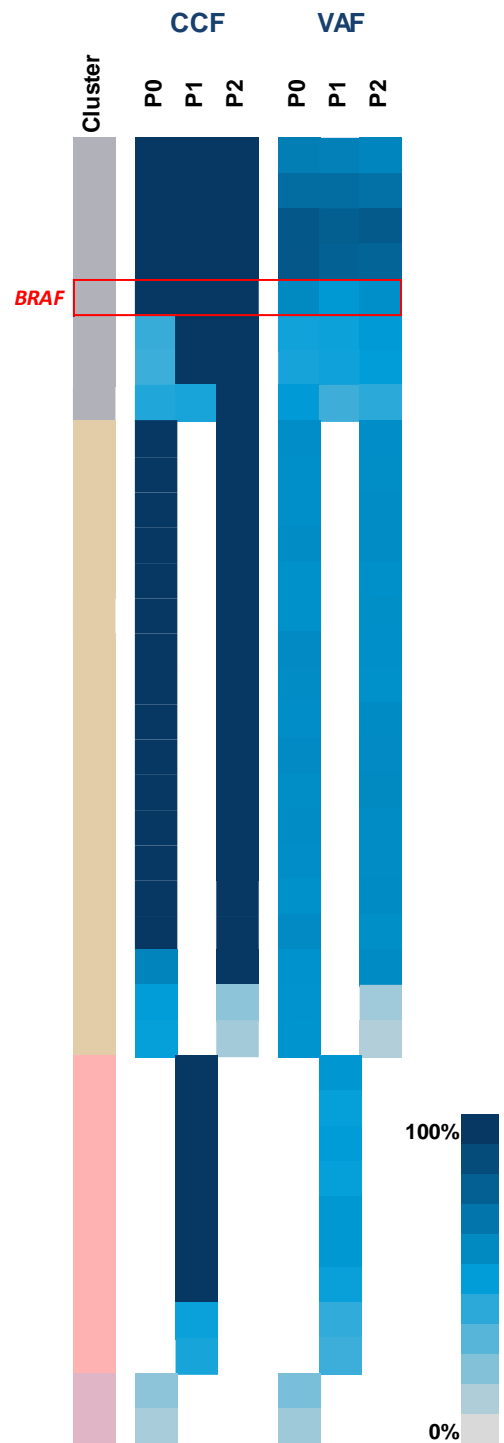
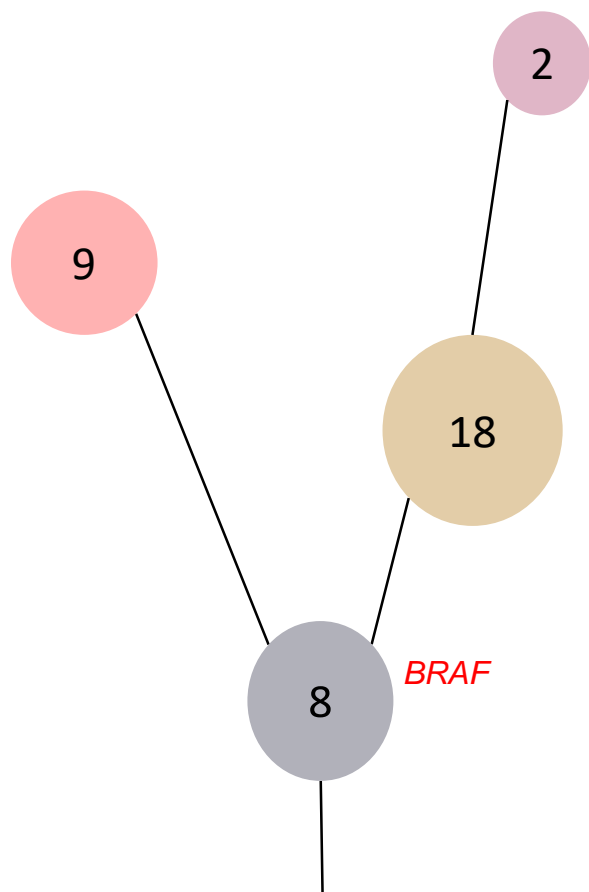


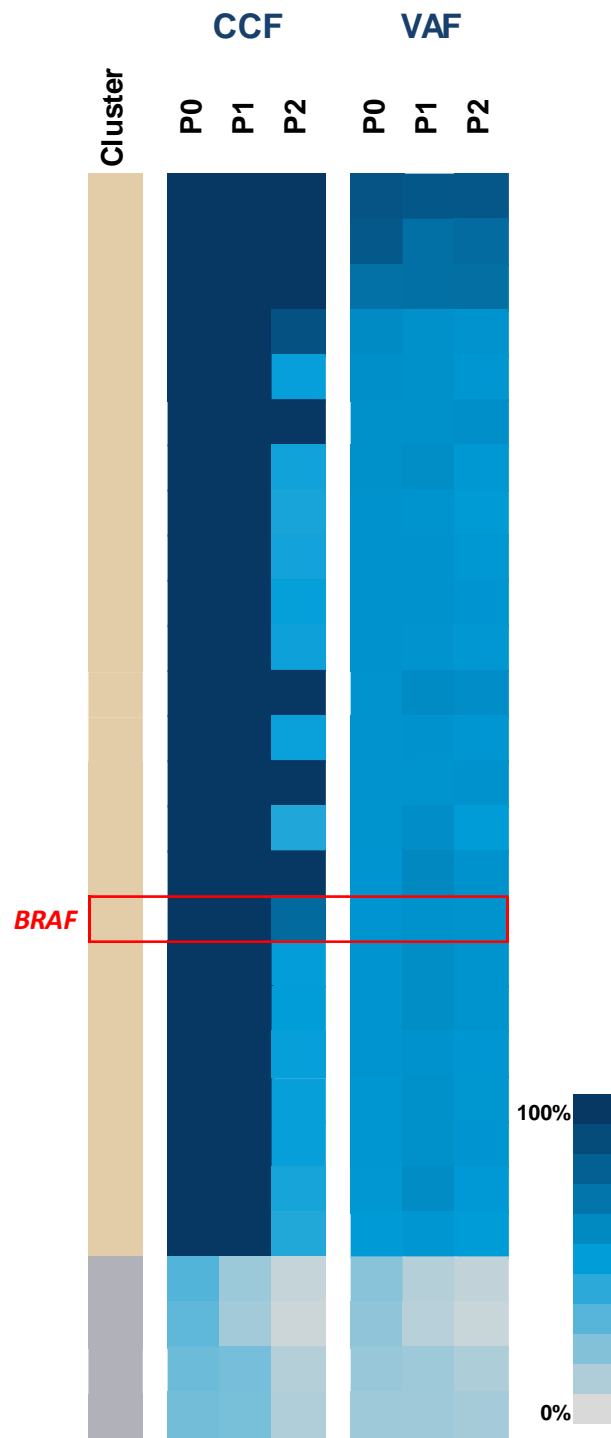
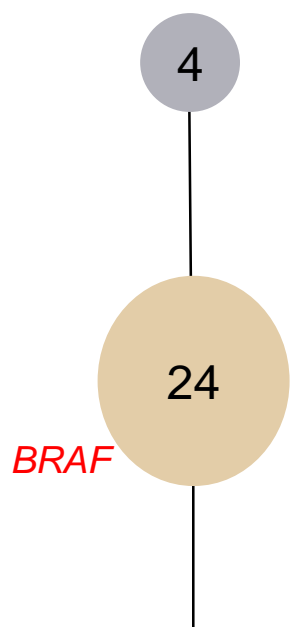
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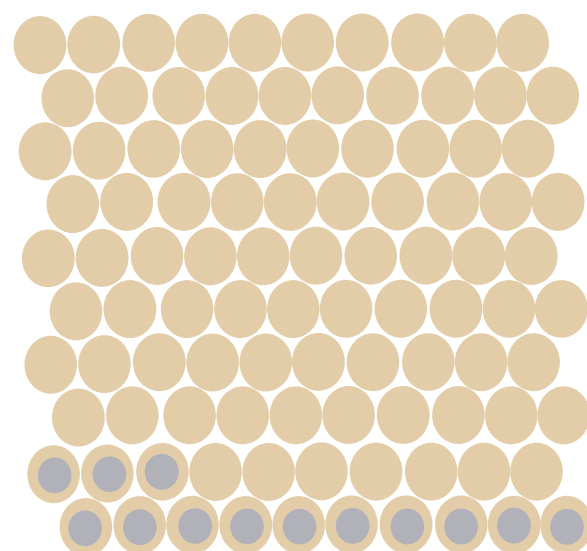
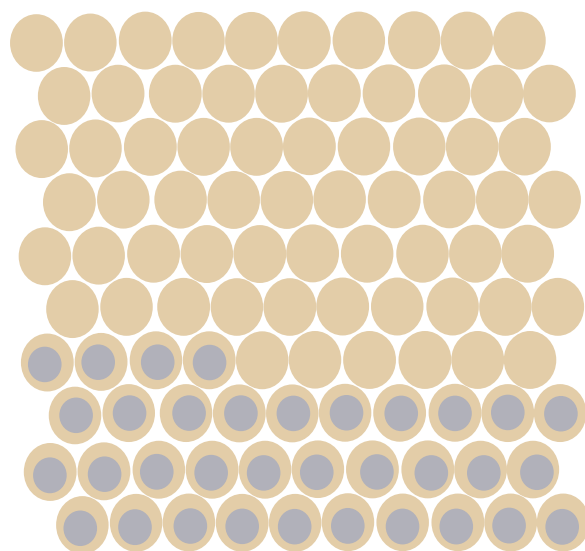
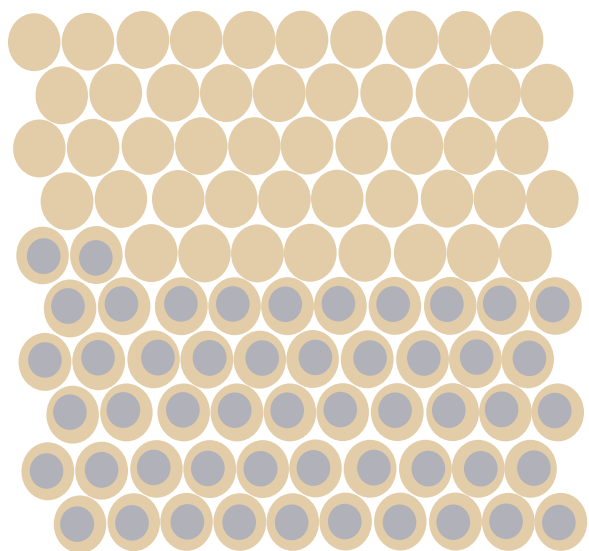
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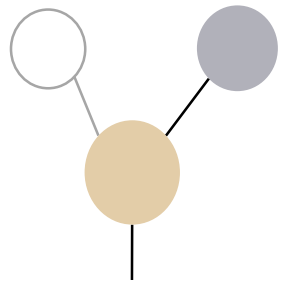
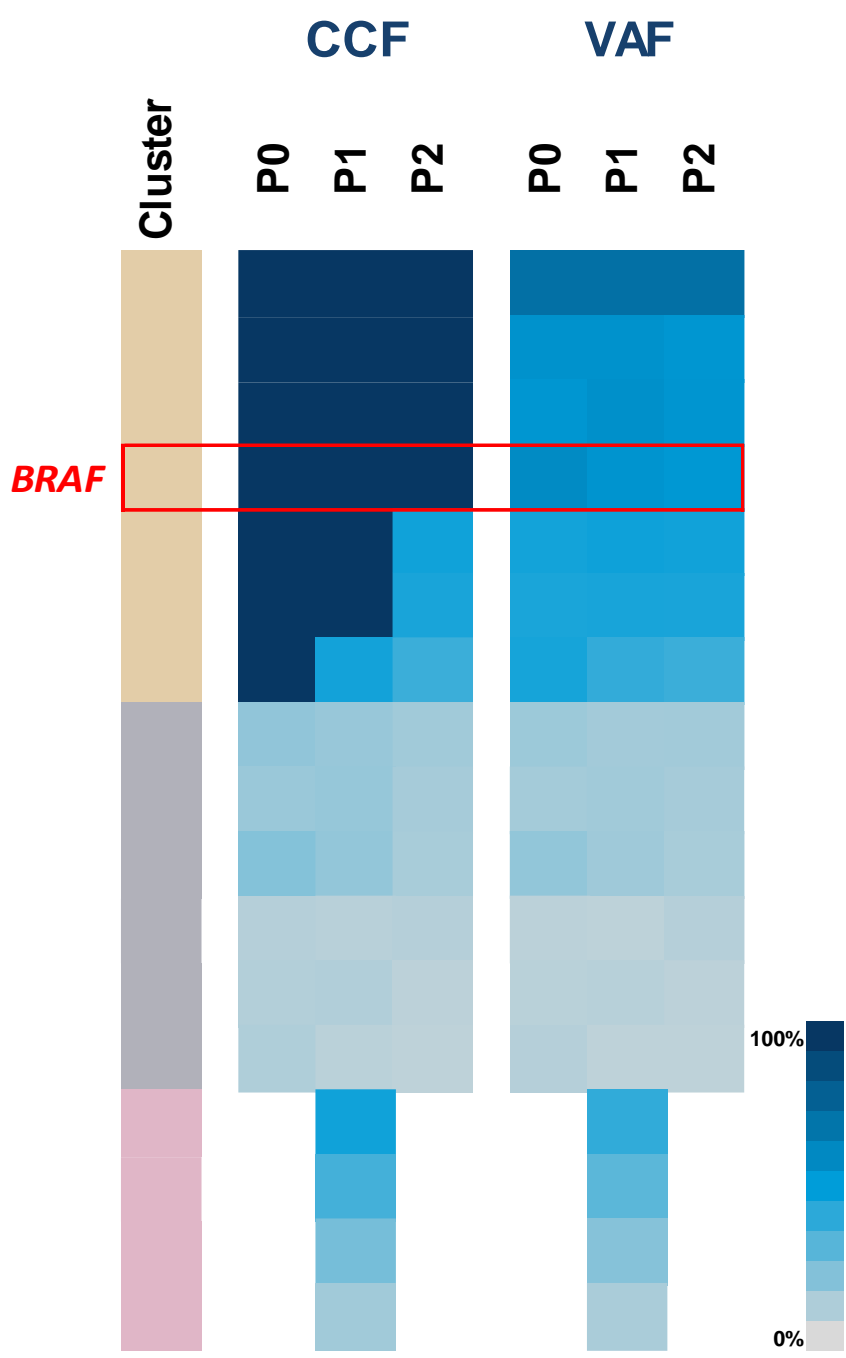
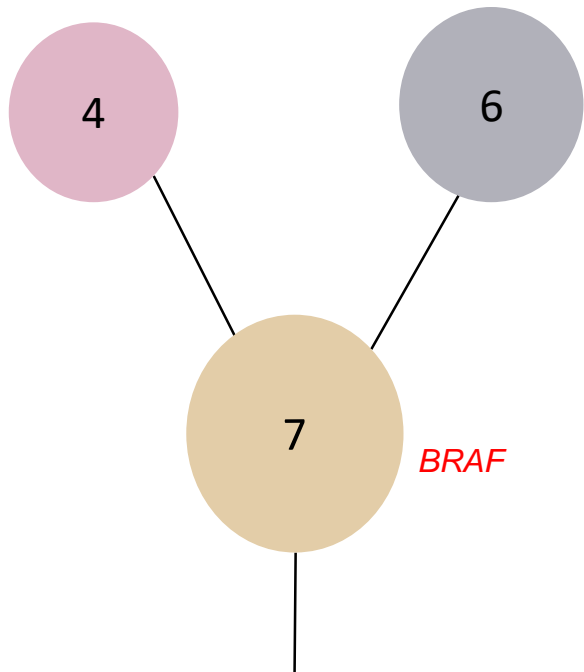


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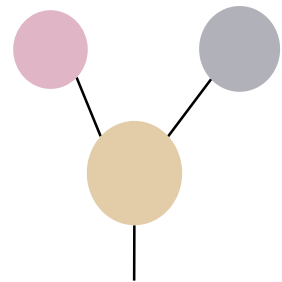


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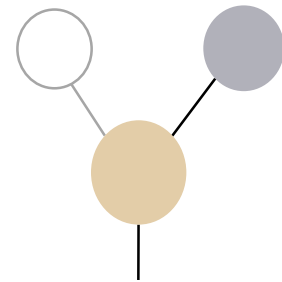




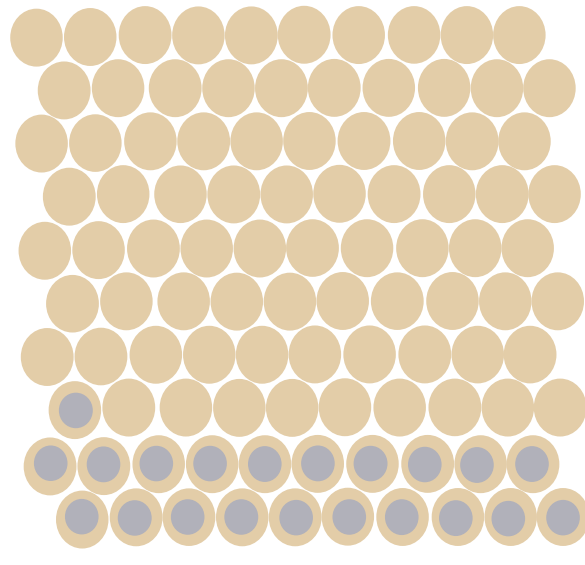
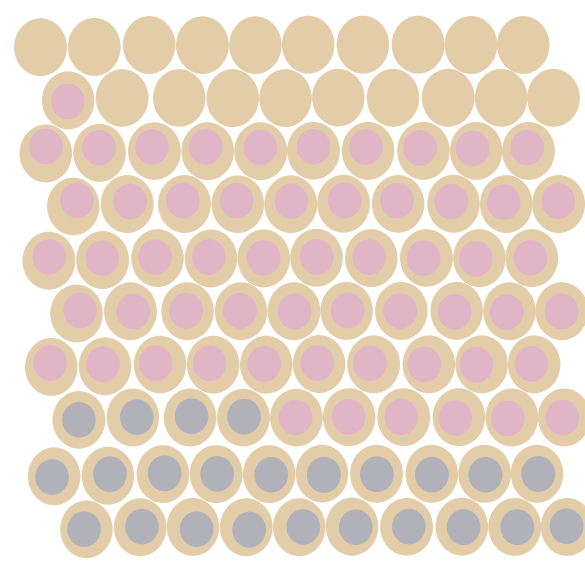
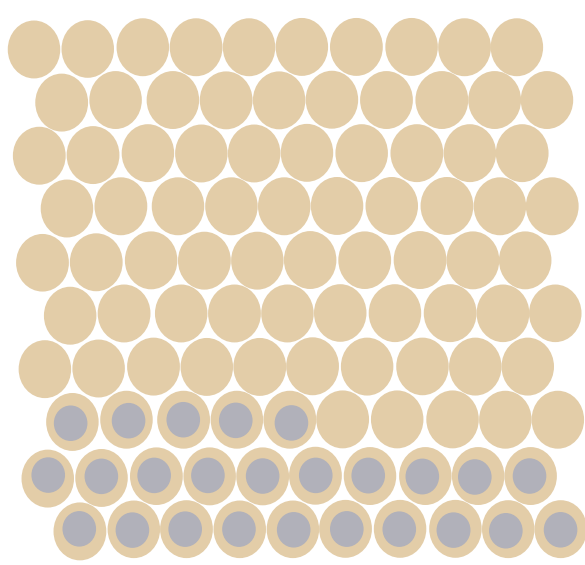
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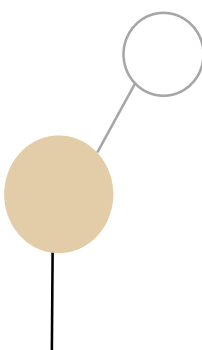
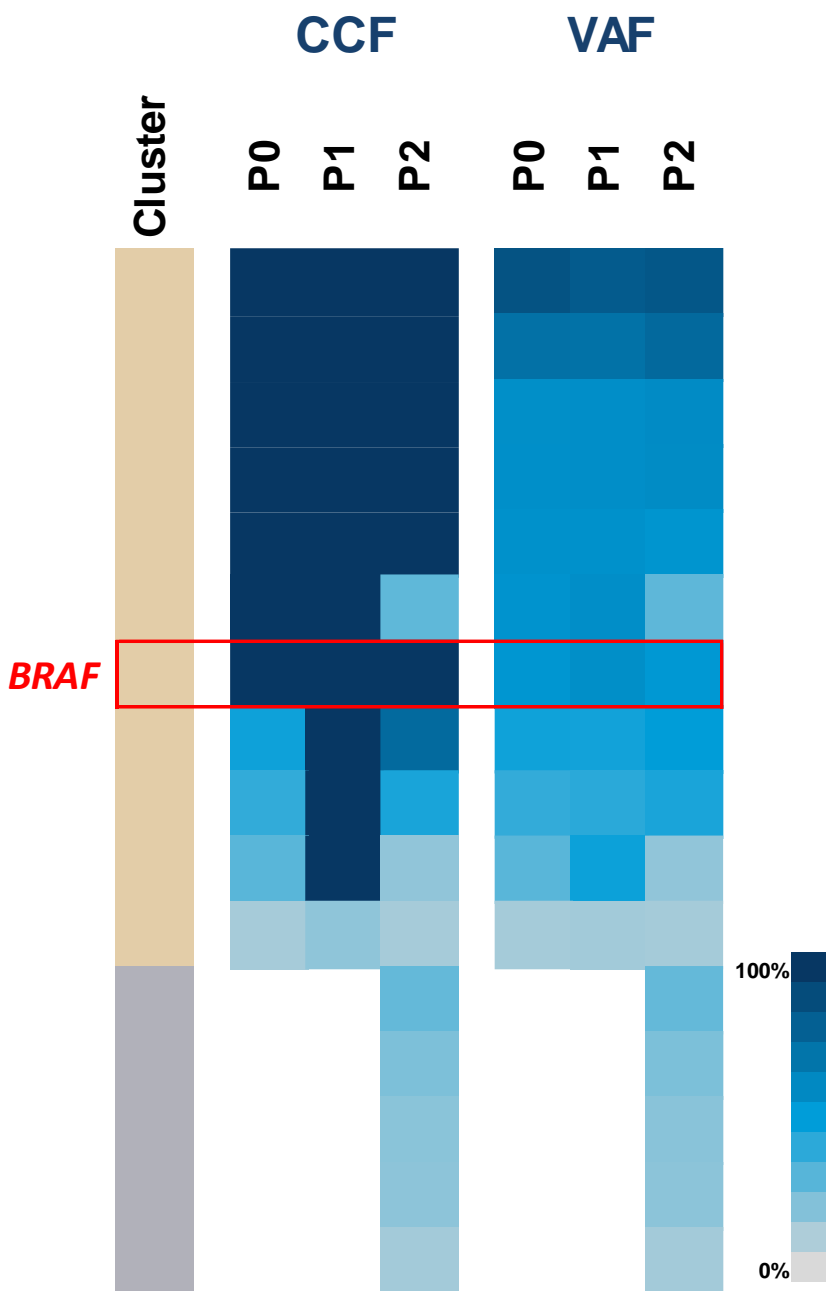
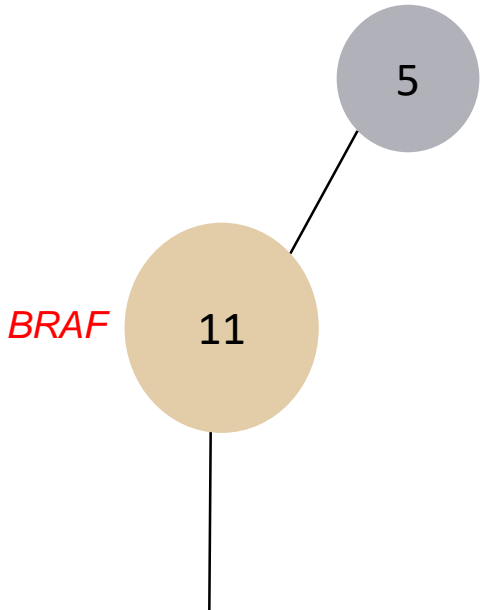


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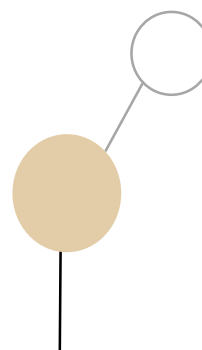


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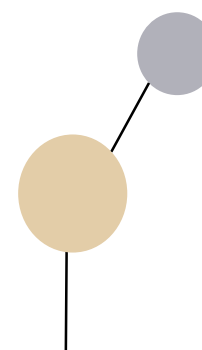




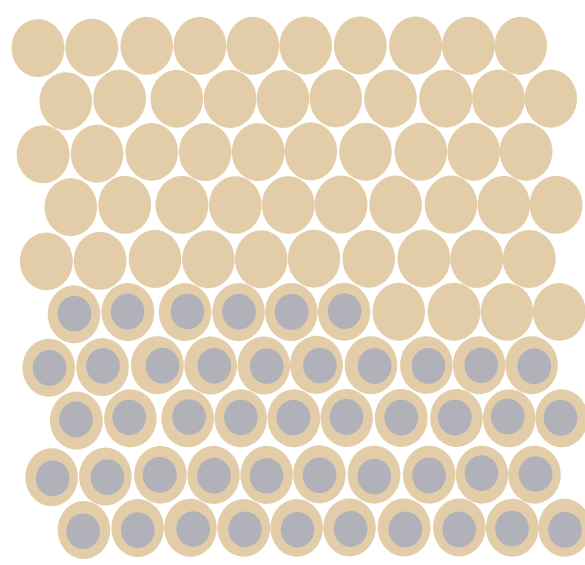
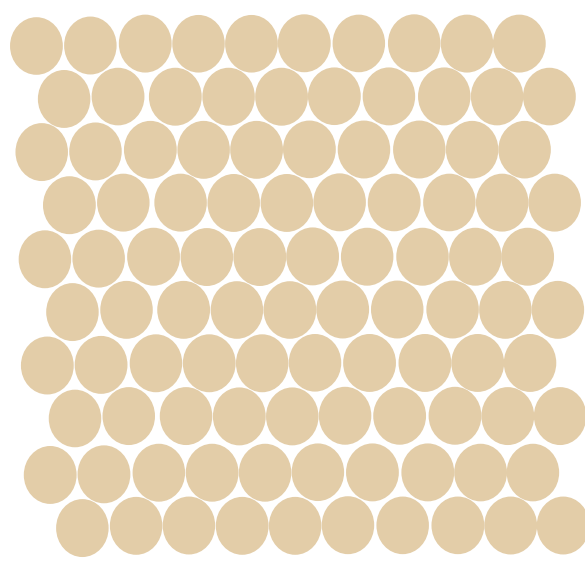
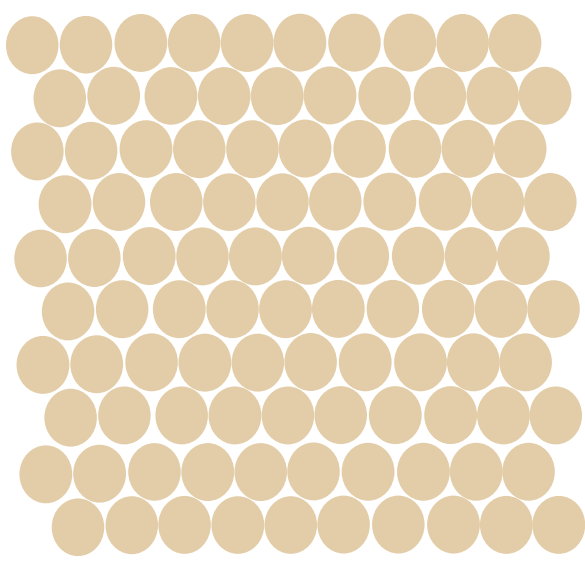
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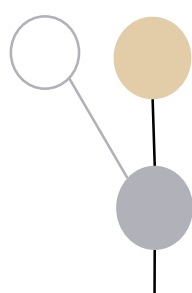
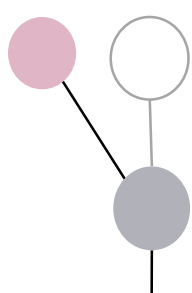
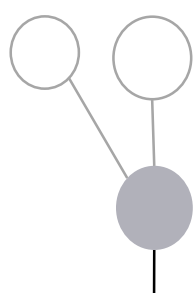
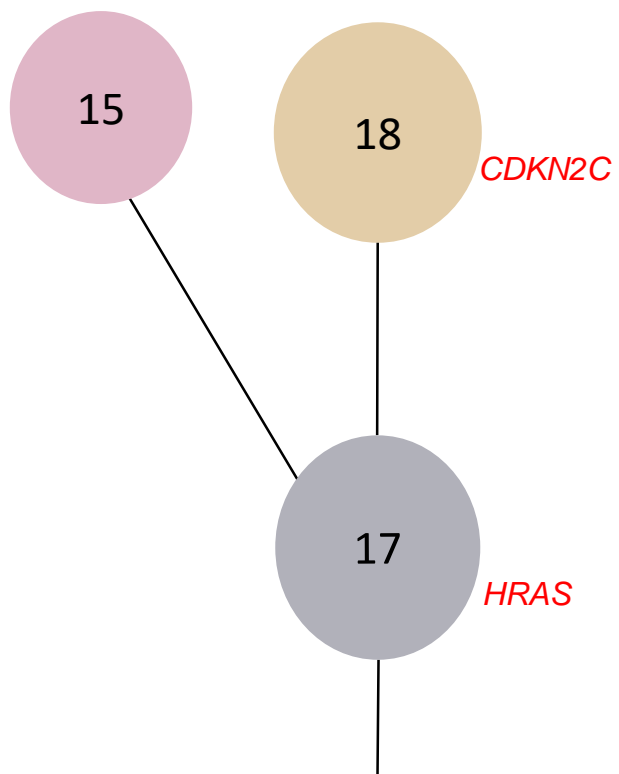


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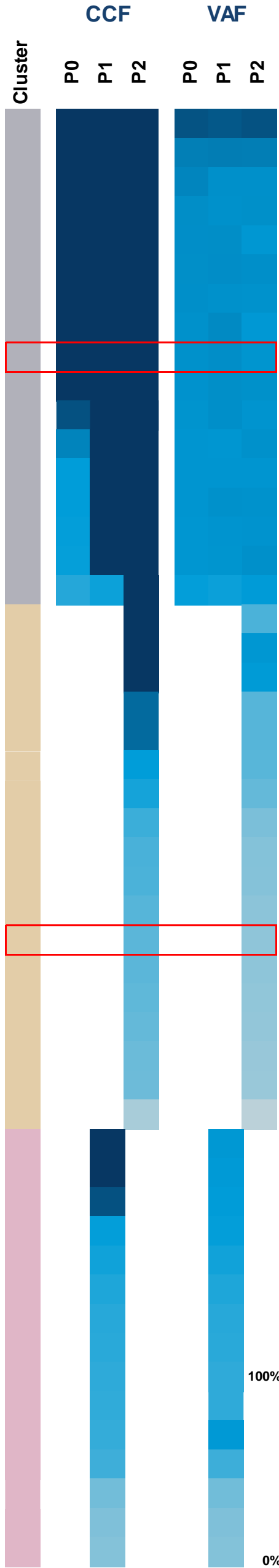
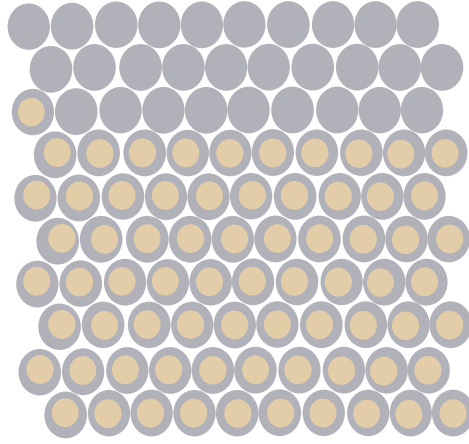
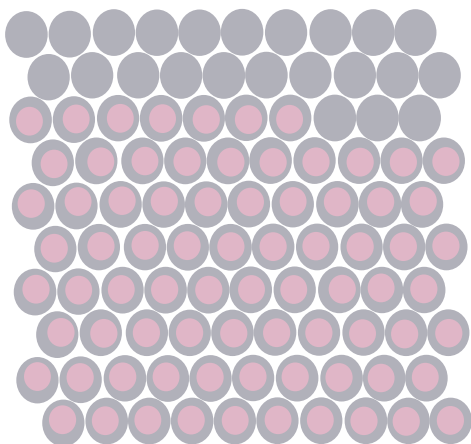
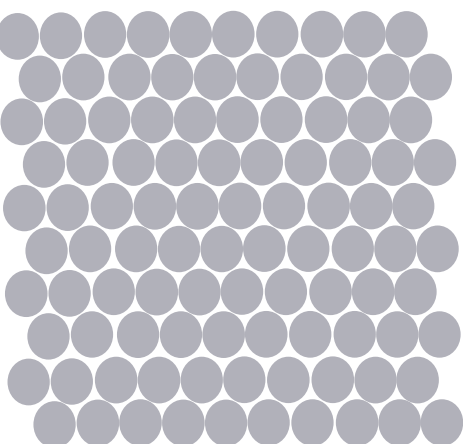




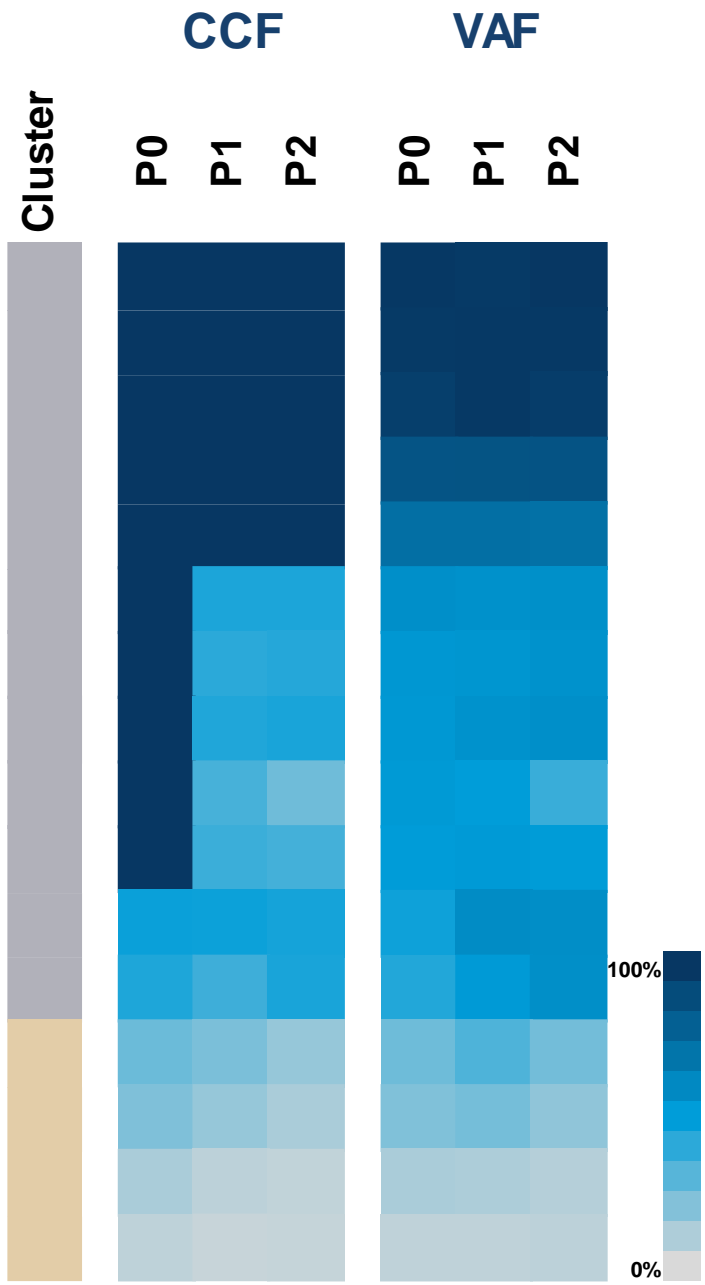
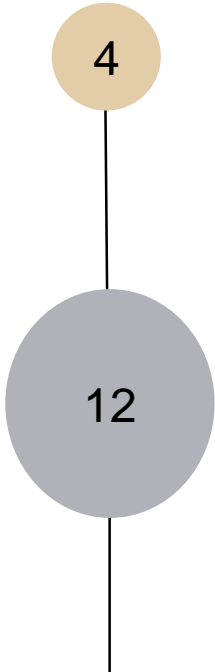
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P2



100%
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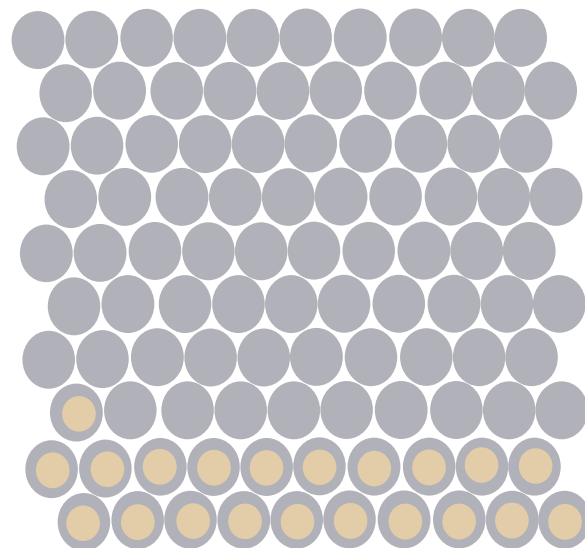
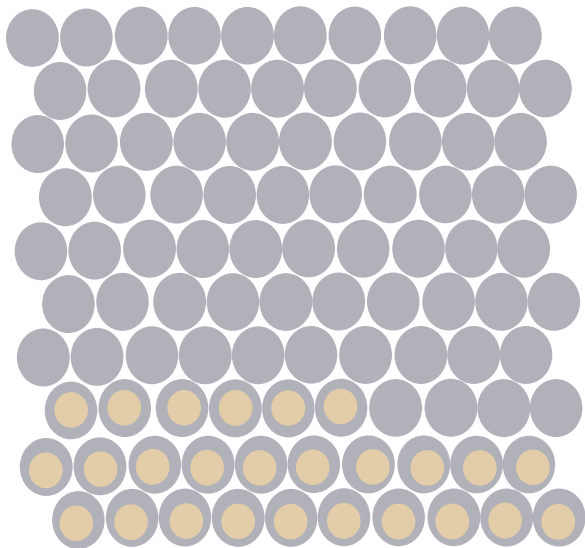
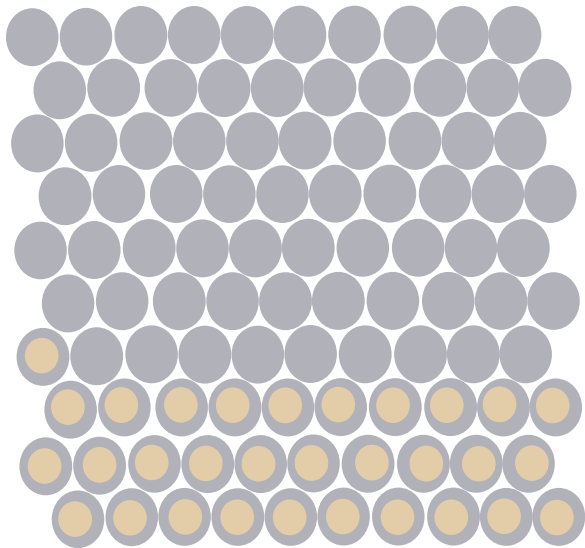
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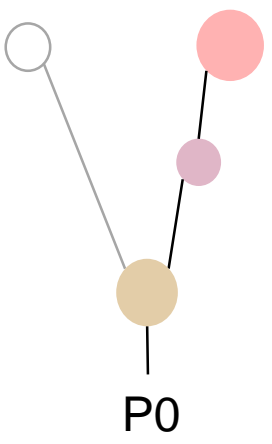
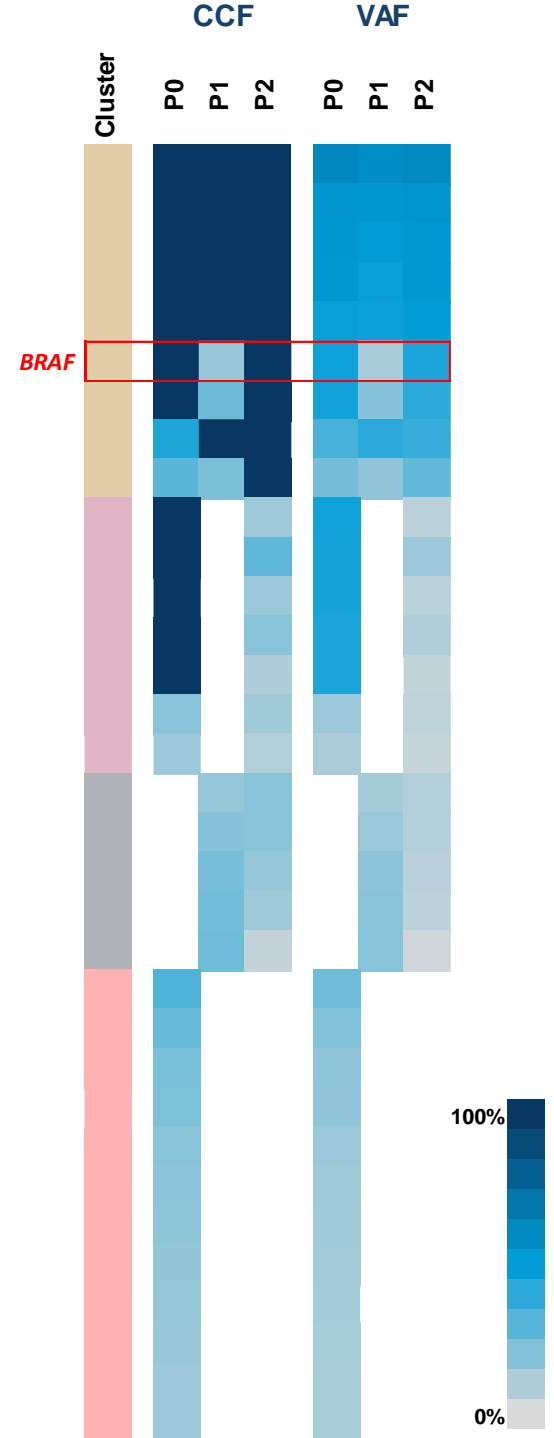
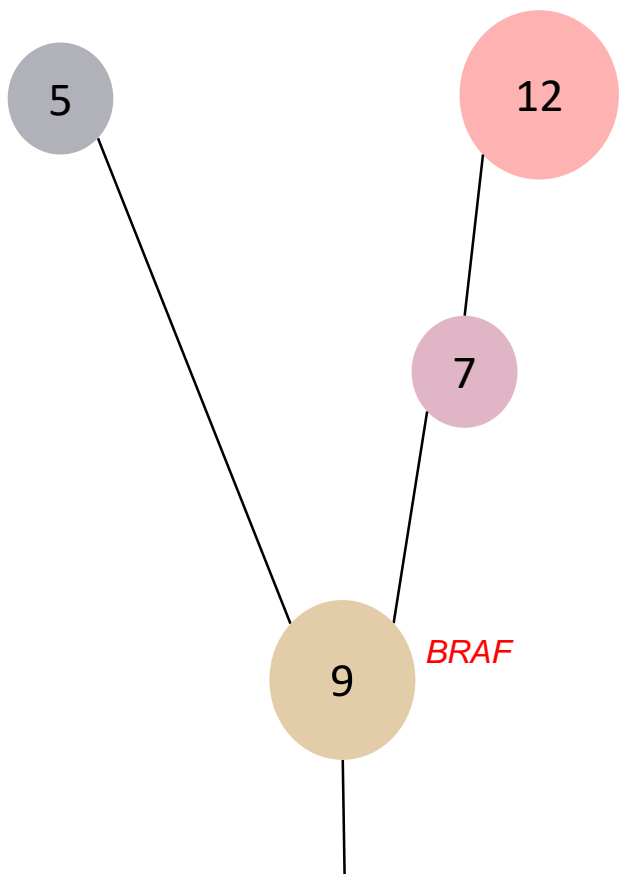


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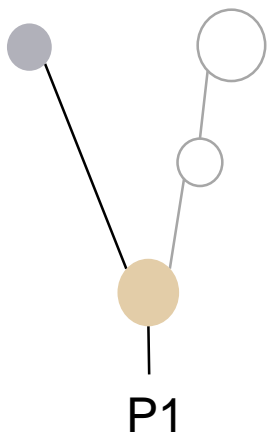


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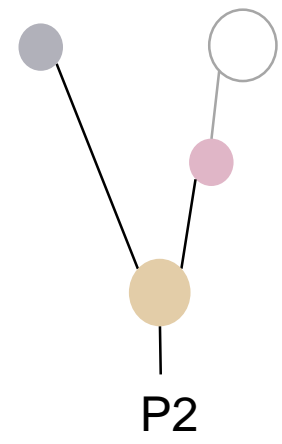




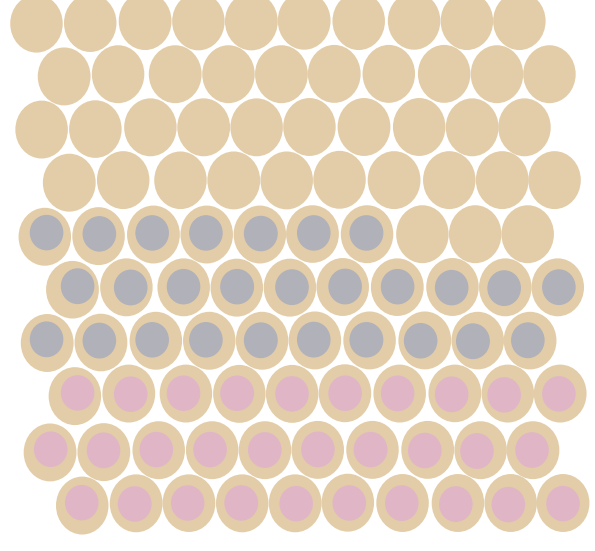
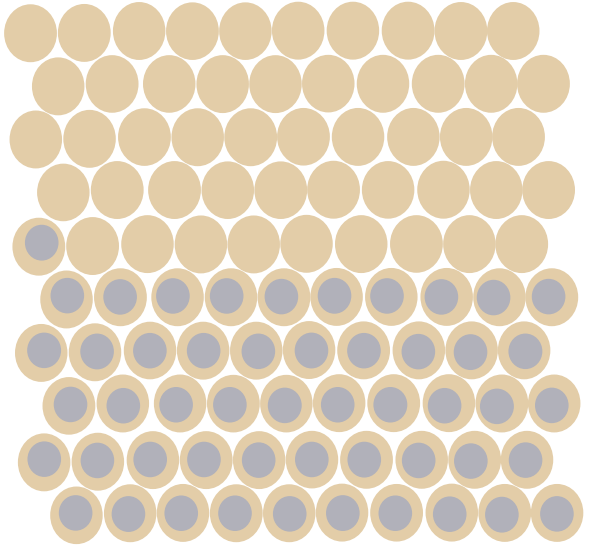
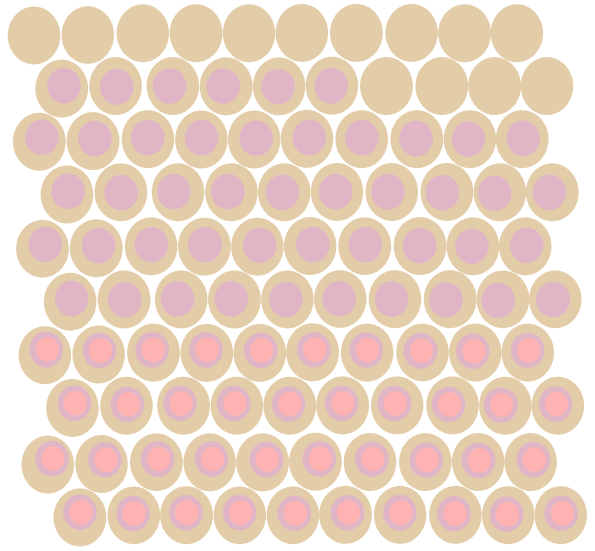
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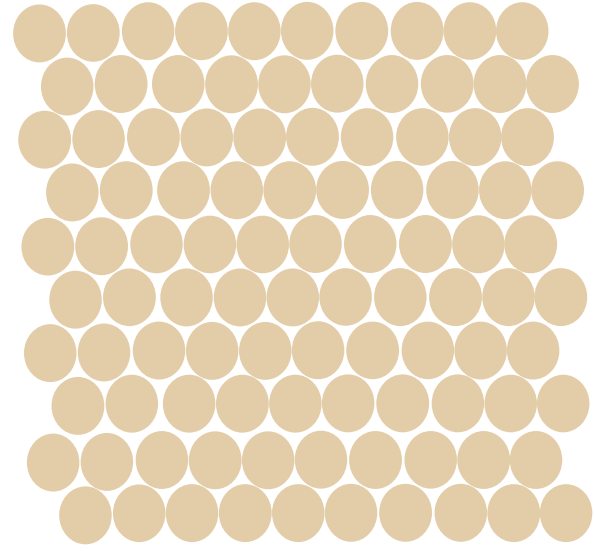
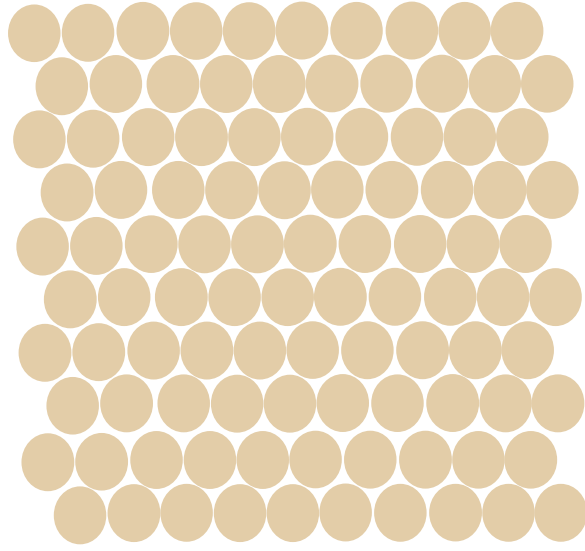
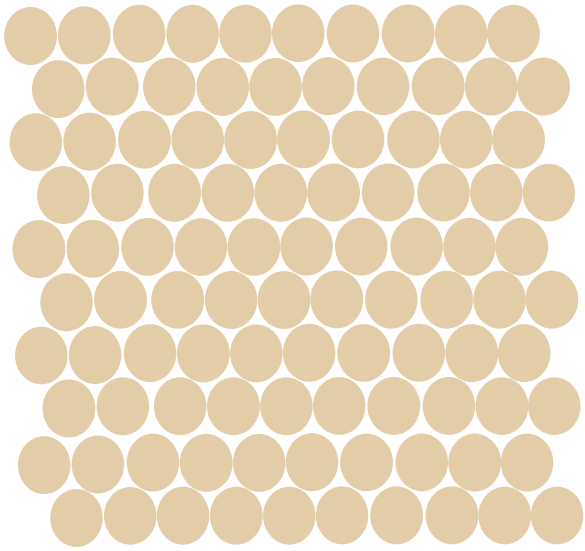
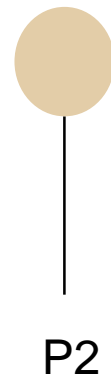
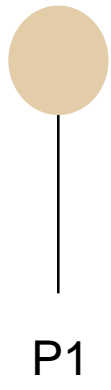
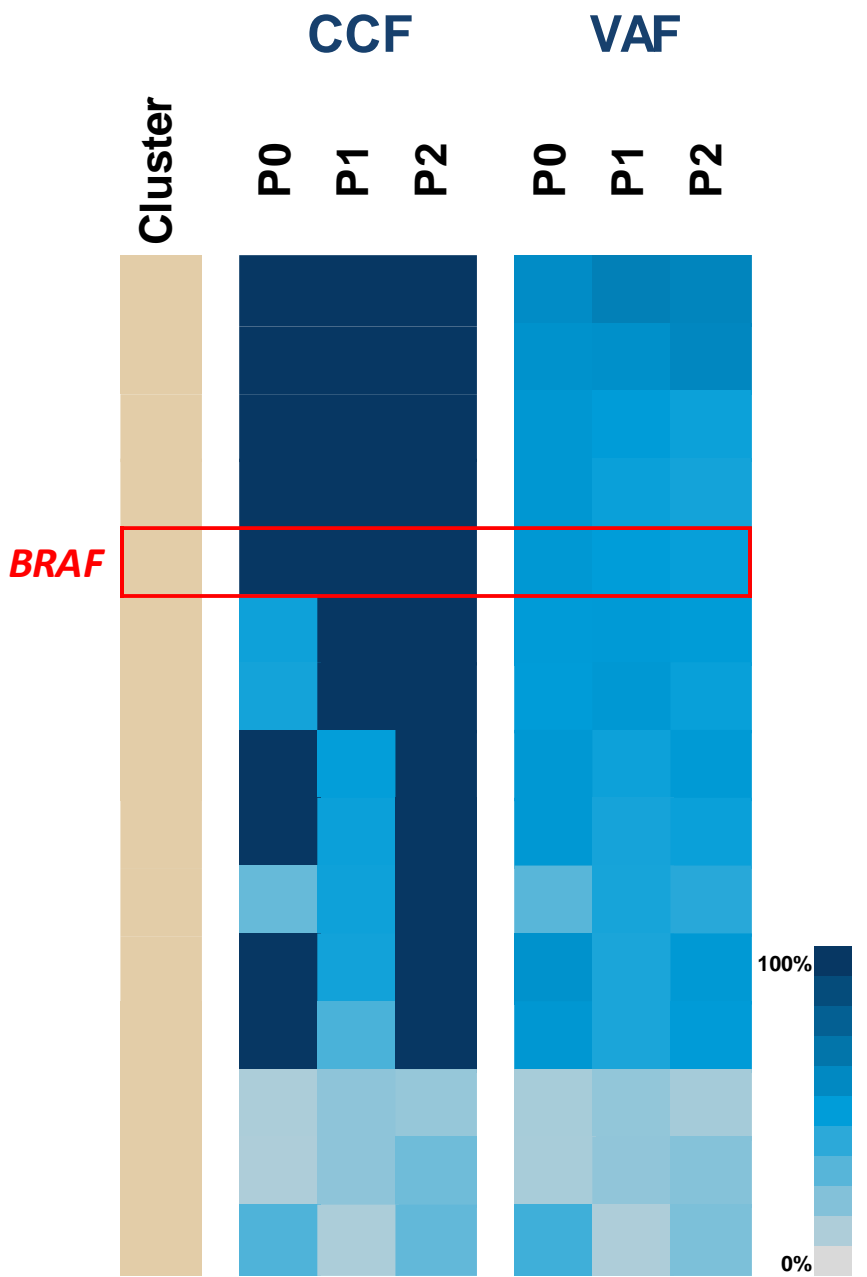
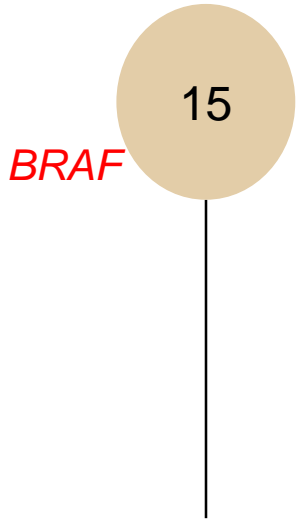


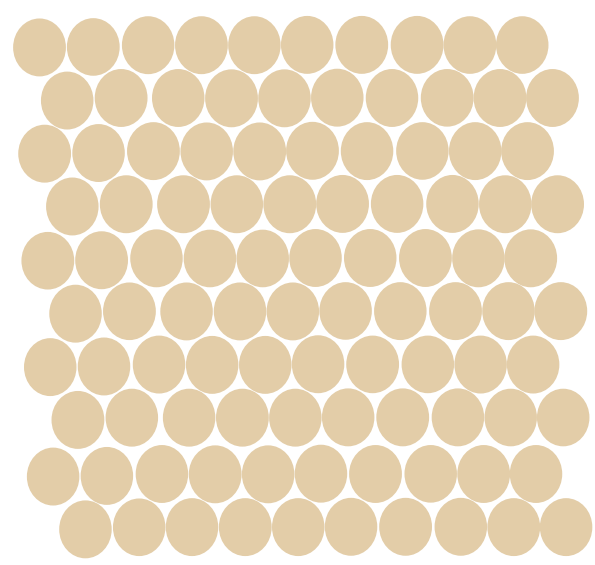
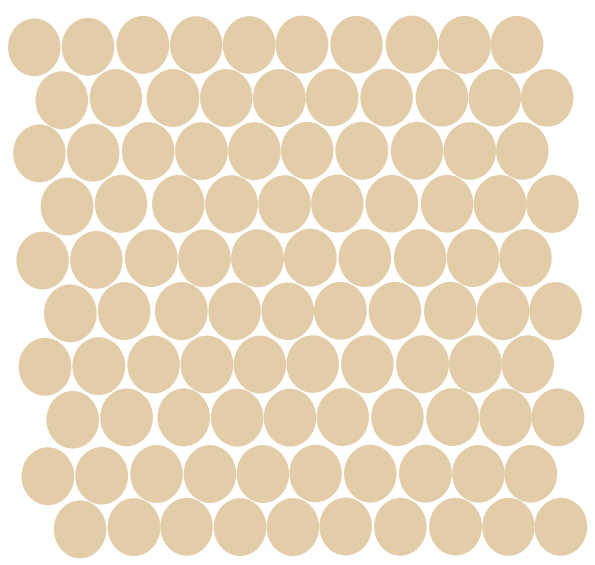
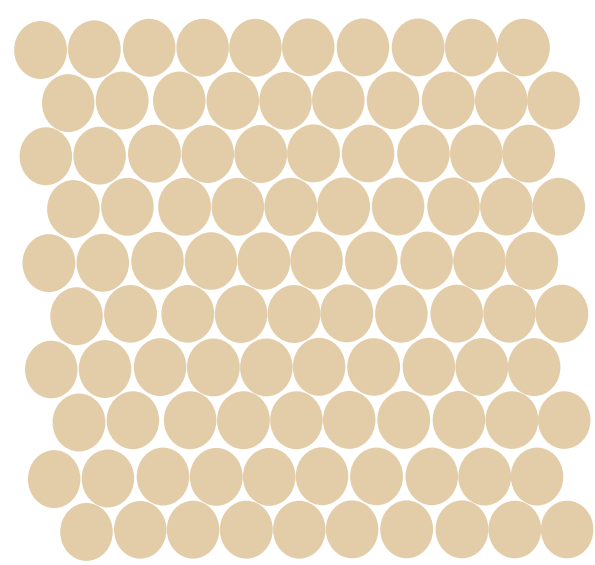
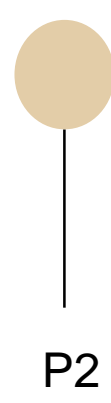
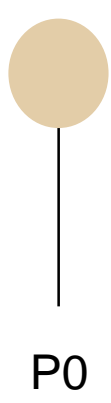
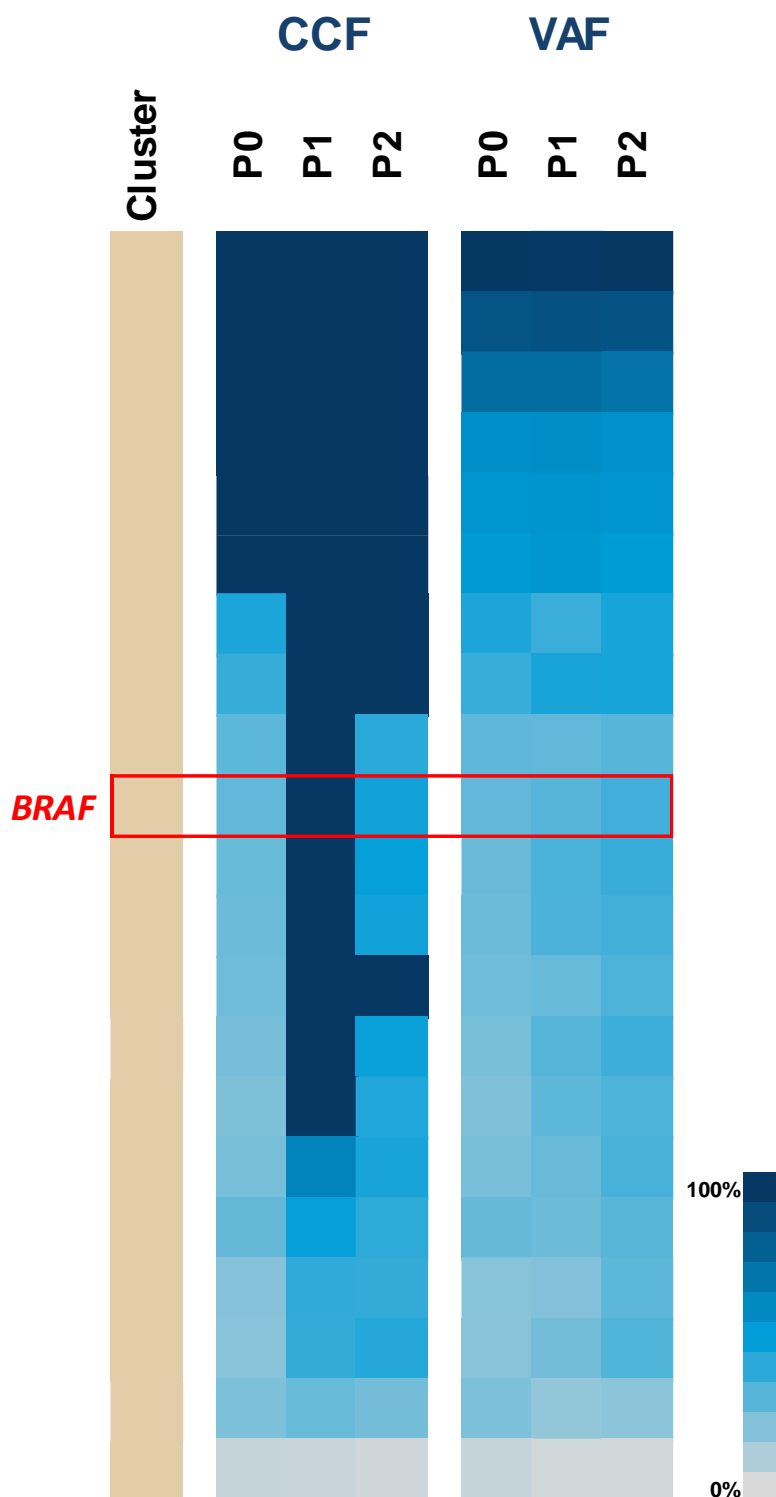
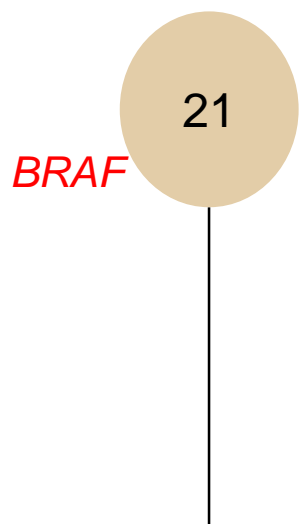
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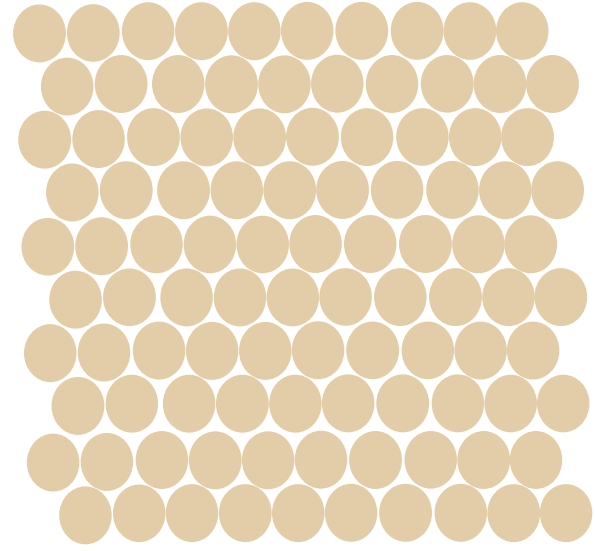
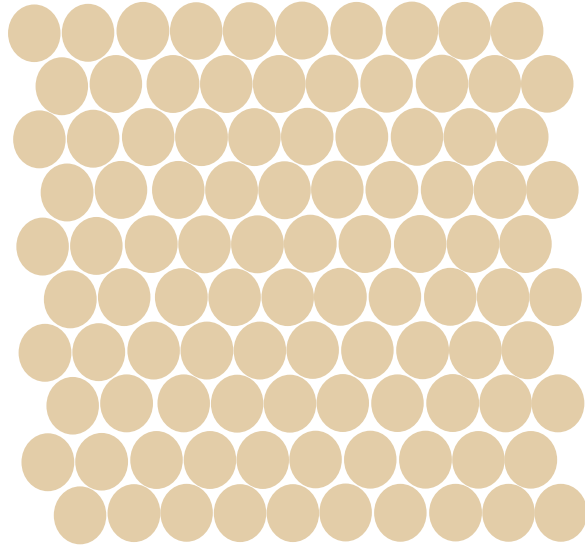
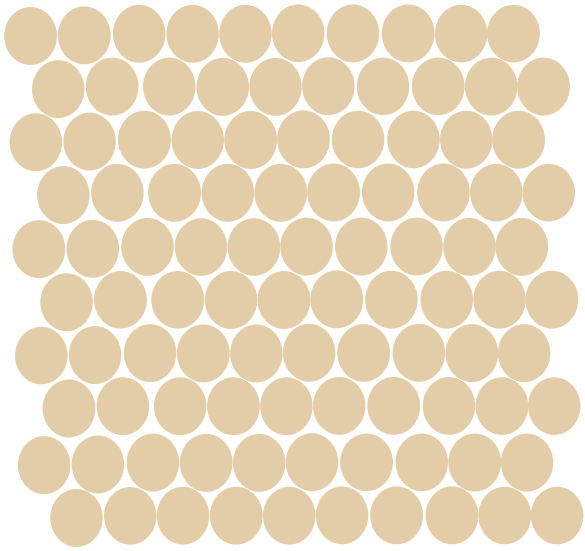
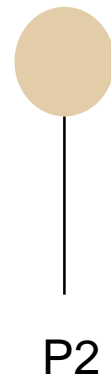
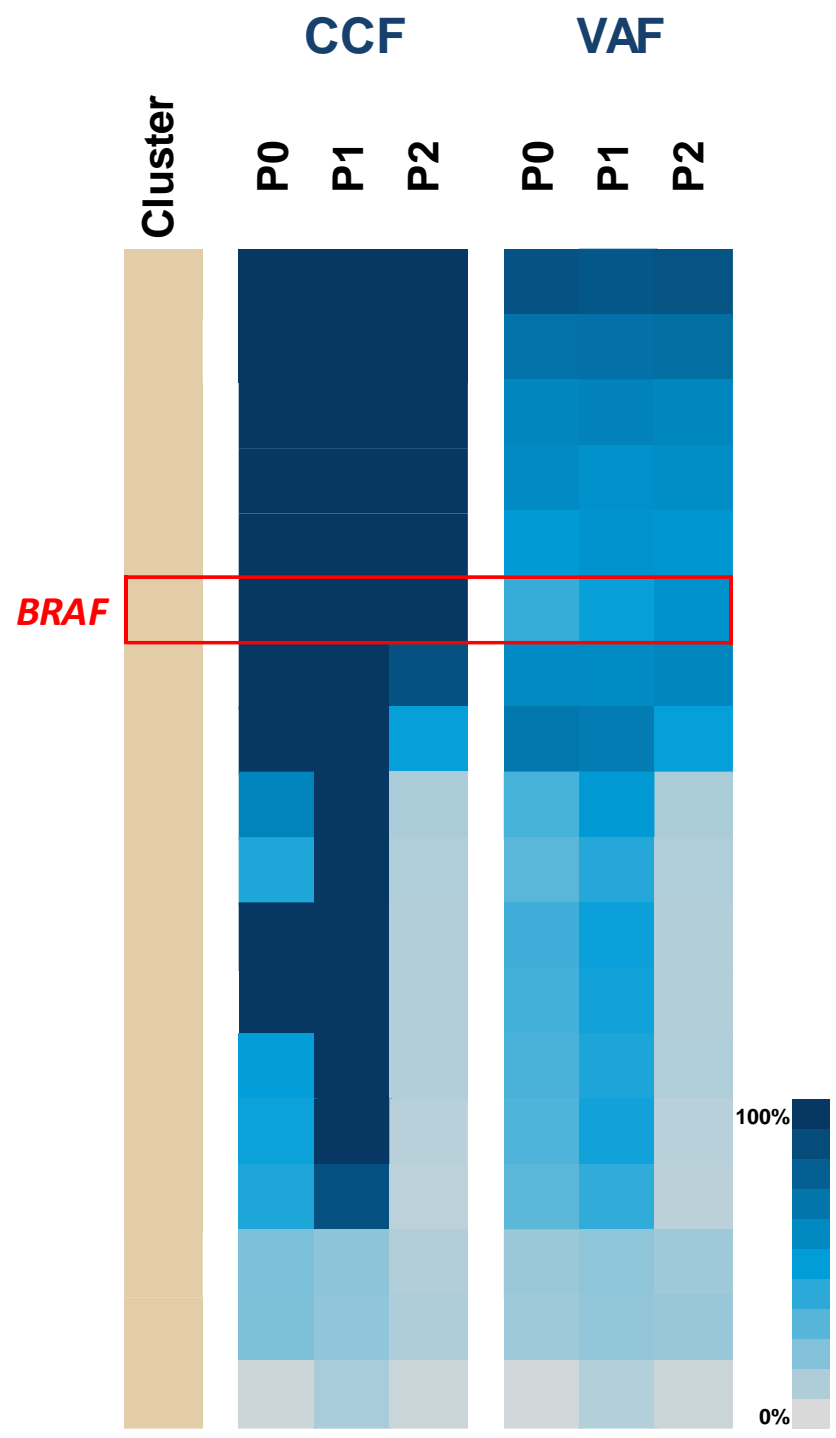
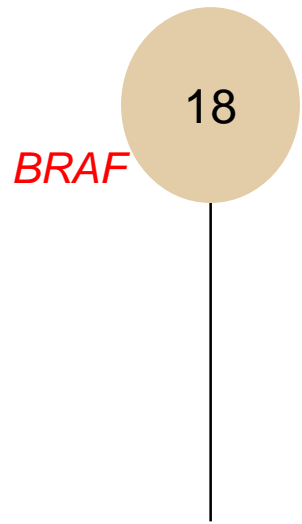


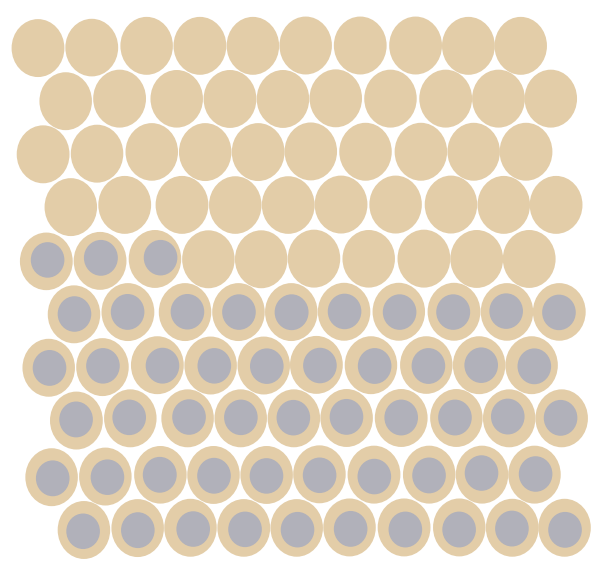
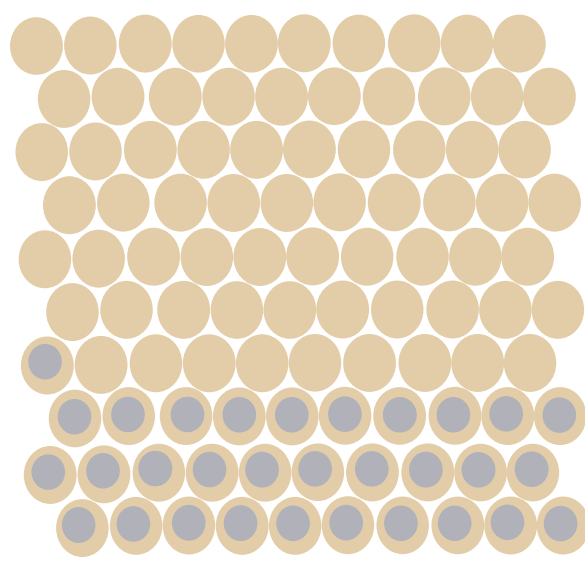
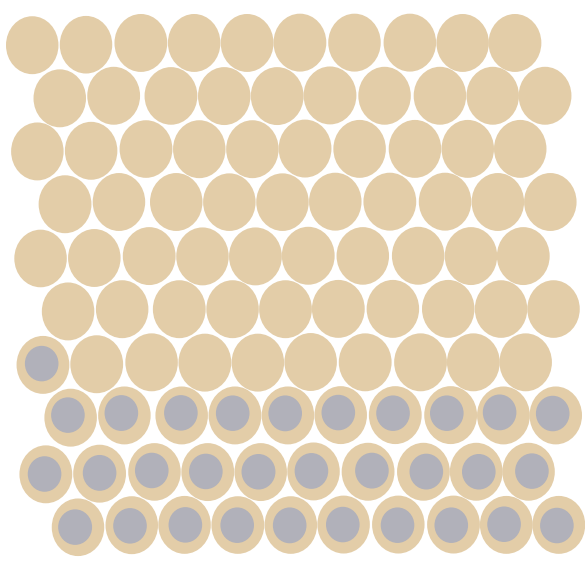
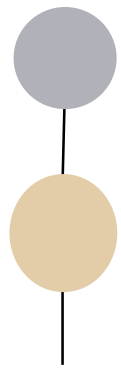
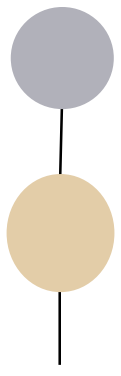
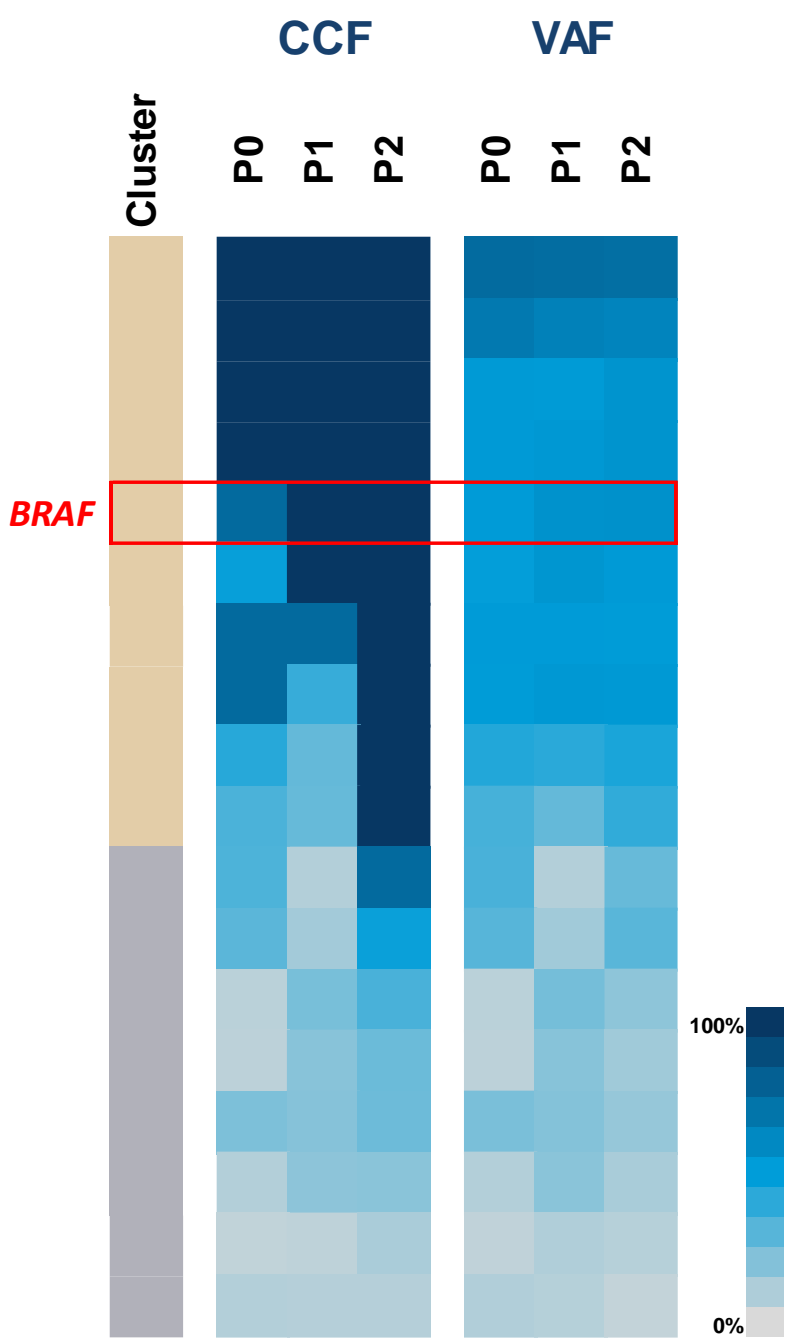
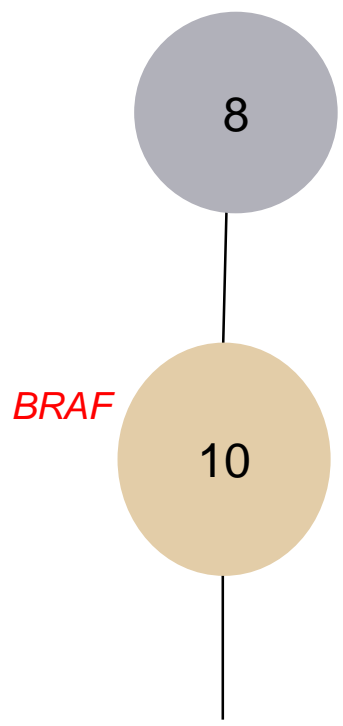
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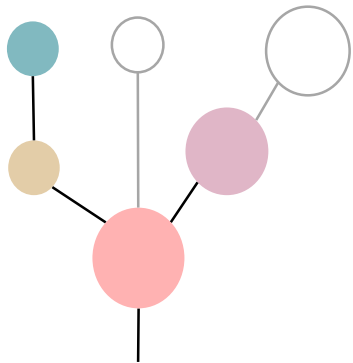
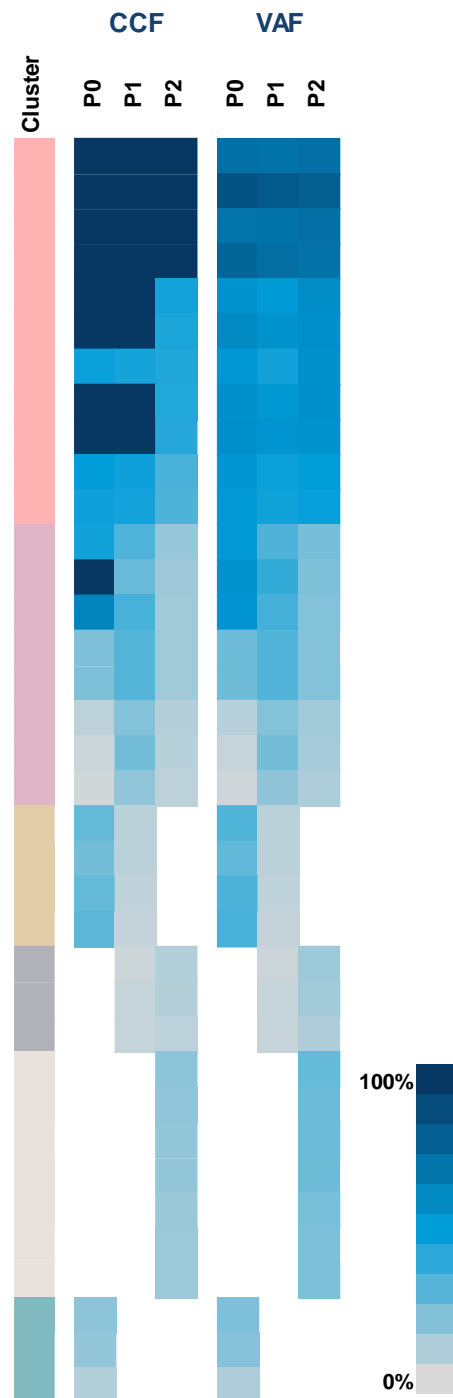
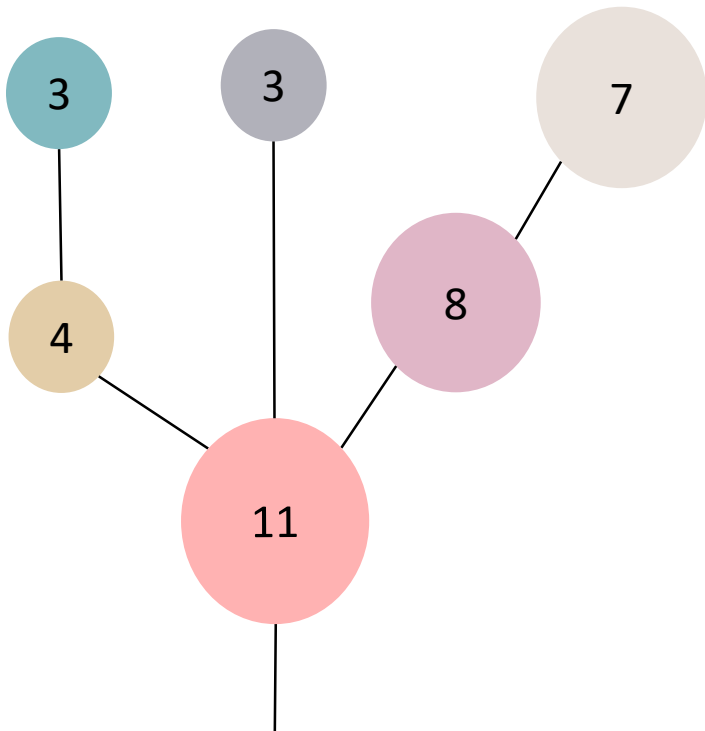




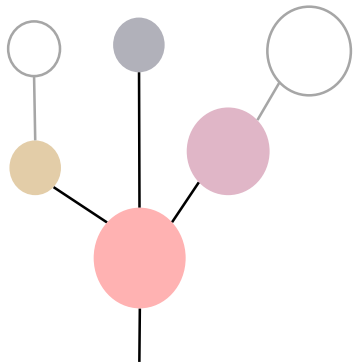




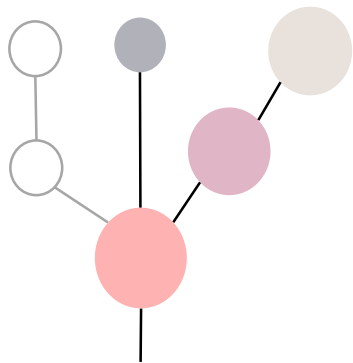




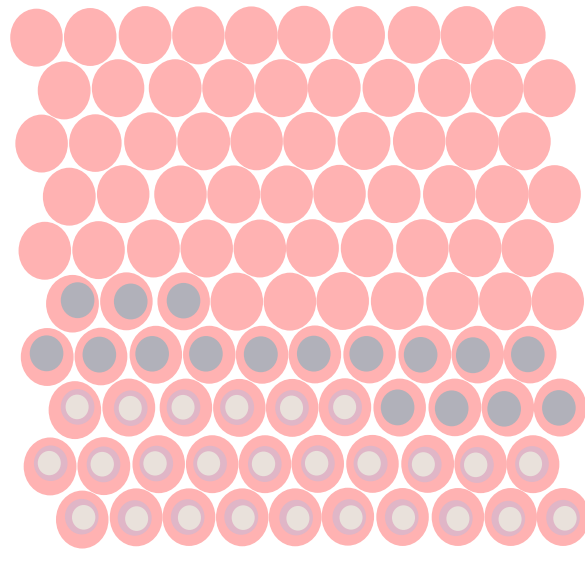
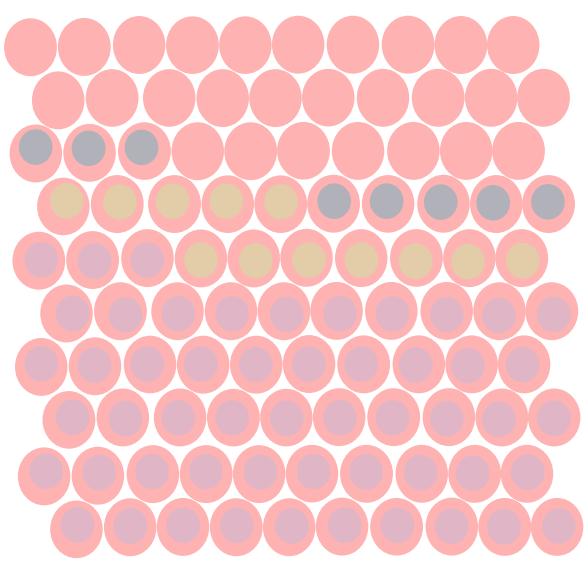
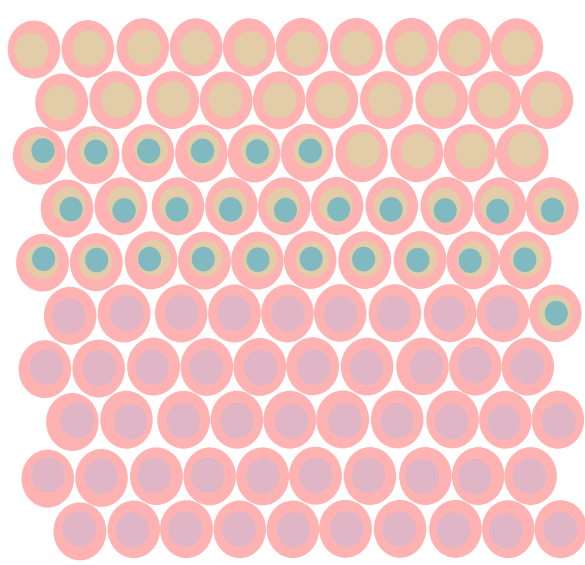
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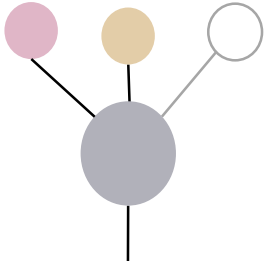
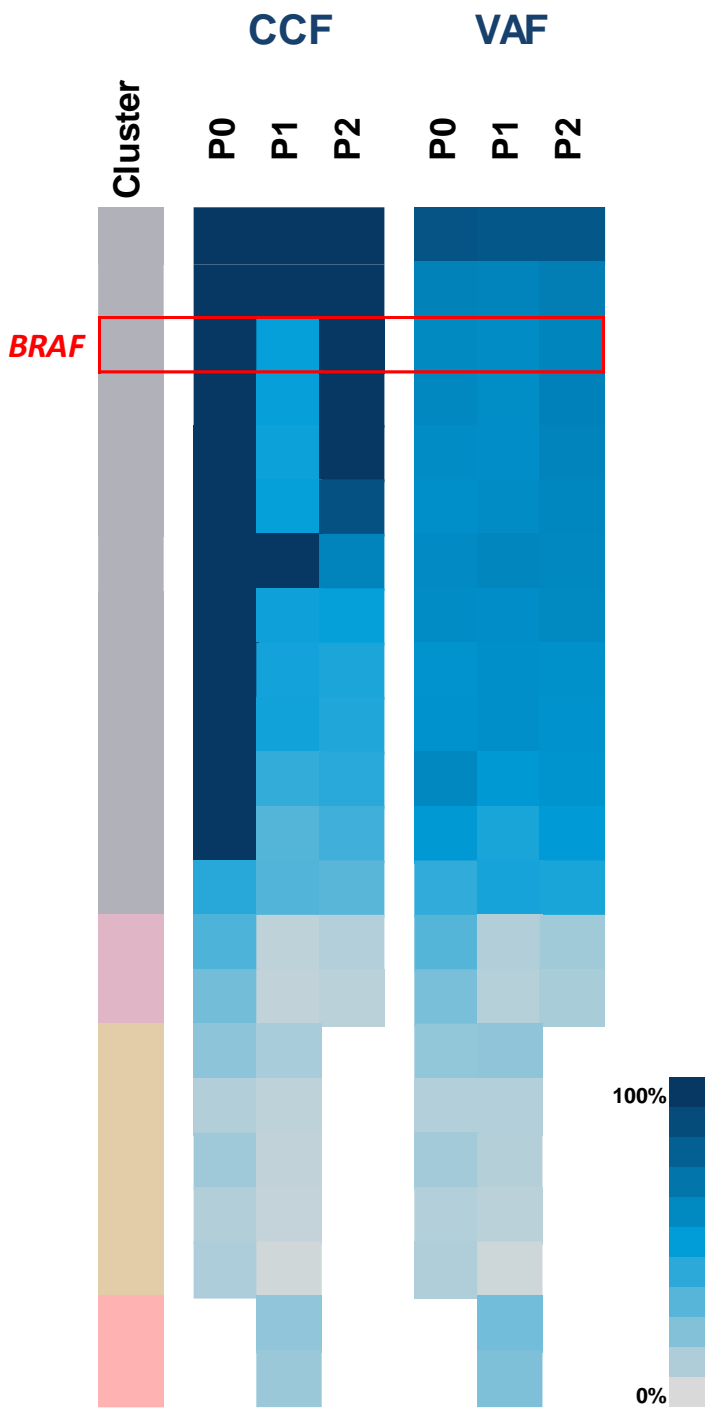
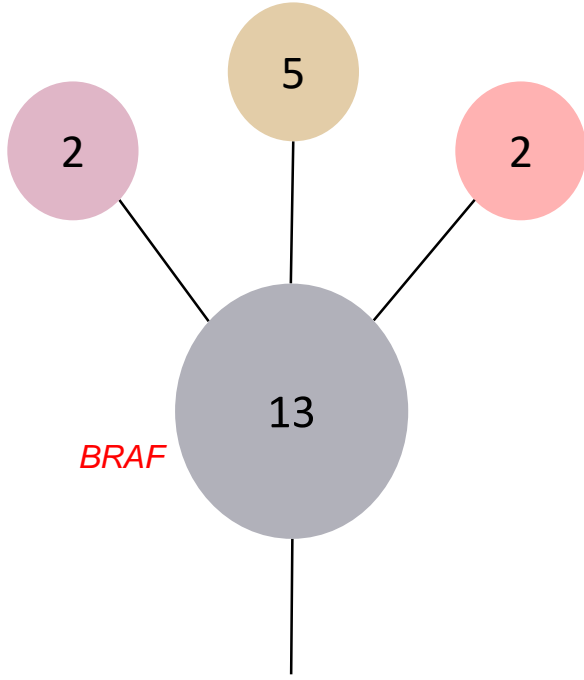


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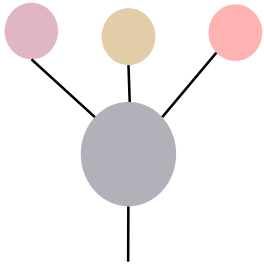


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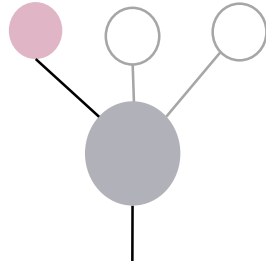




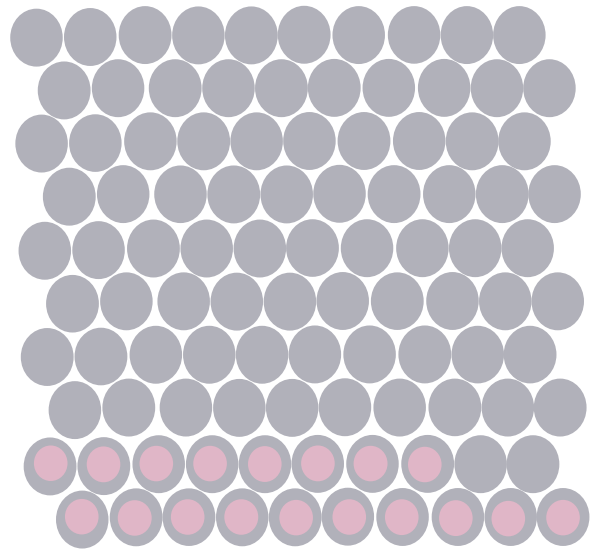
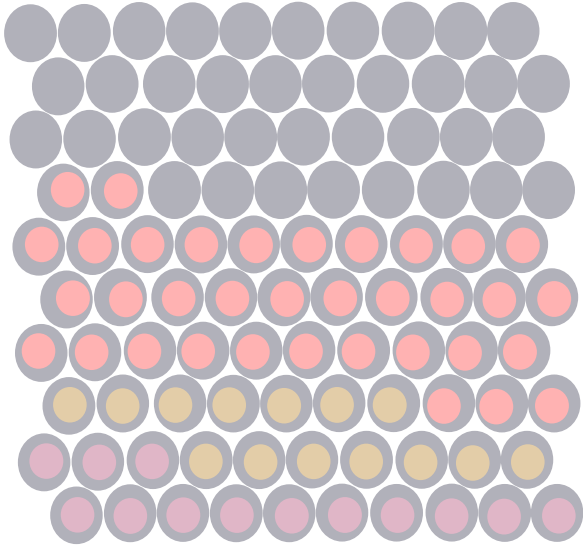
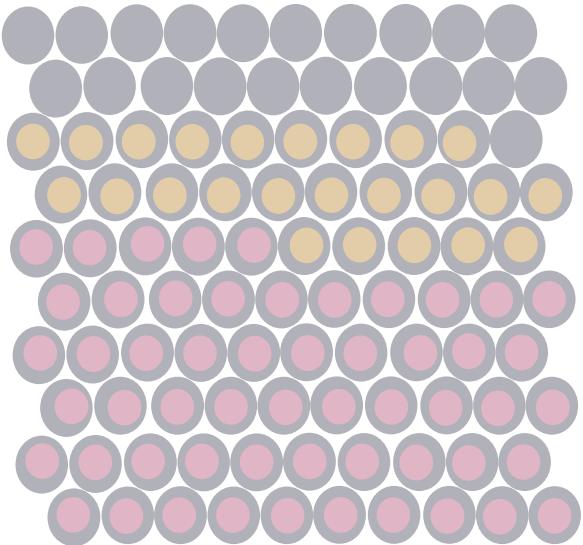
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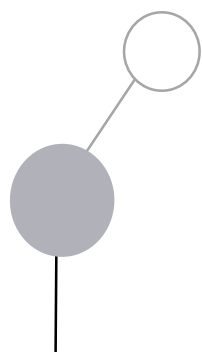
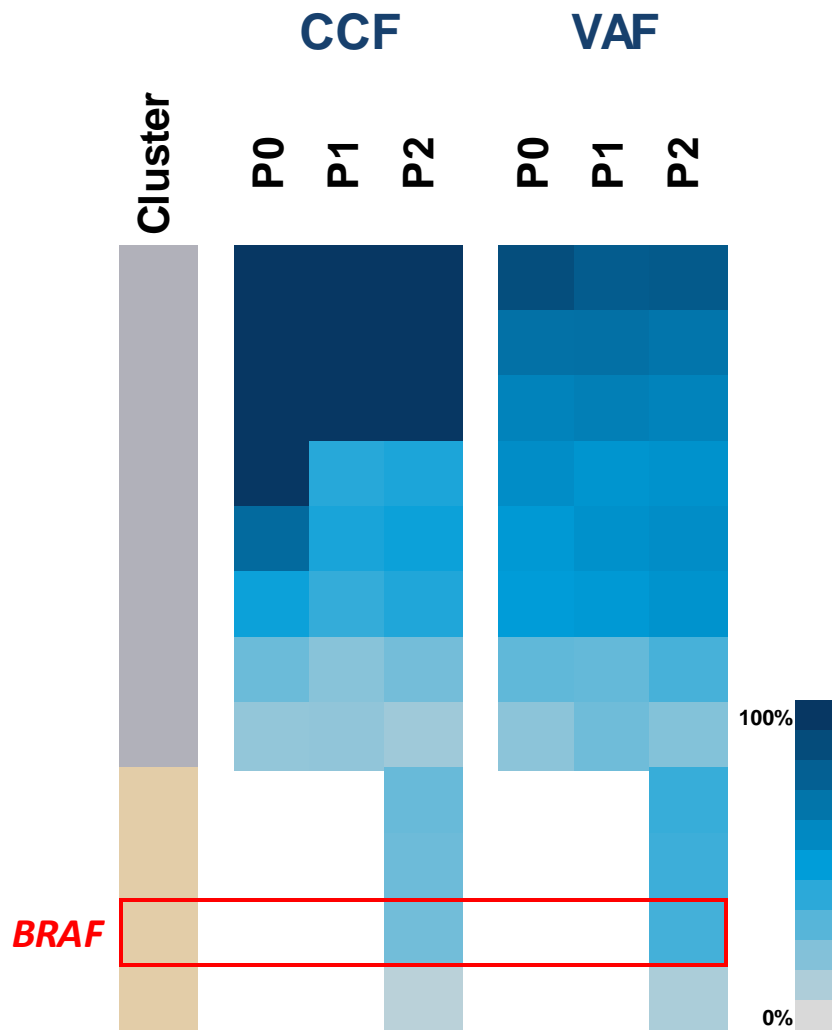
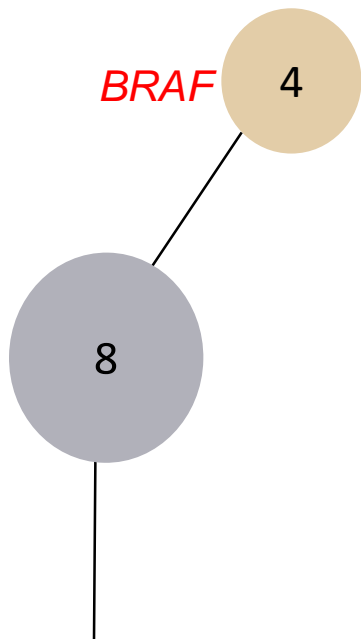


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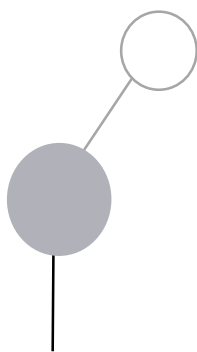


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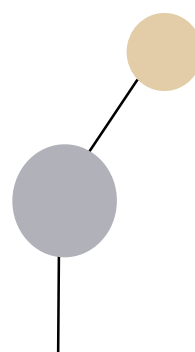




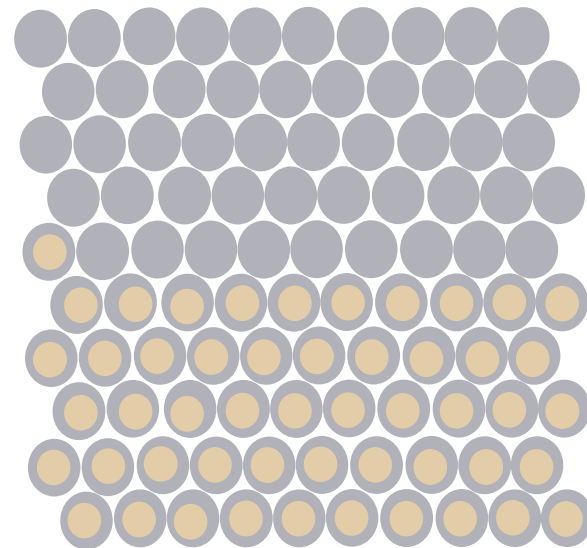
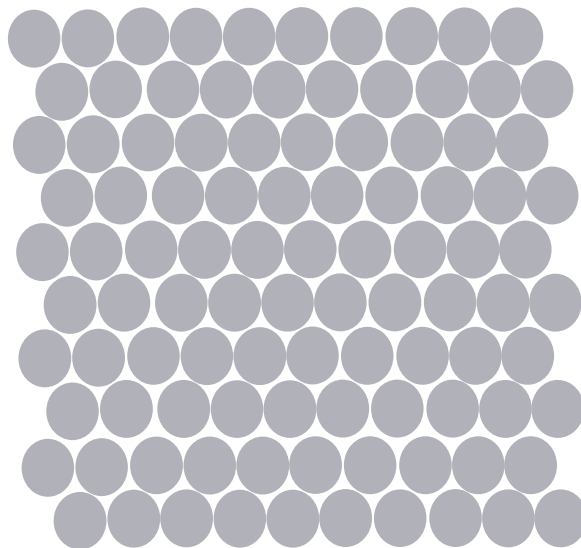
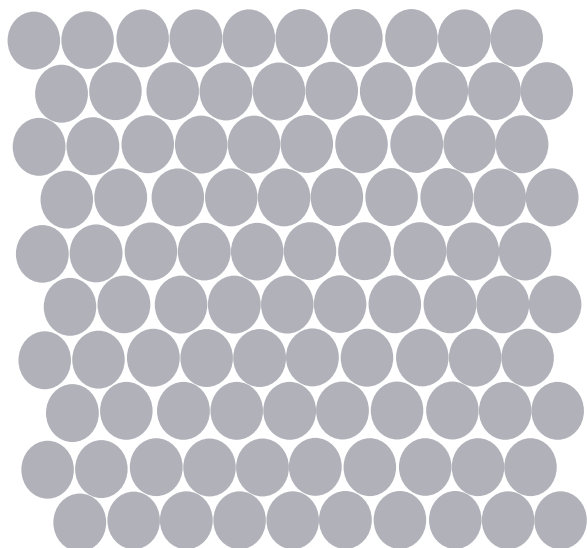
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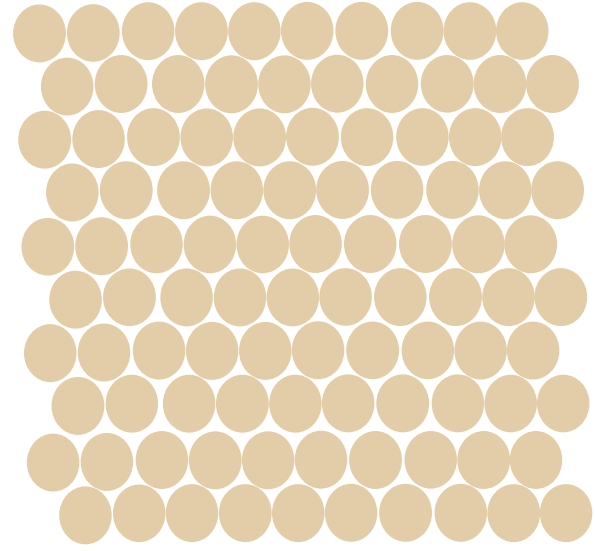
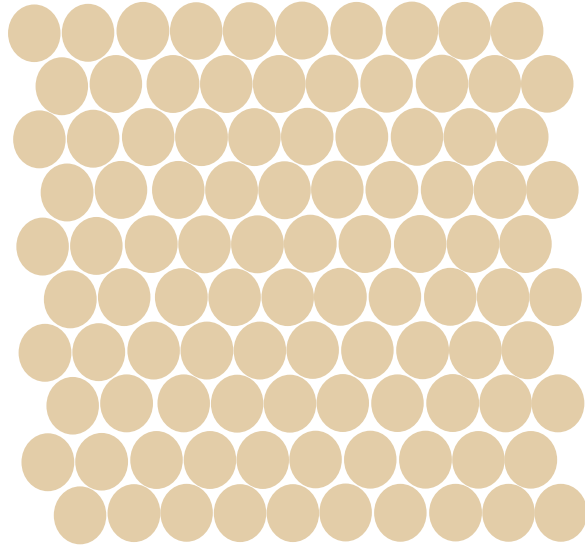
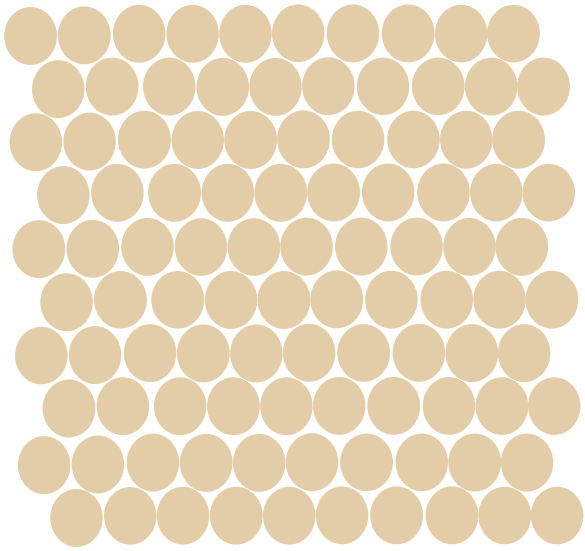
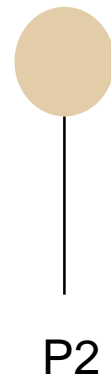
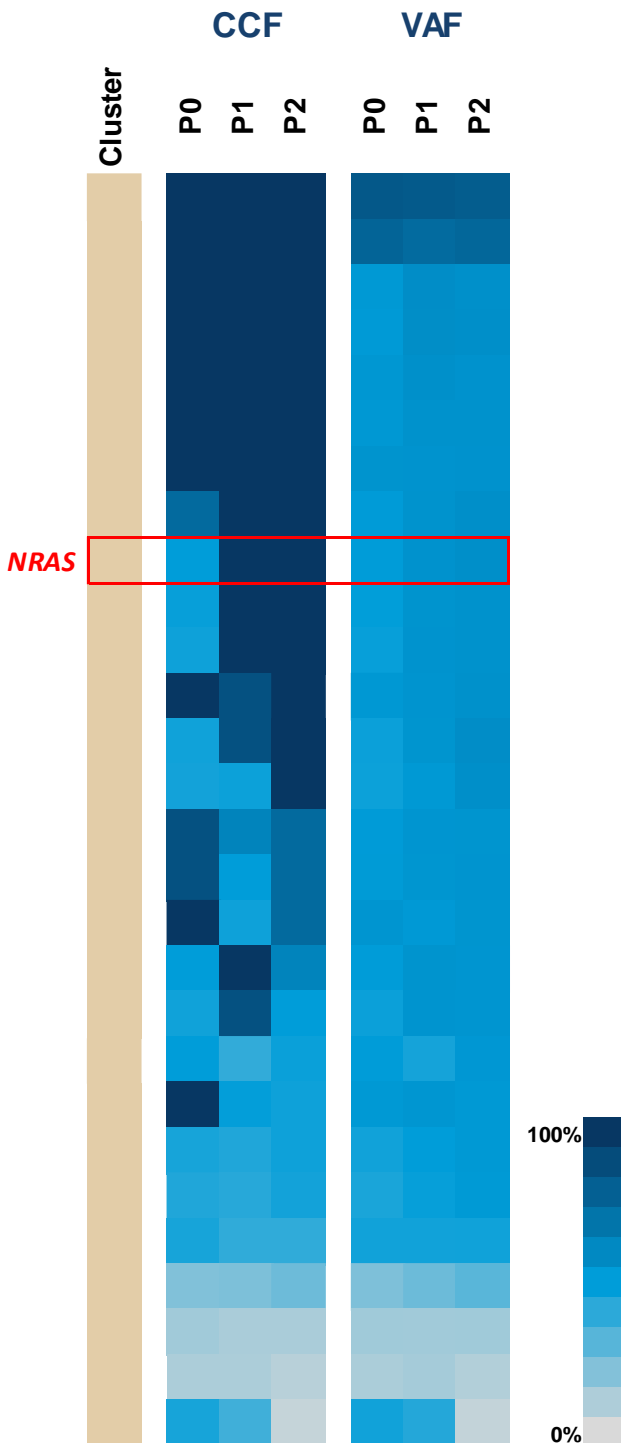
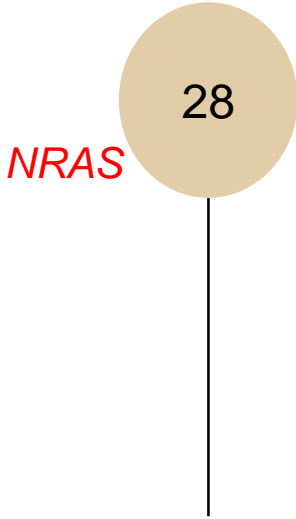


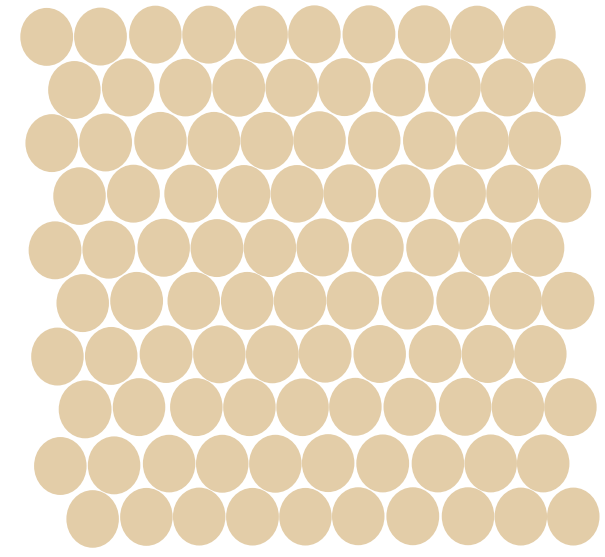
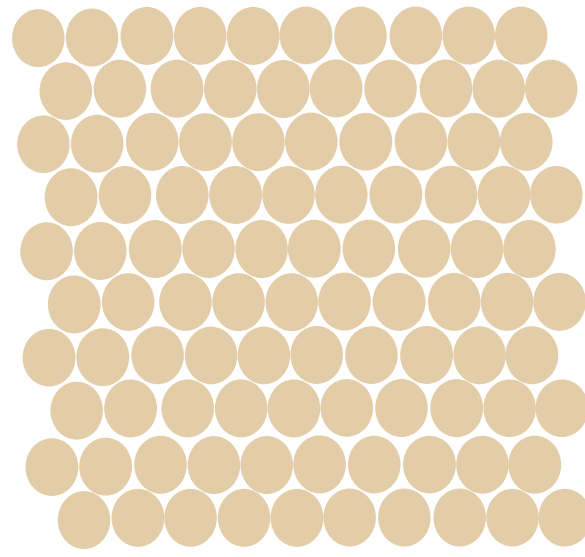
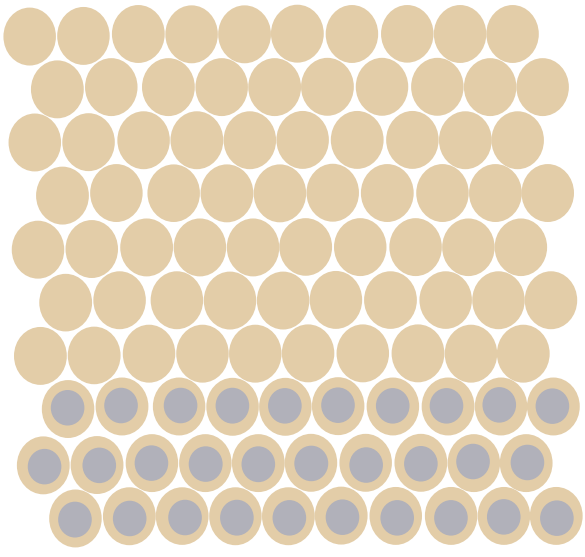
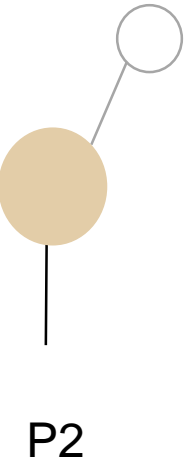
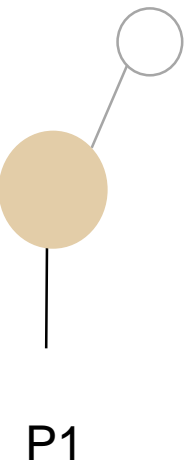
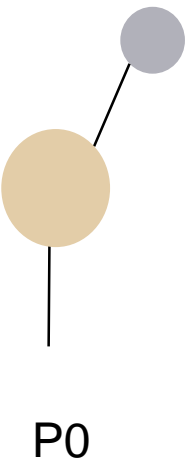
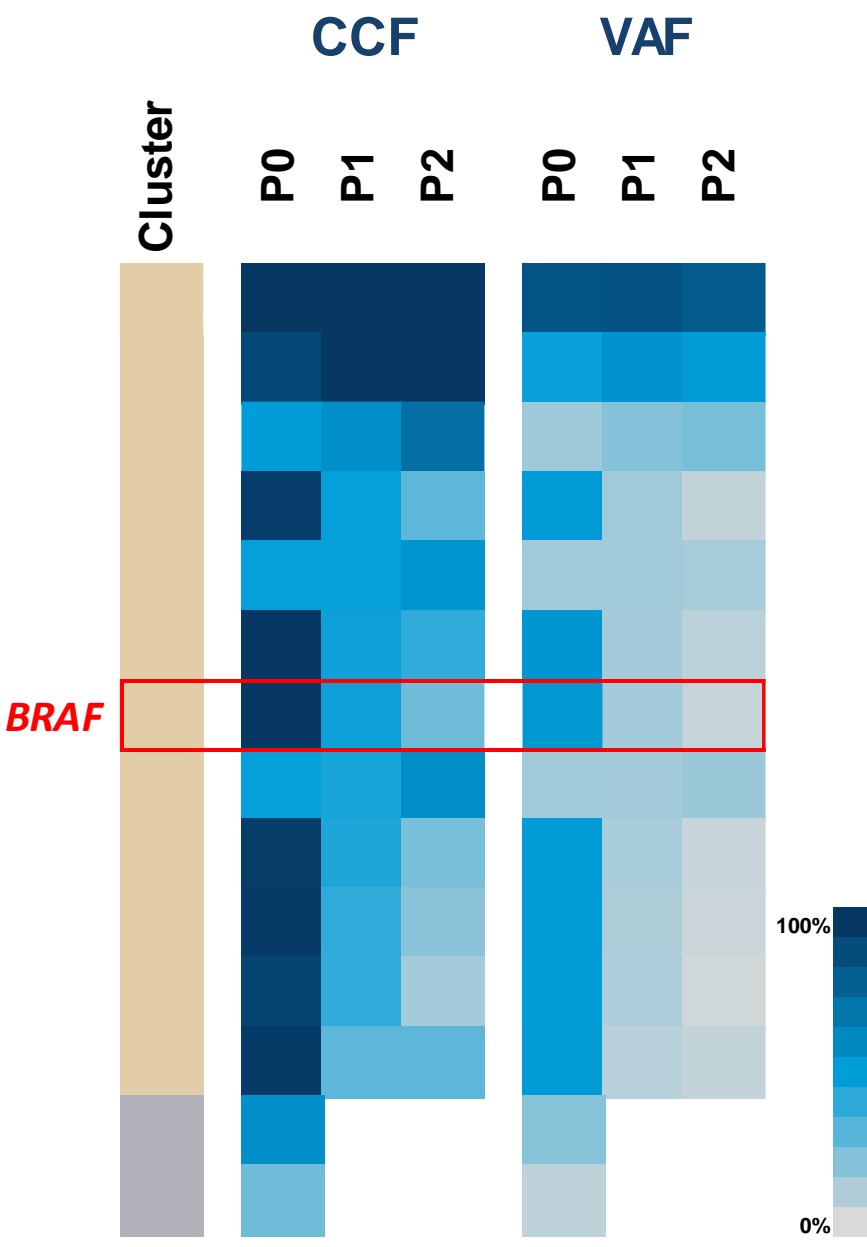
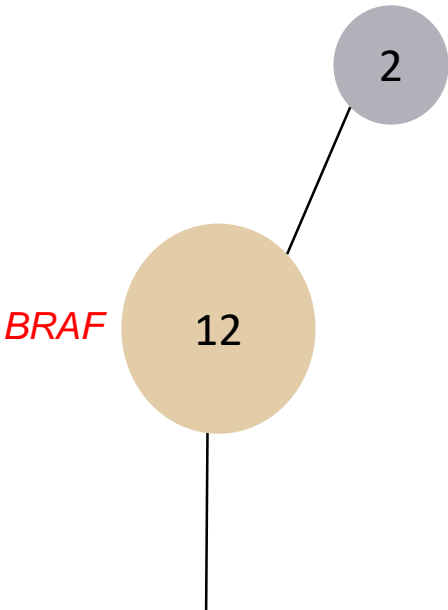
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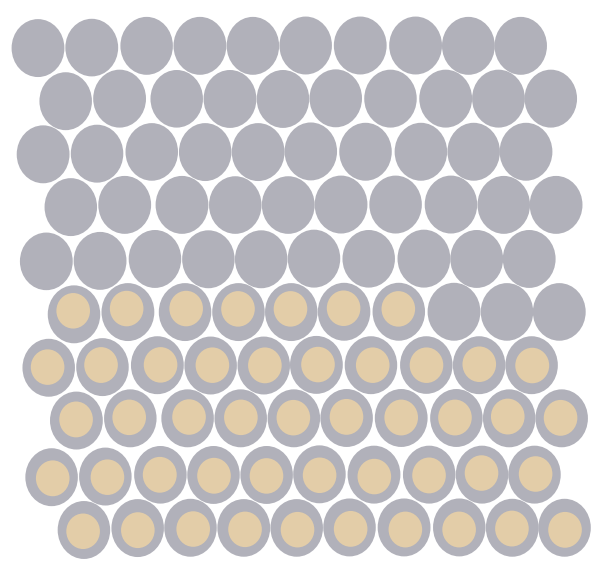
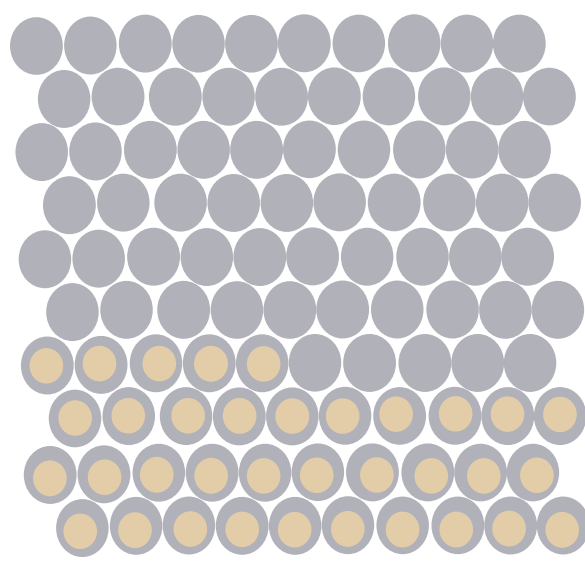
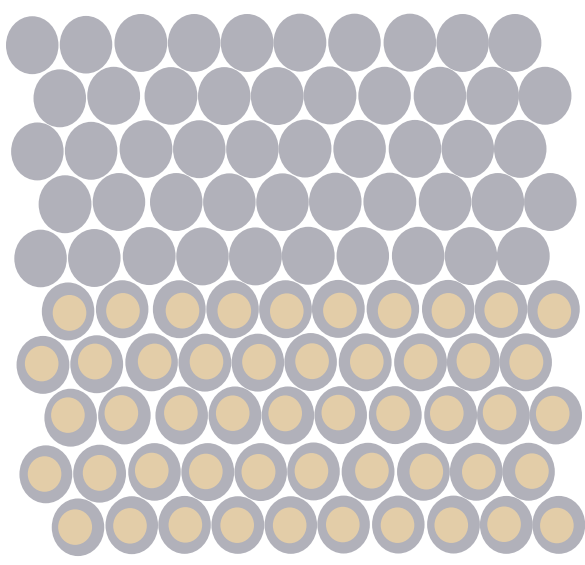
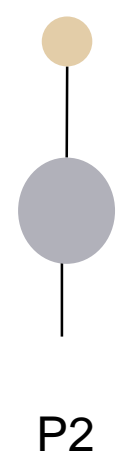
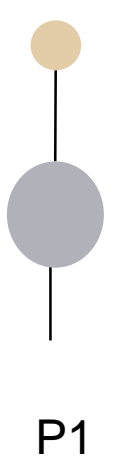
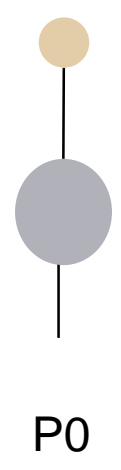
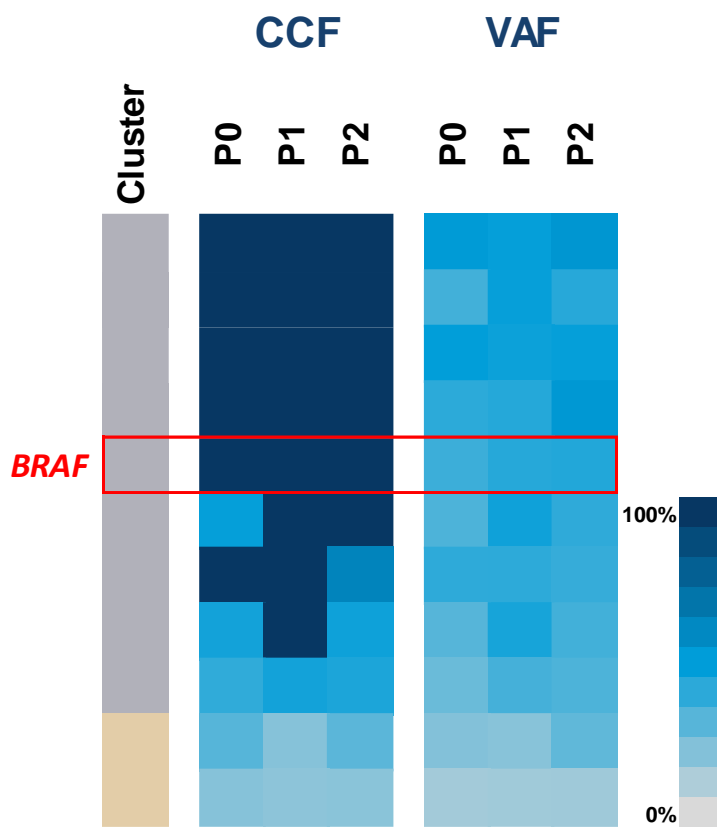
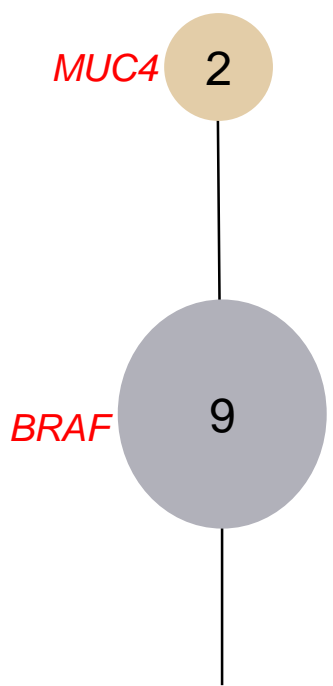
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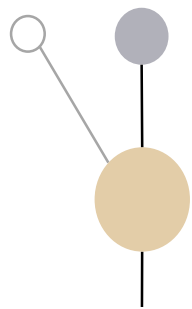
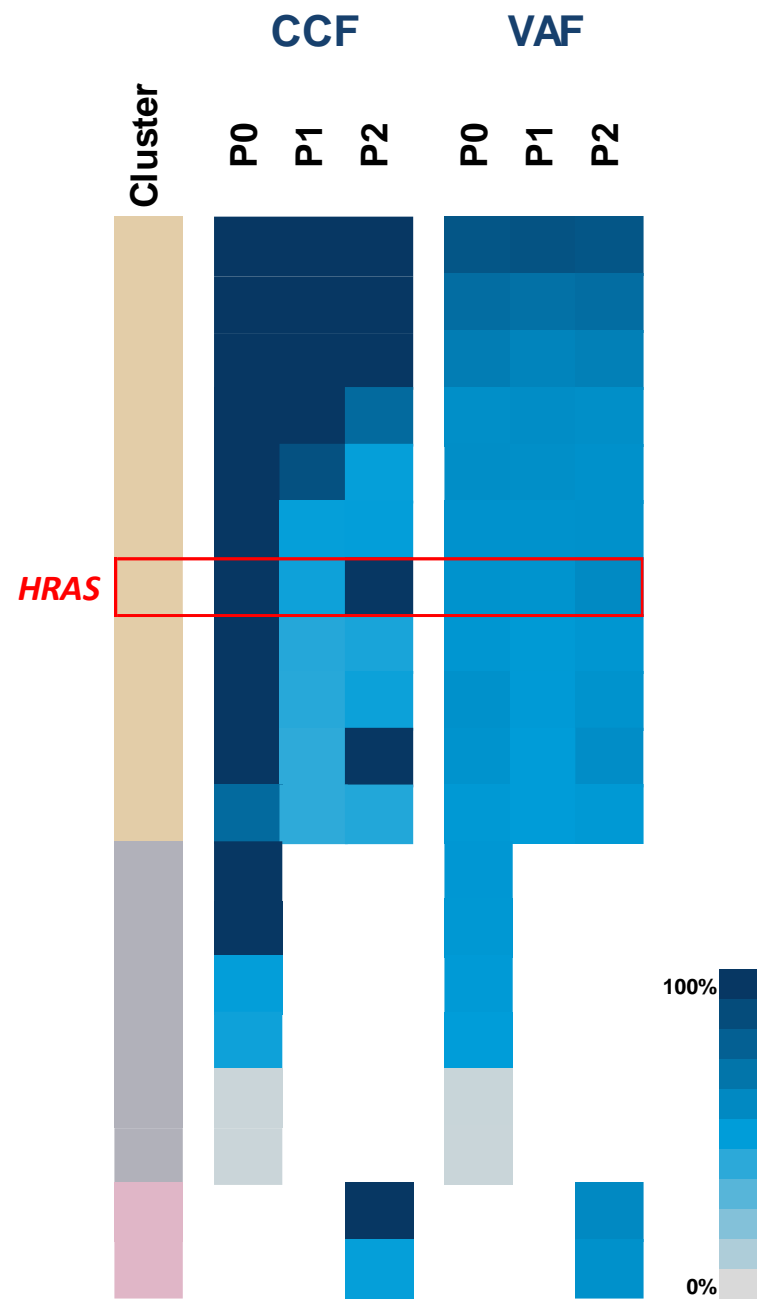
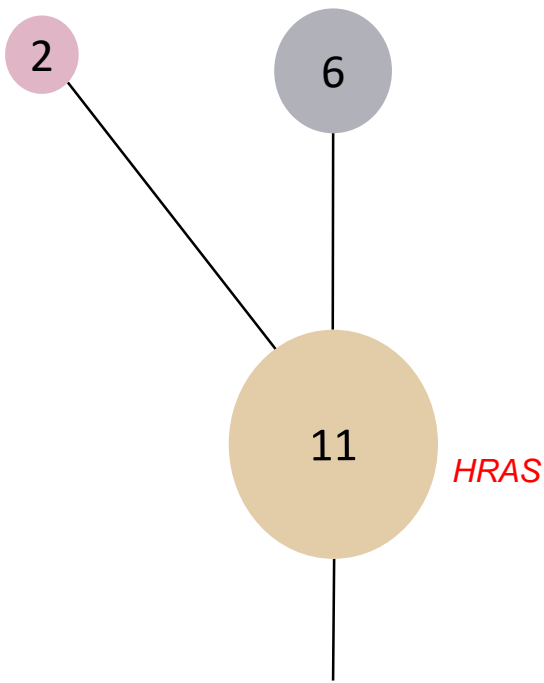




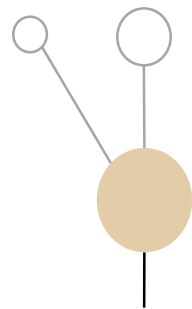


Cluster
 Gene Type
 MUC4 Amp

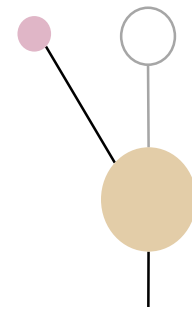




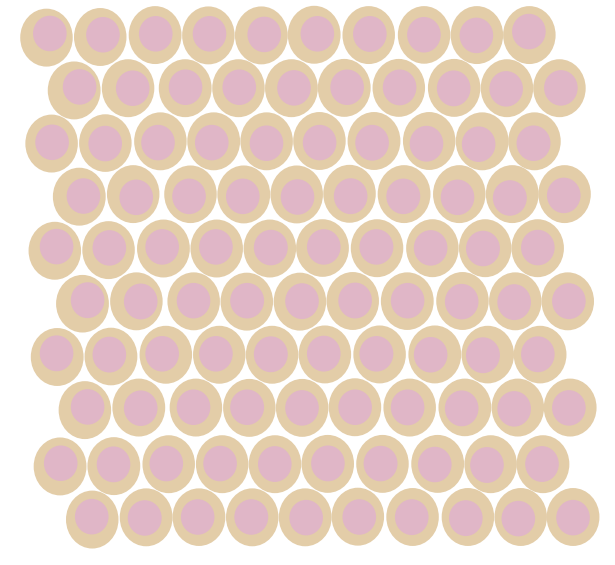
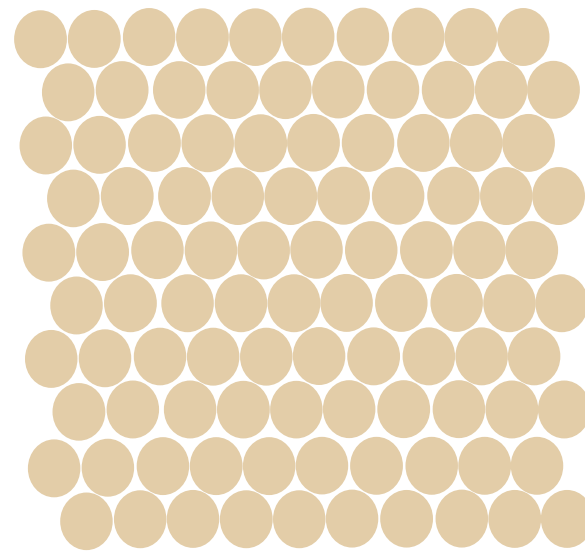
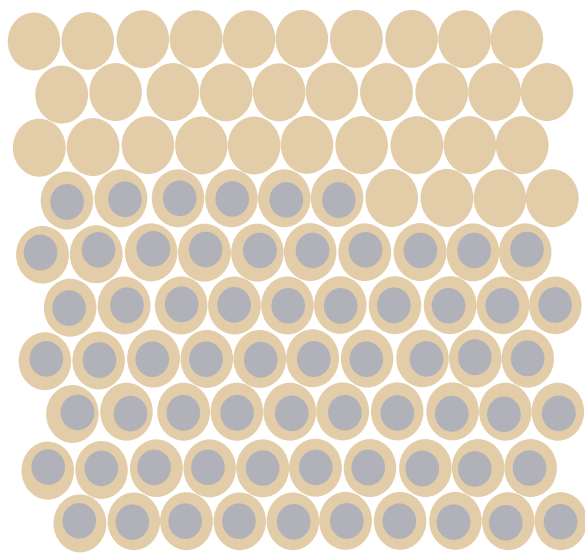
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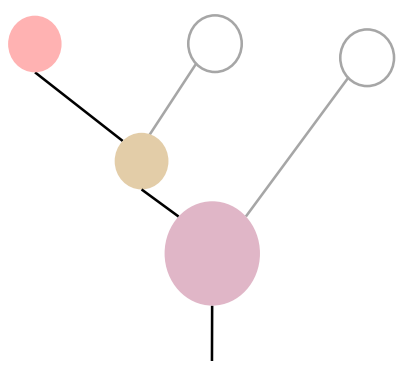
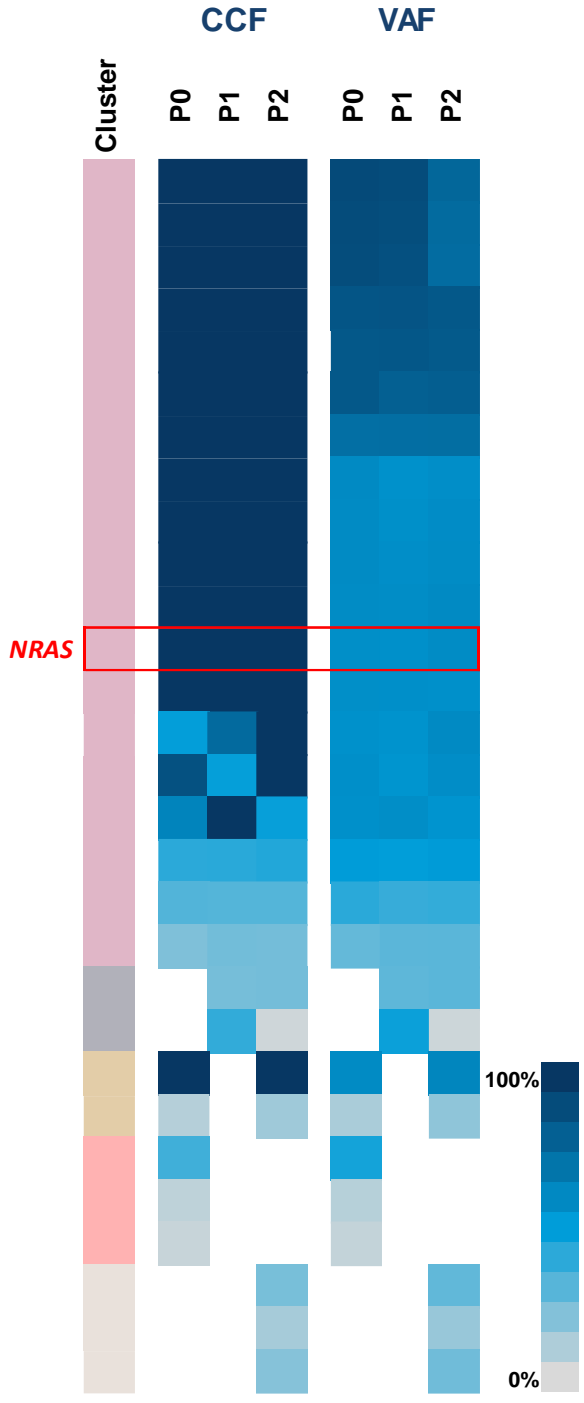
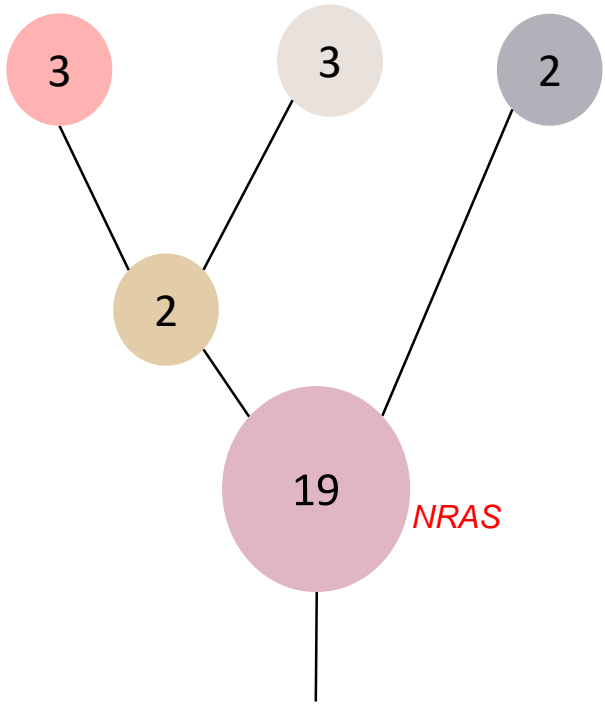


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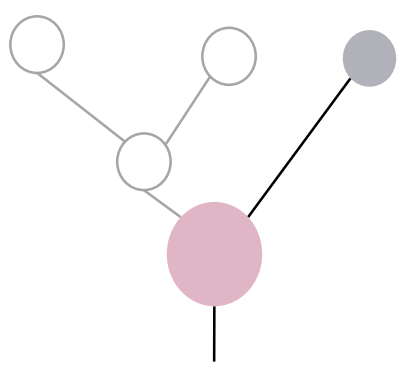


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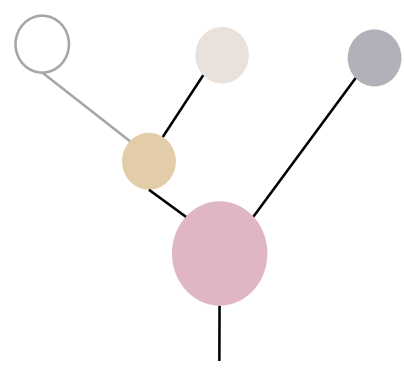




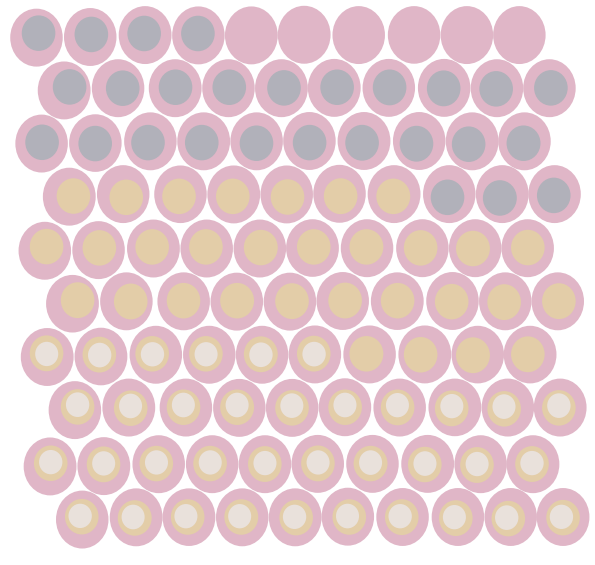
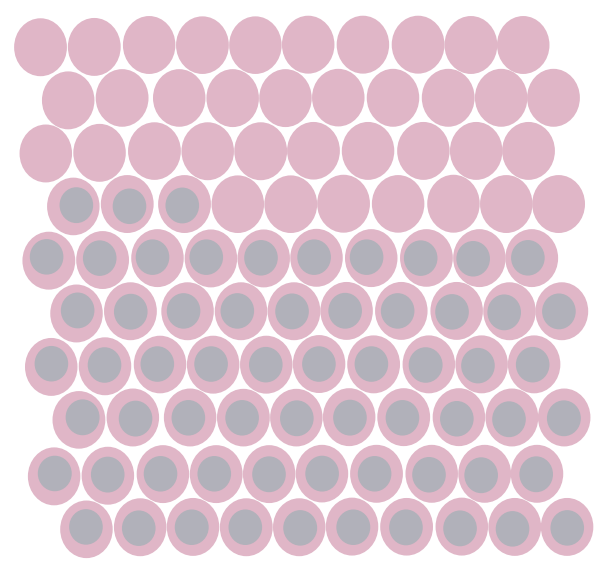
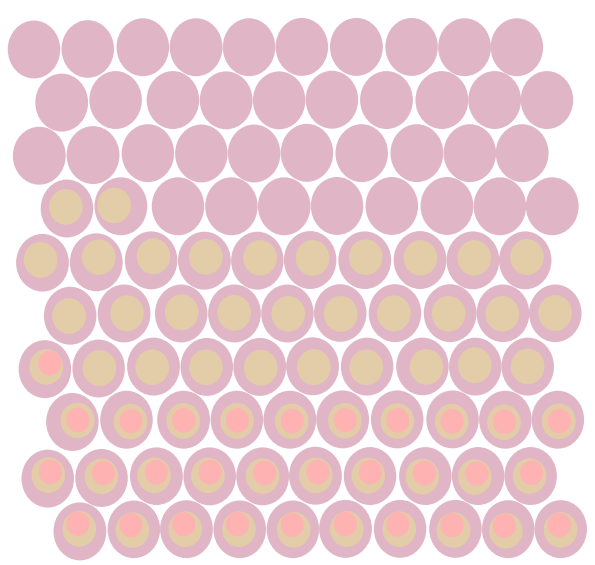
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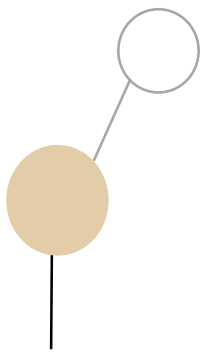
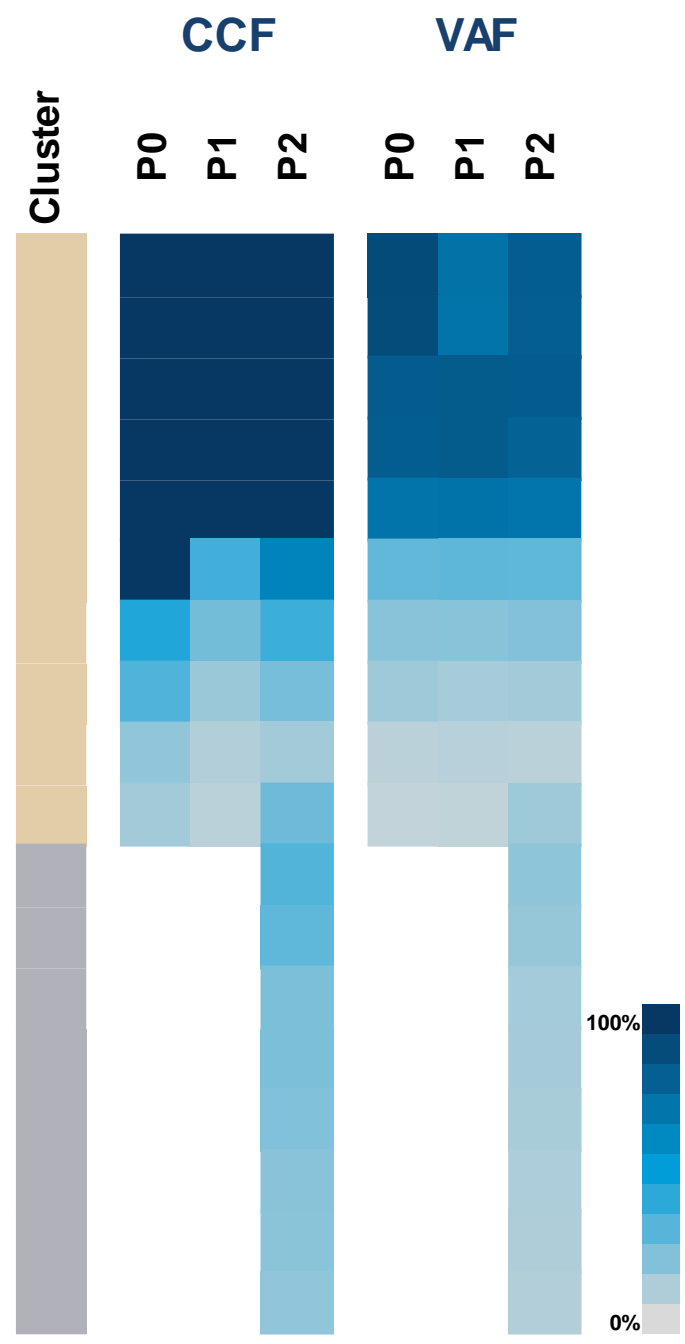
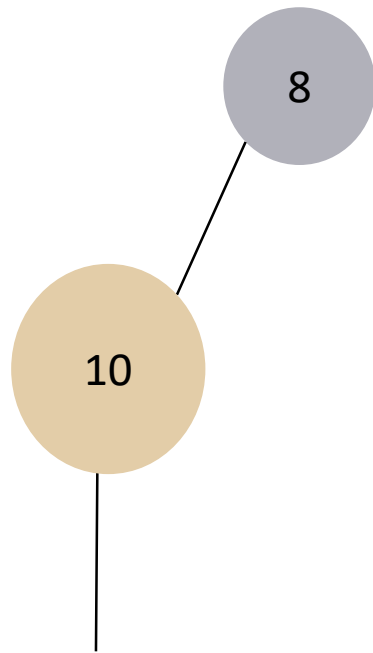


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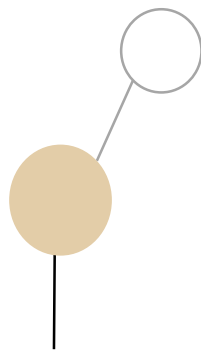


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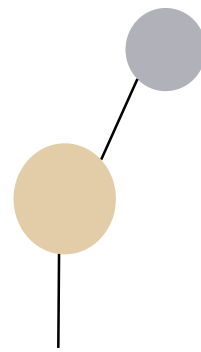




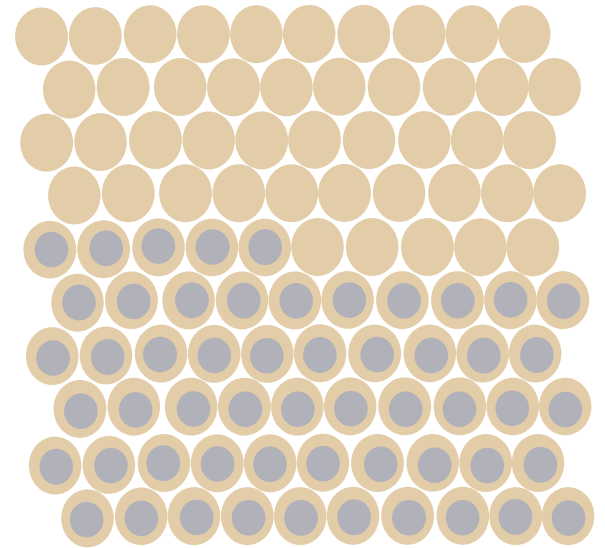
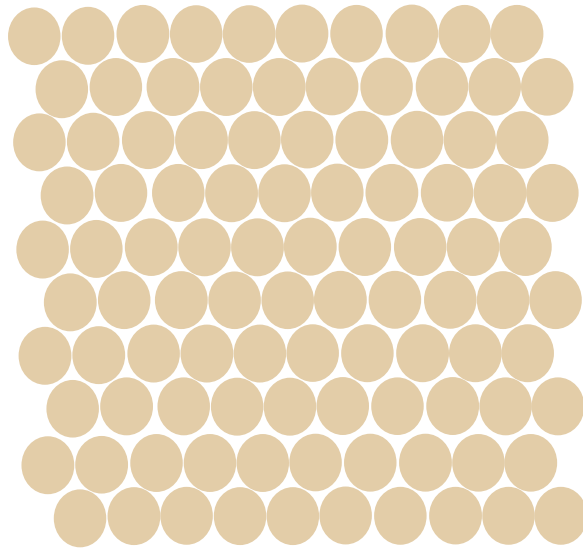
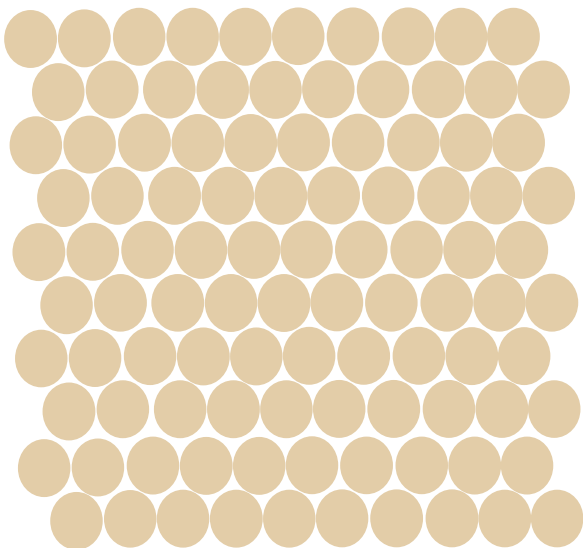
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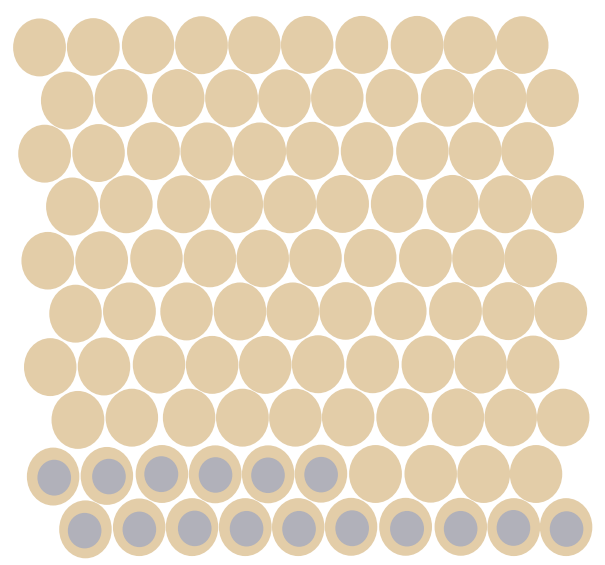
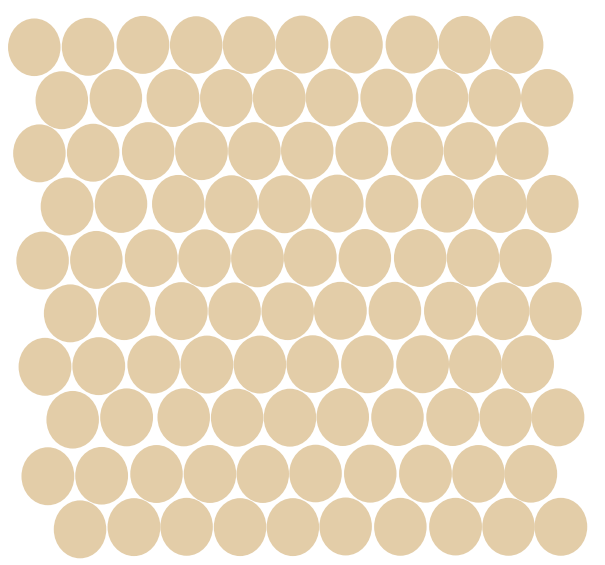
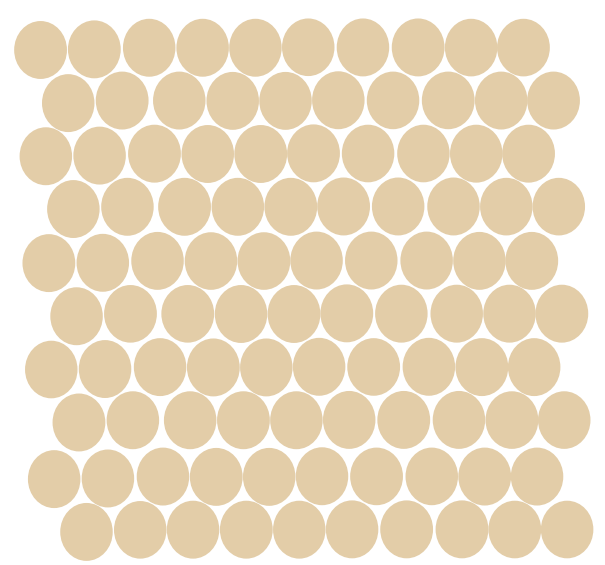
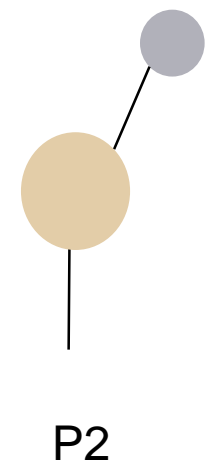
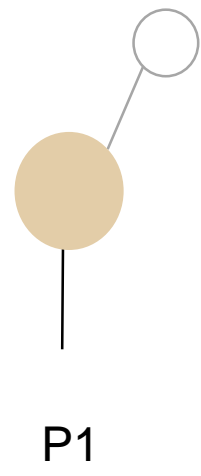
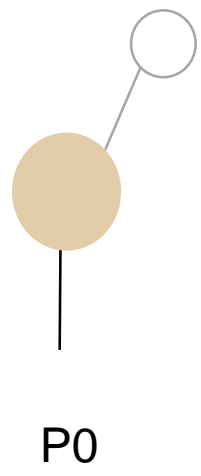
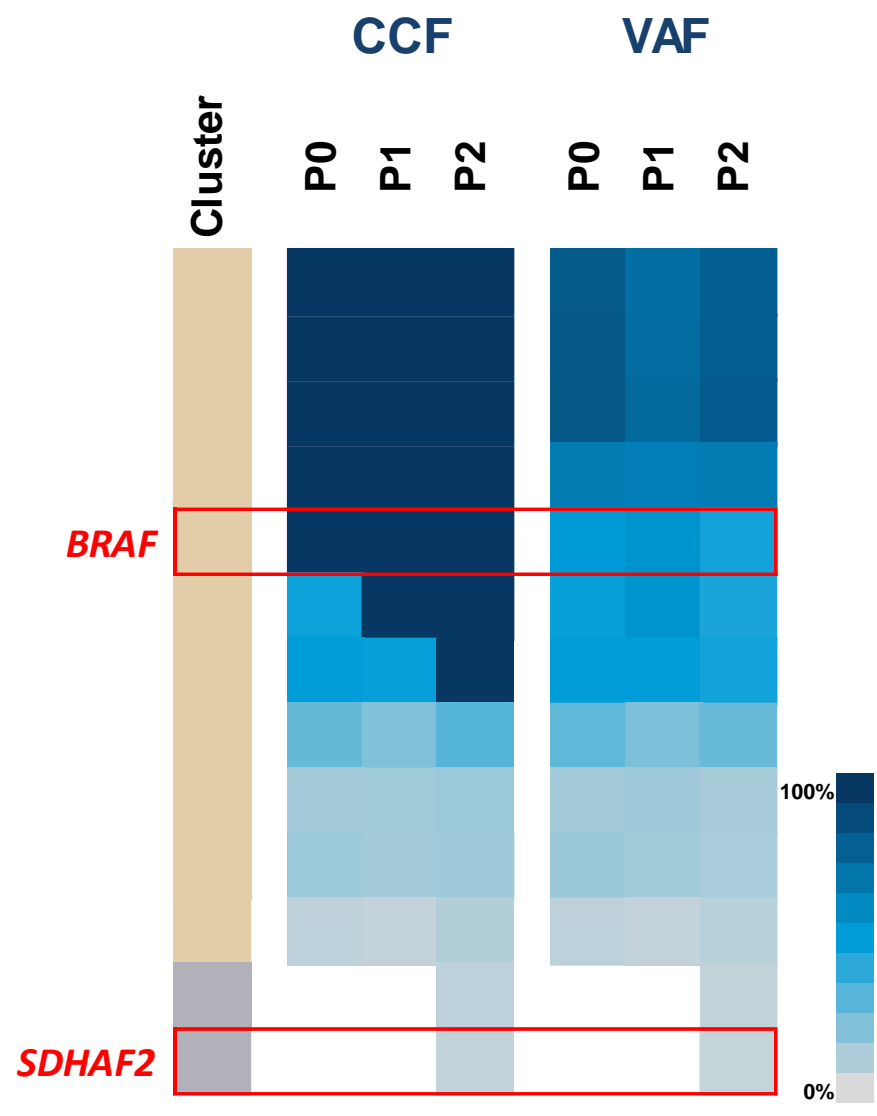
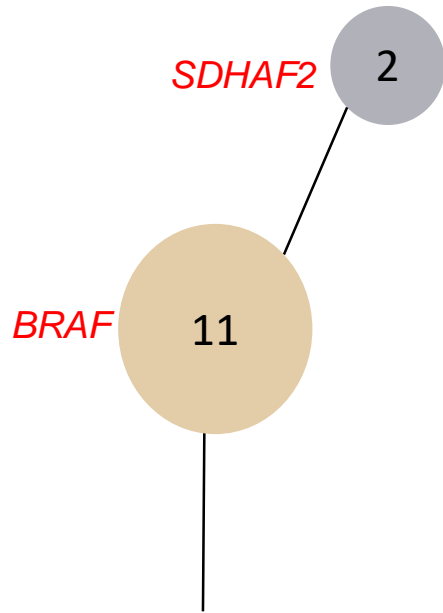


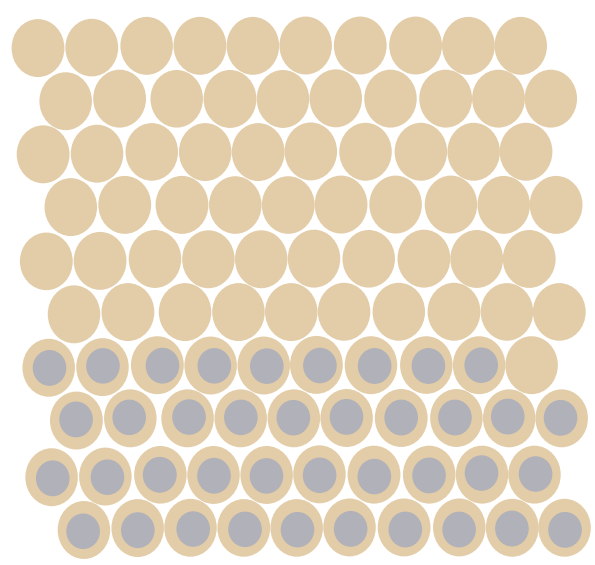
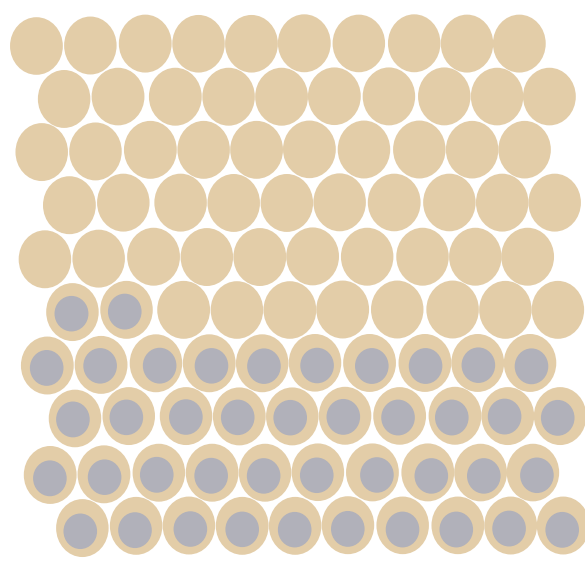
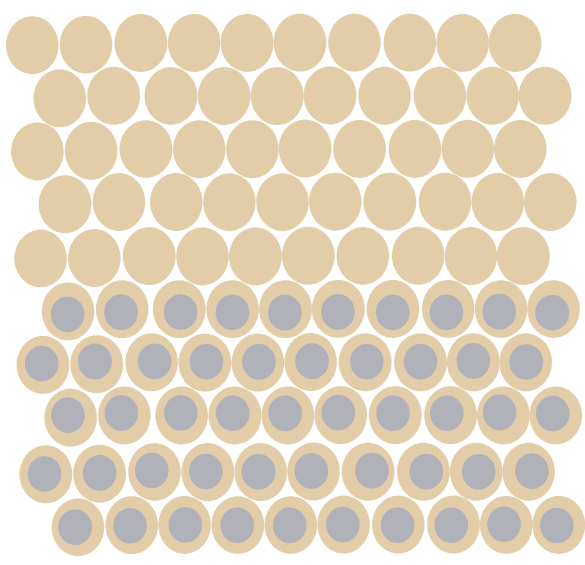
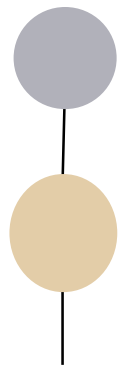
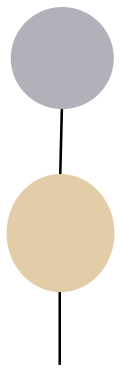
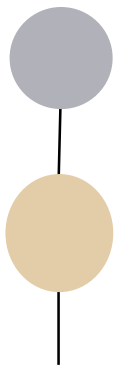
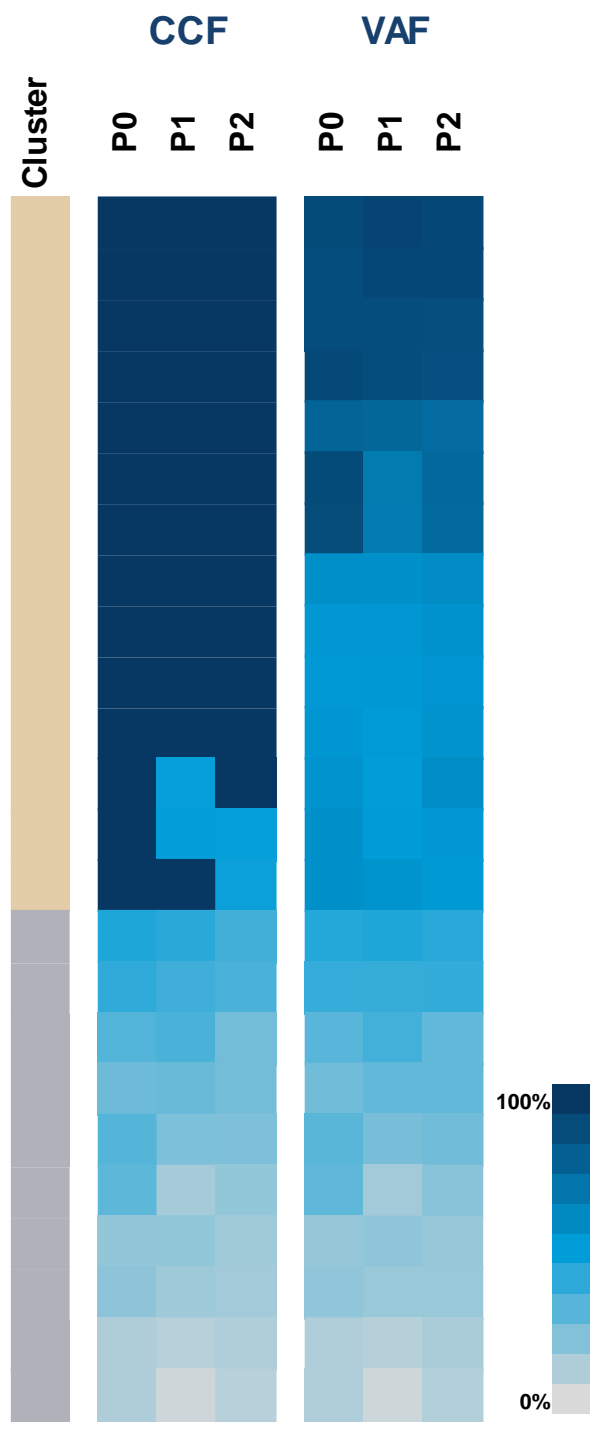
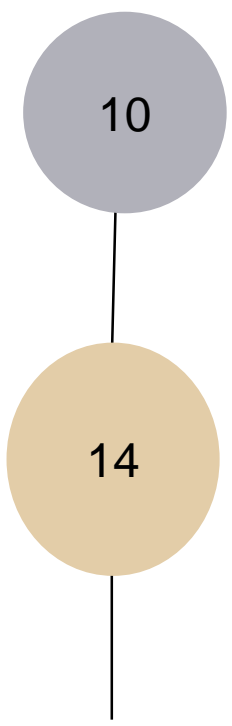
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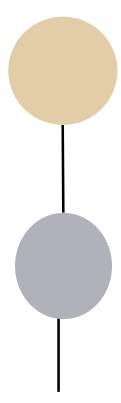
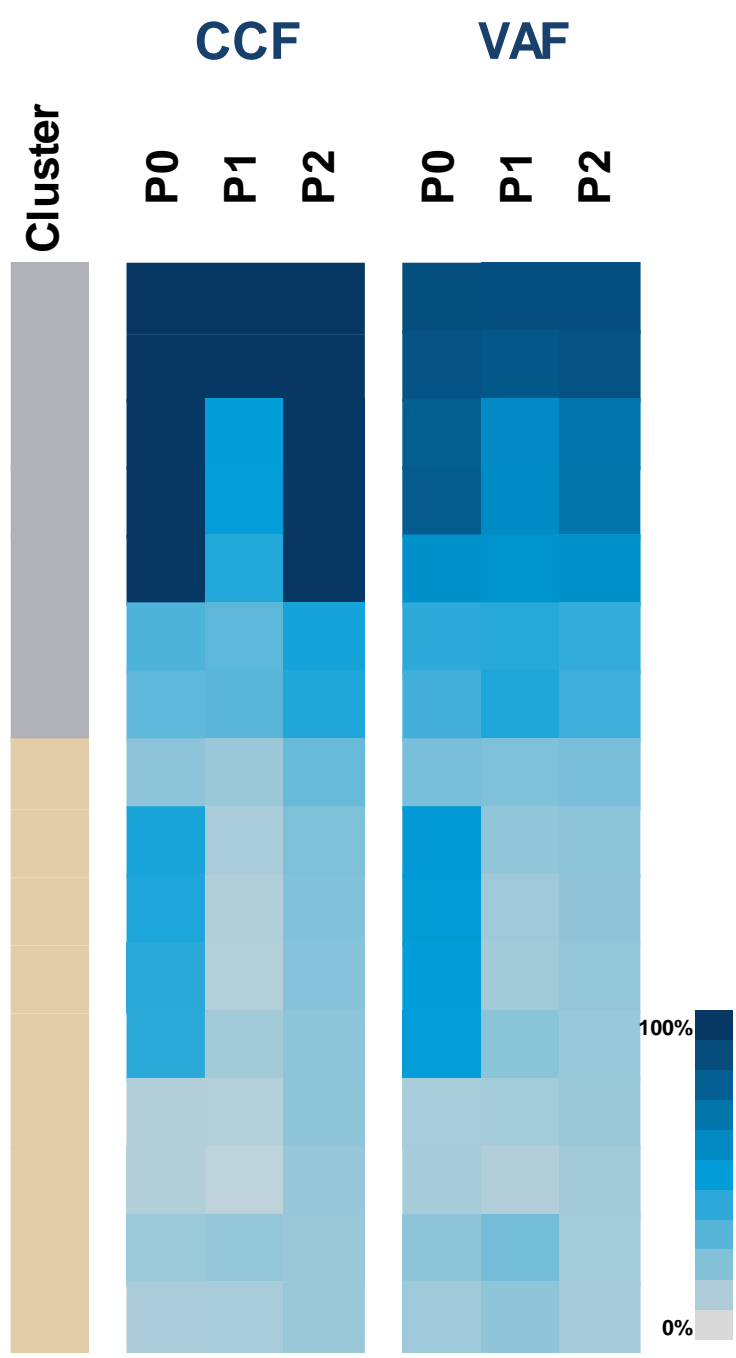
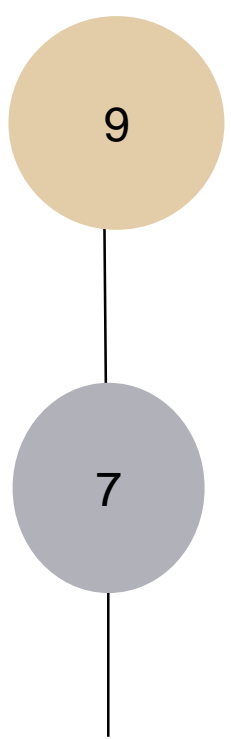


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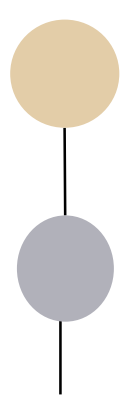




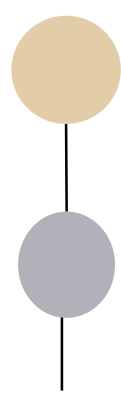




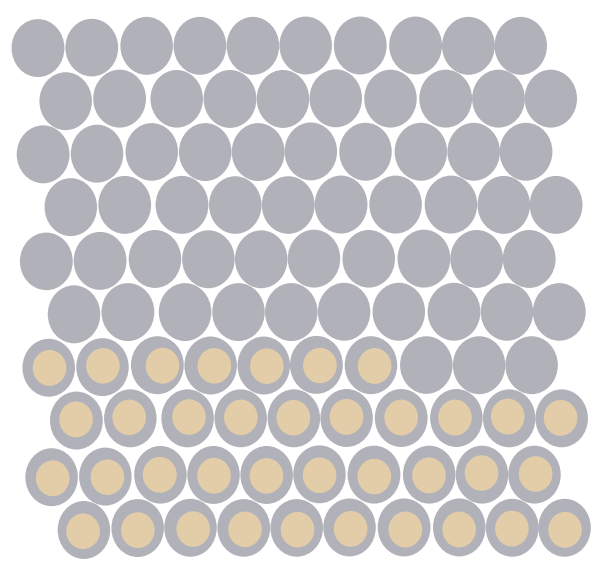
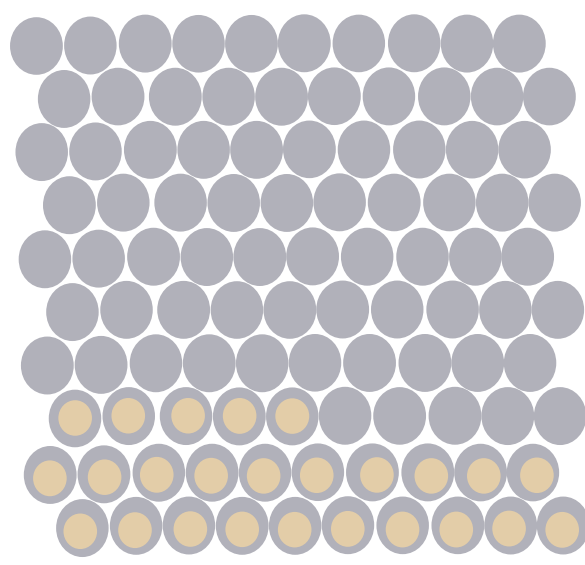
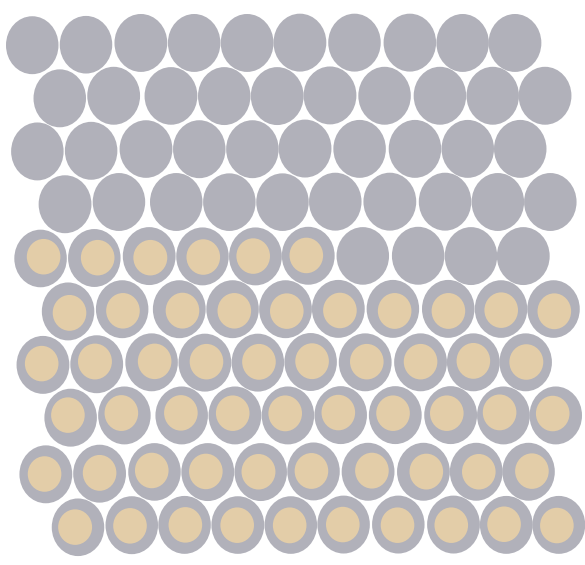
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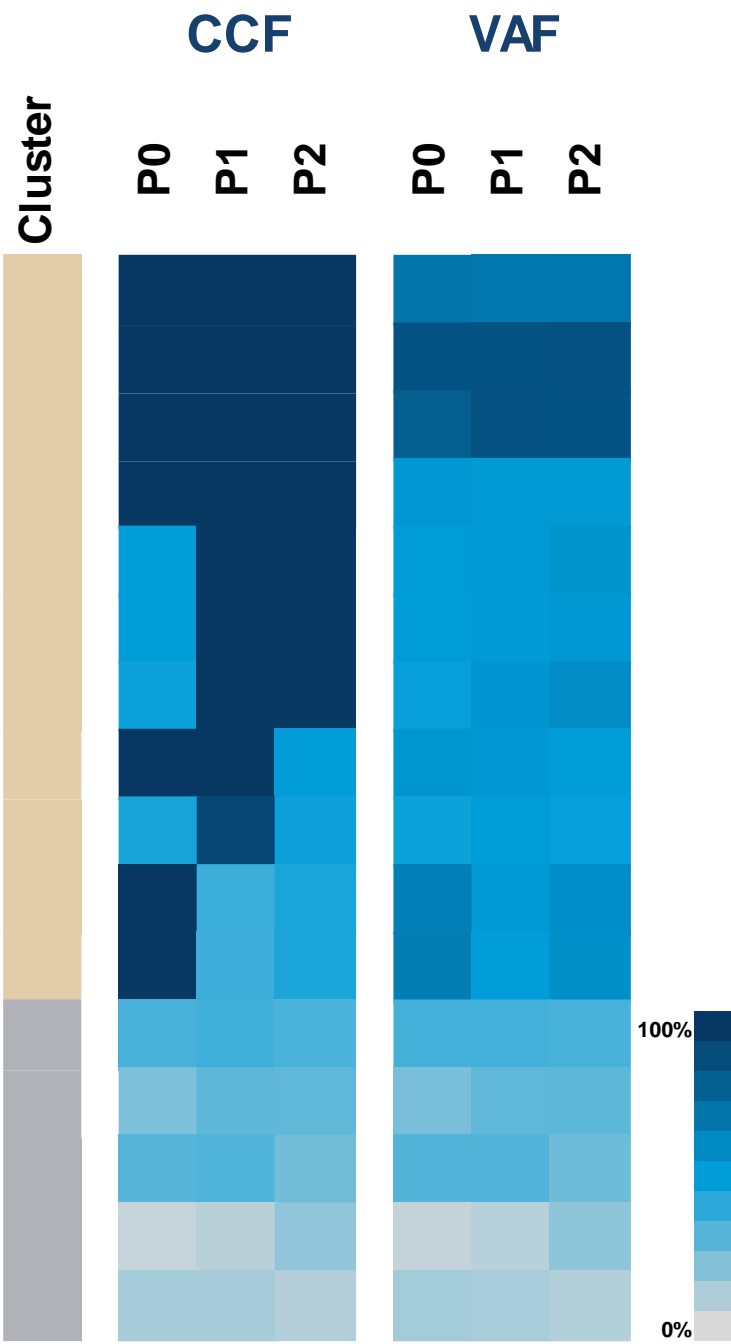
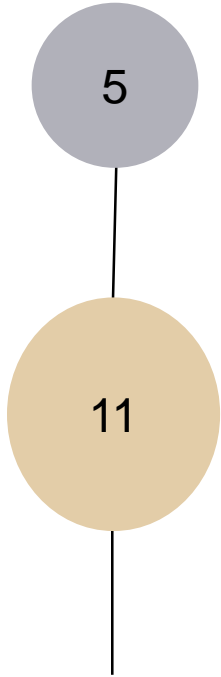


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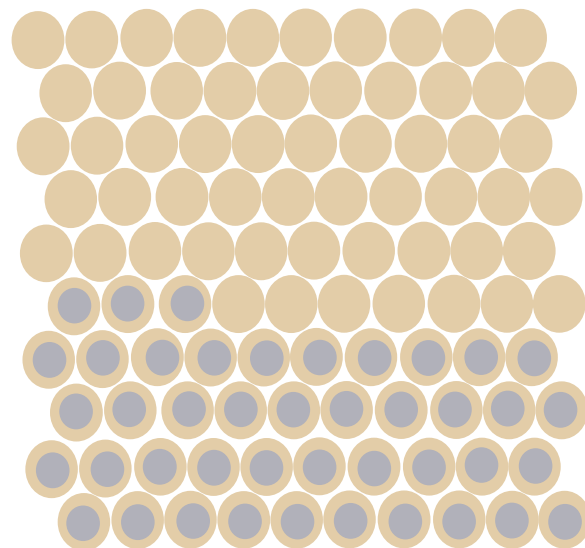
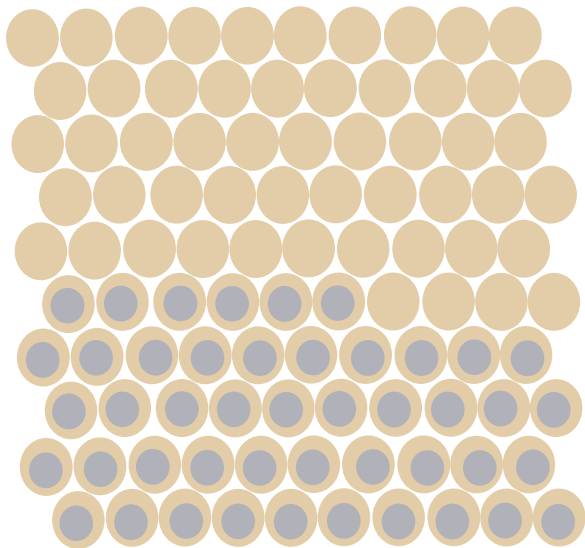
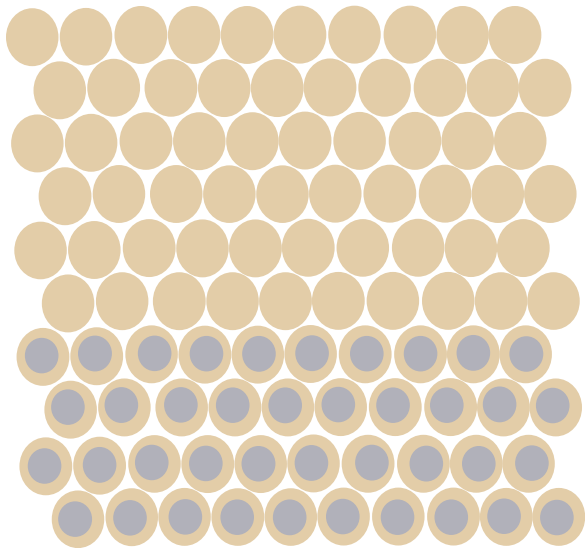
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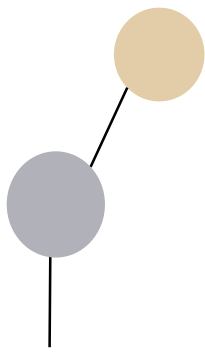
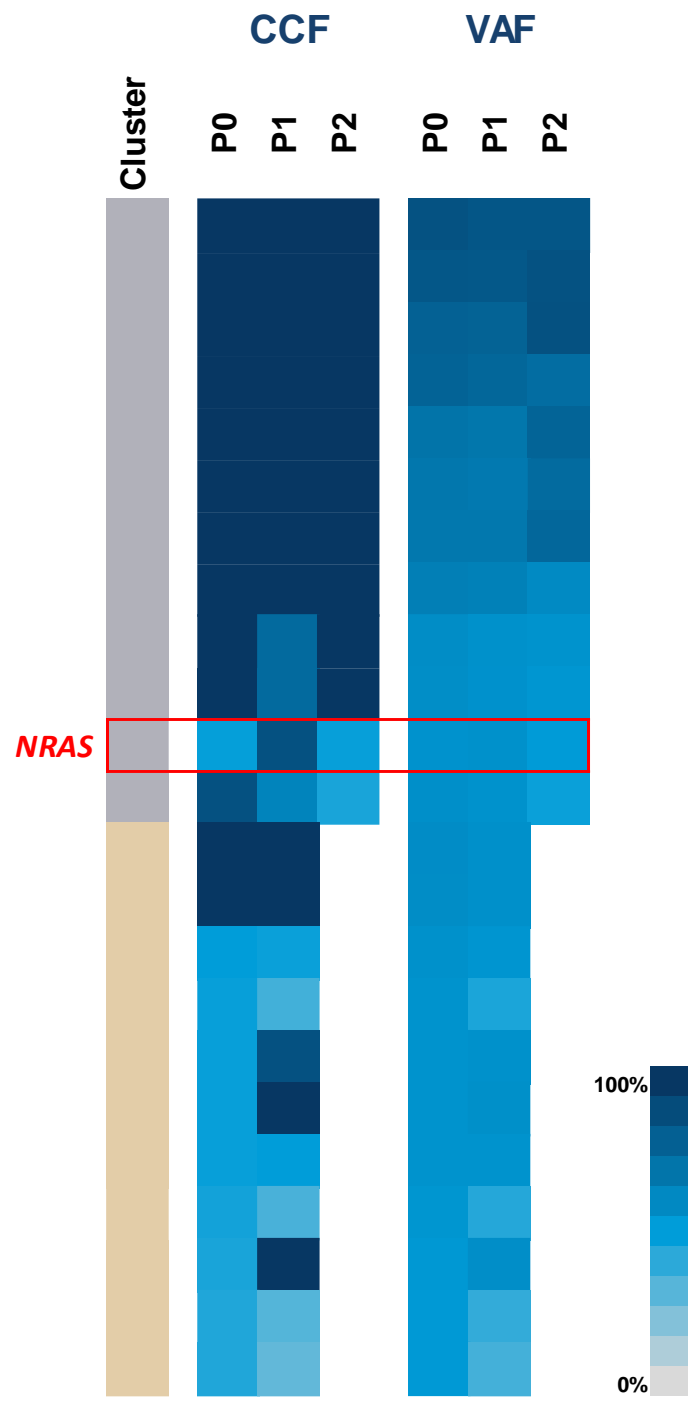
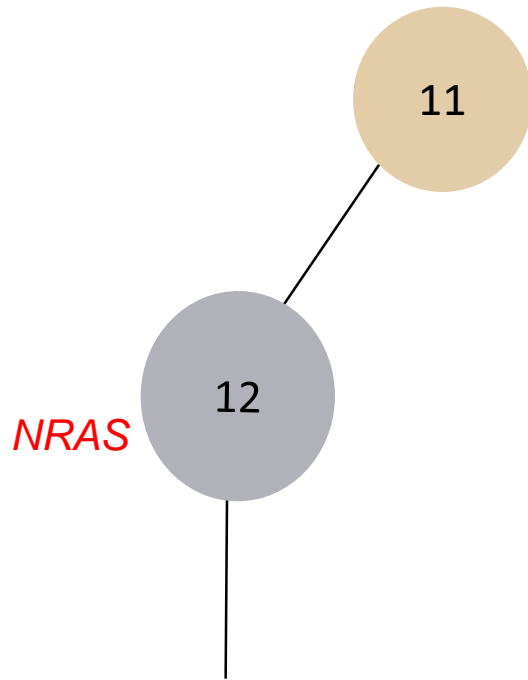


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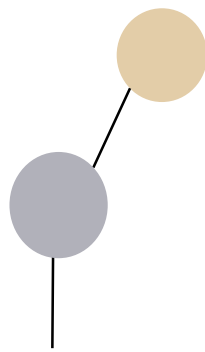


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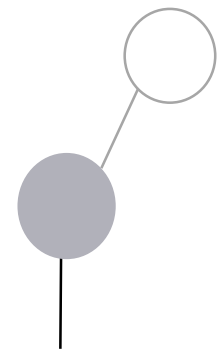




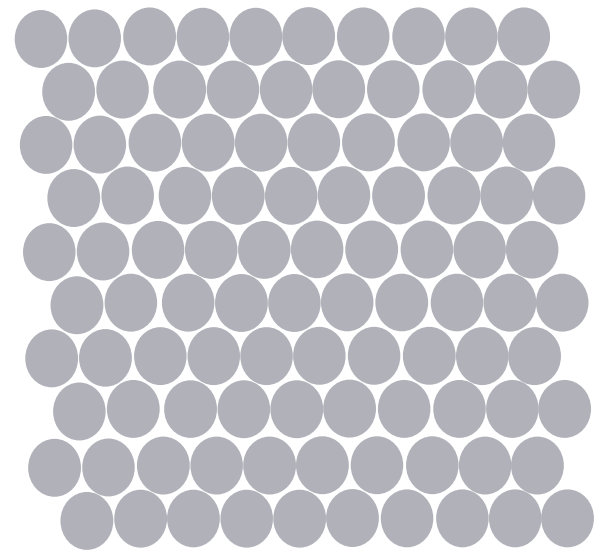
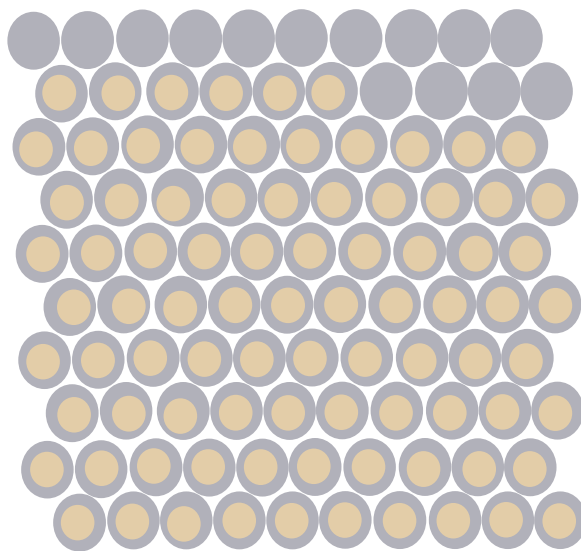
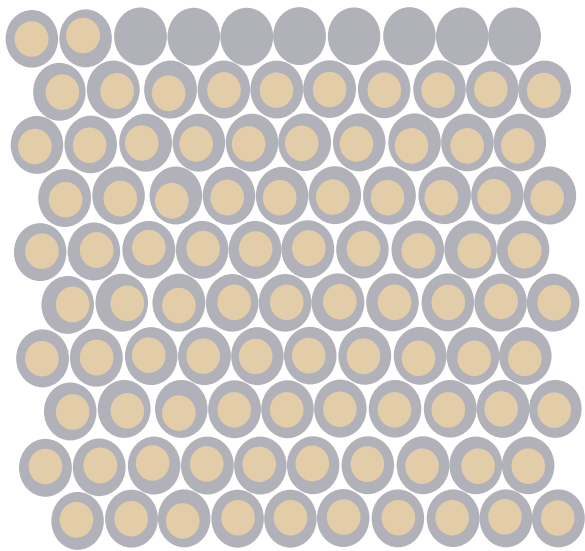
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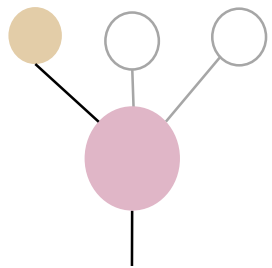
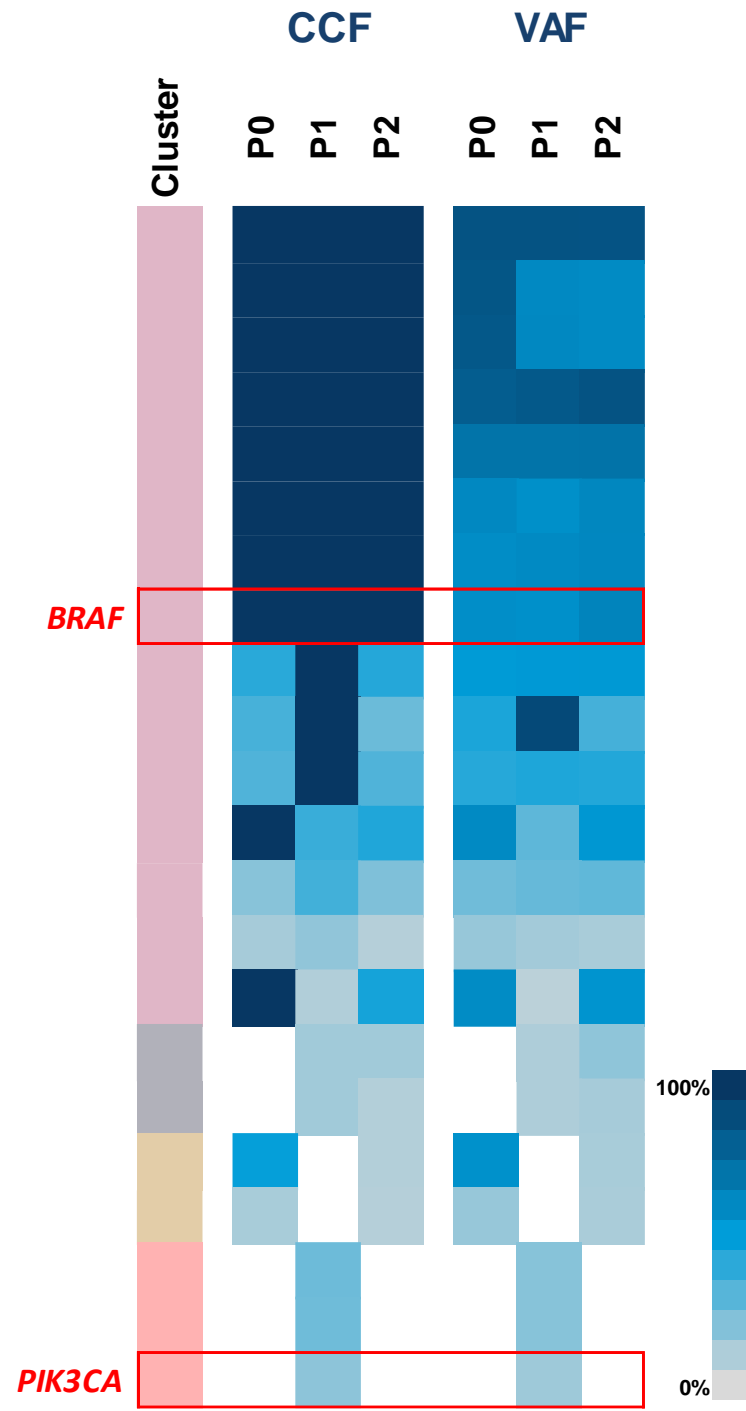
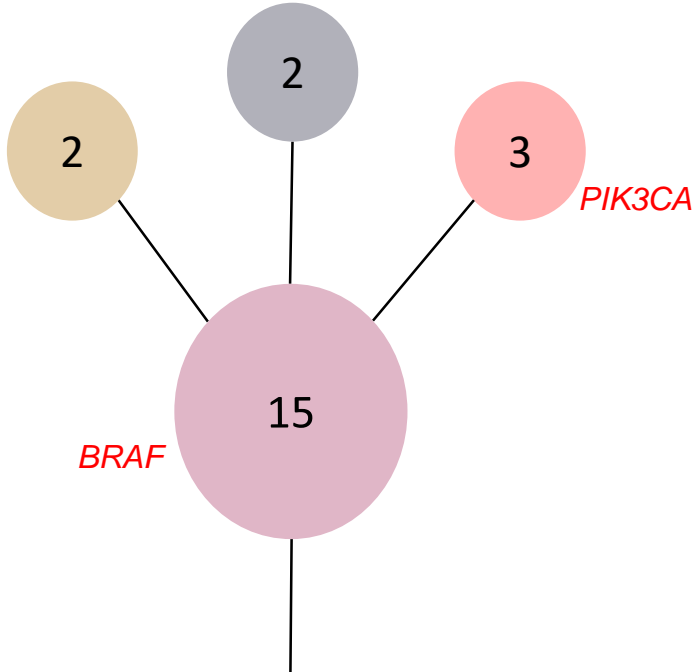


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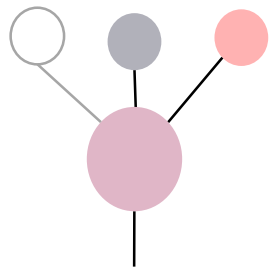


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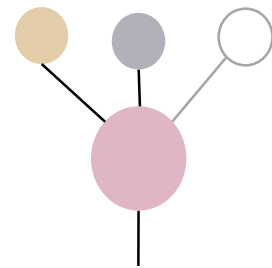




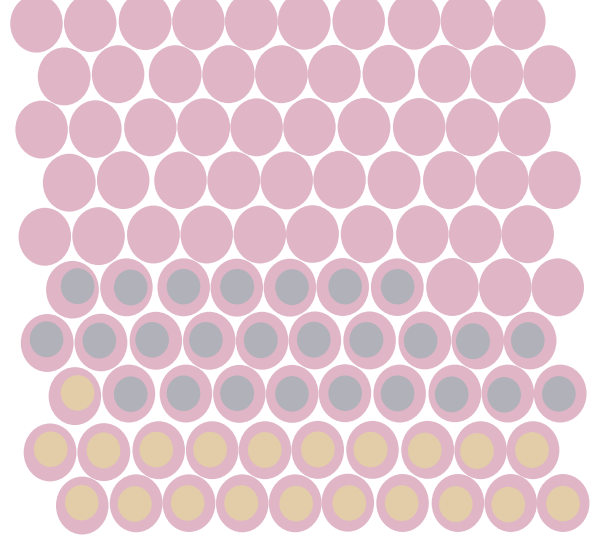
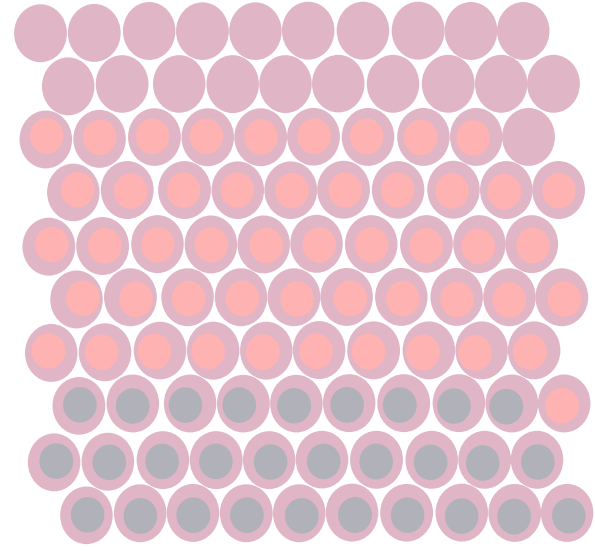
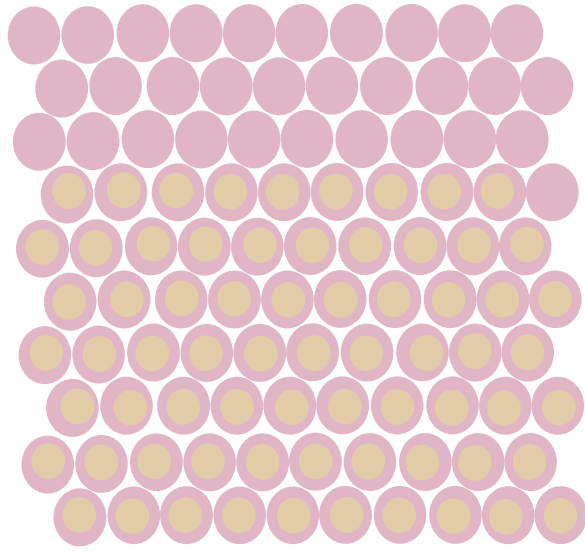
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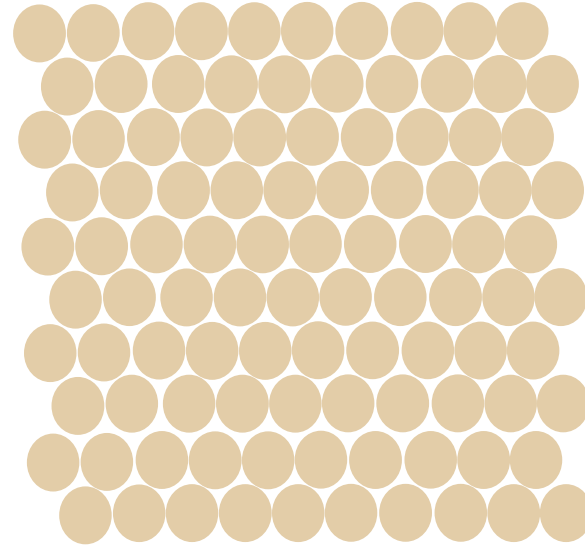
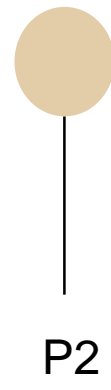
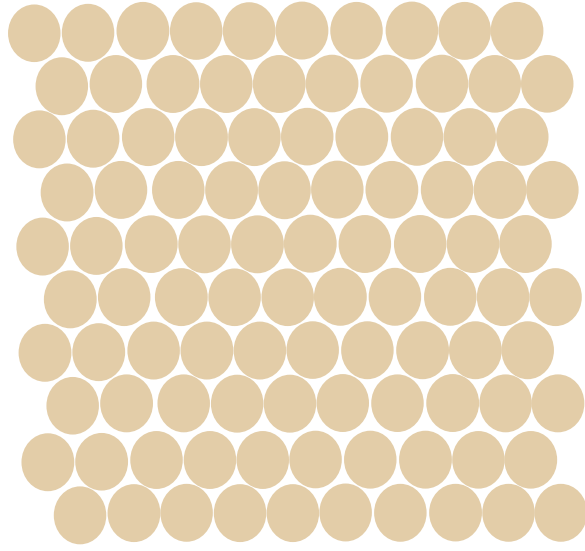
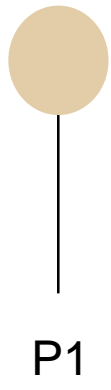
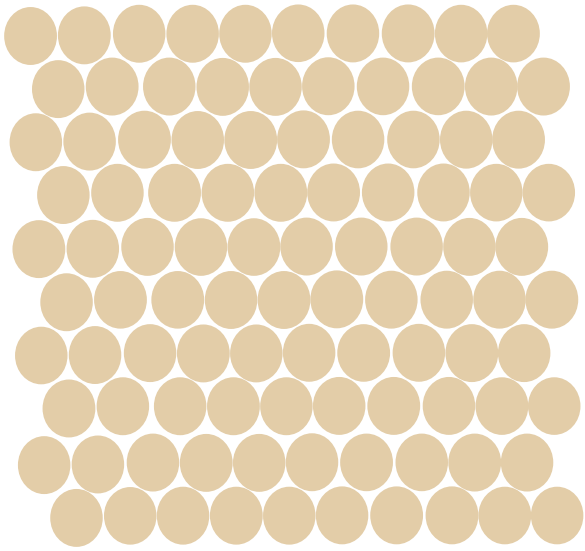
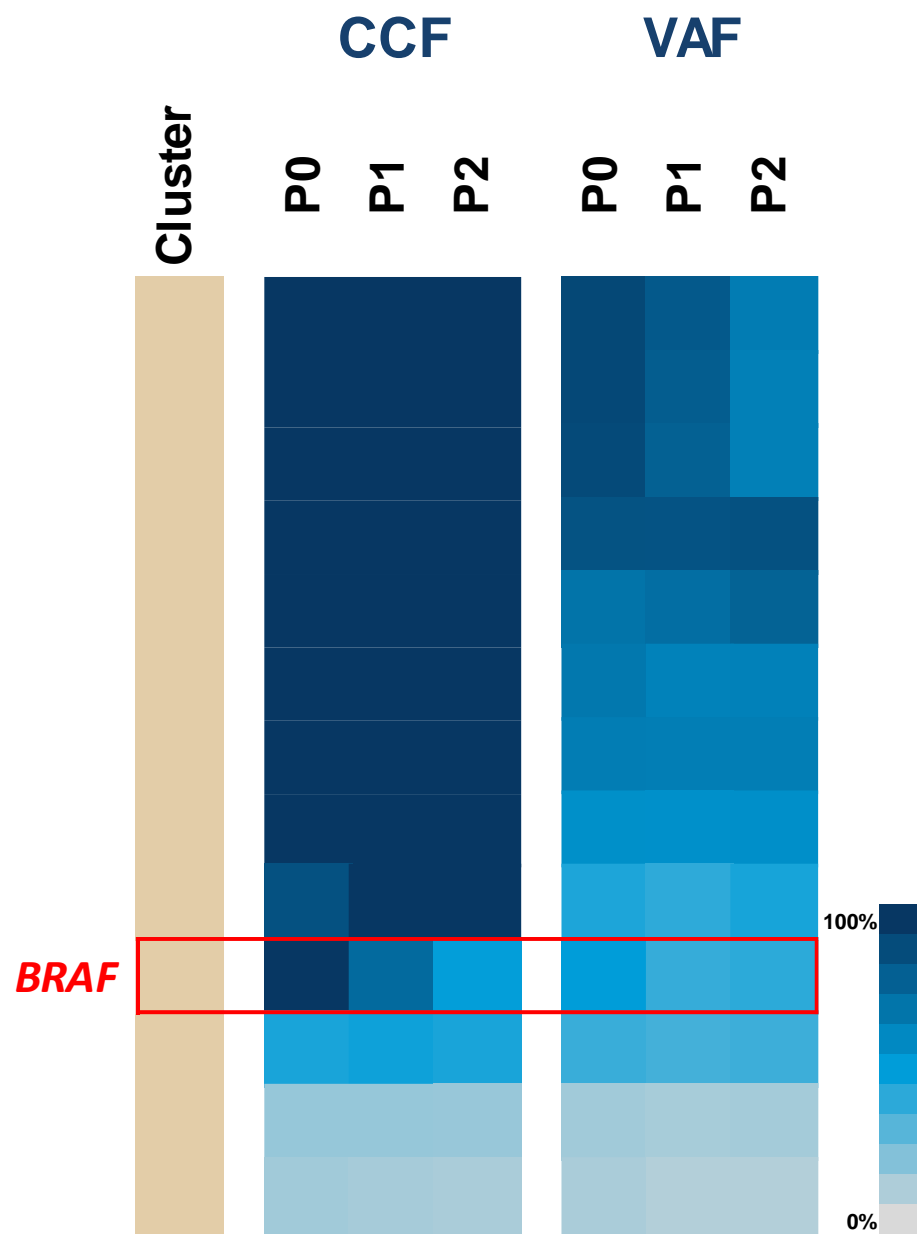
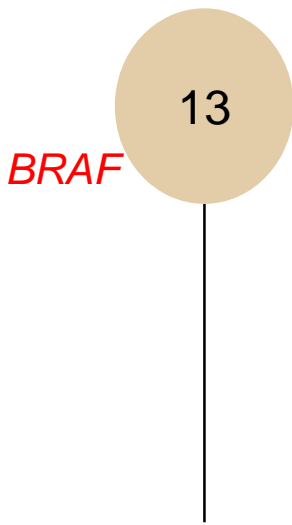


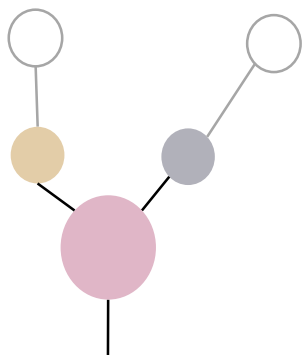
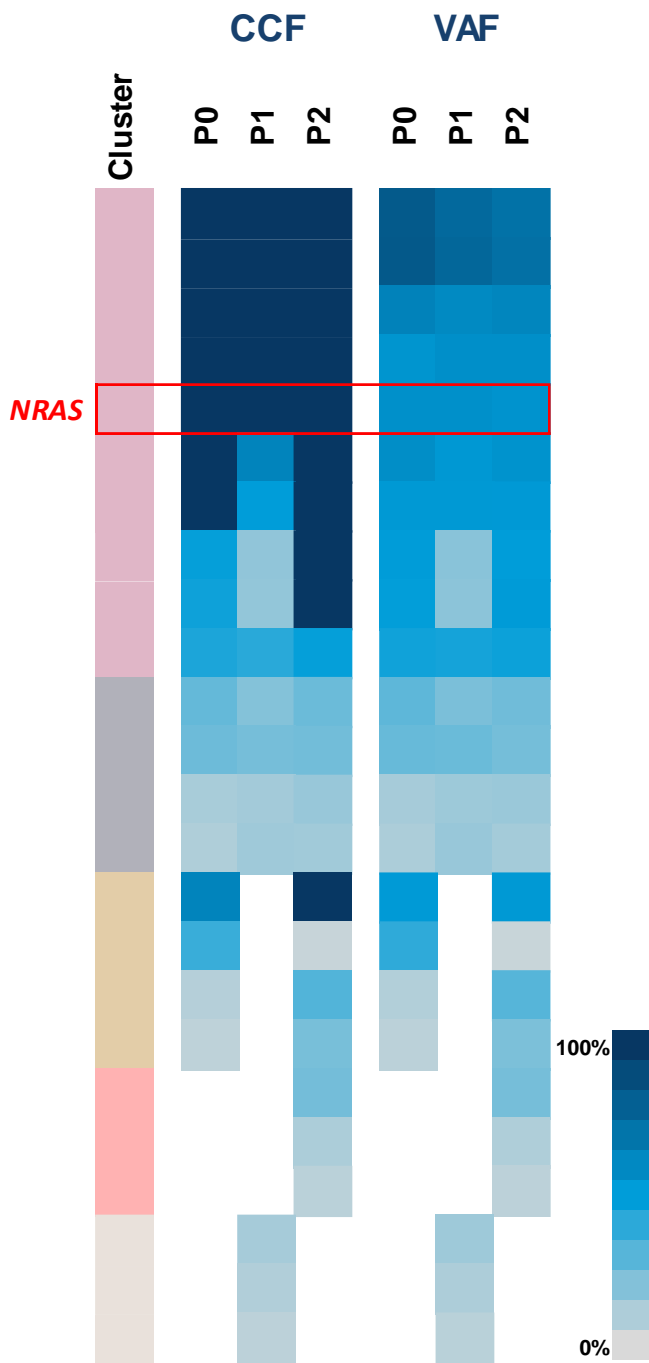
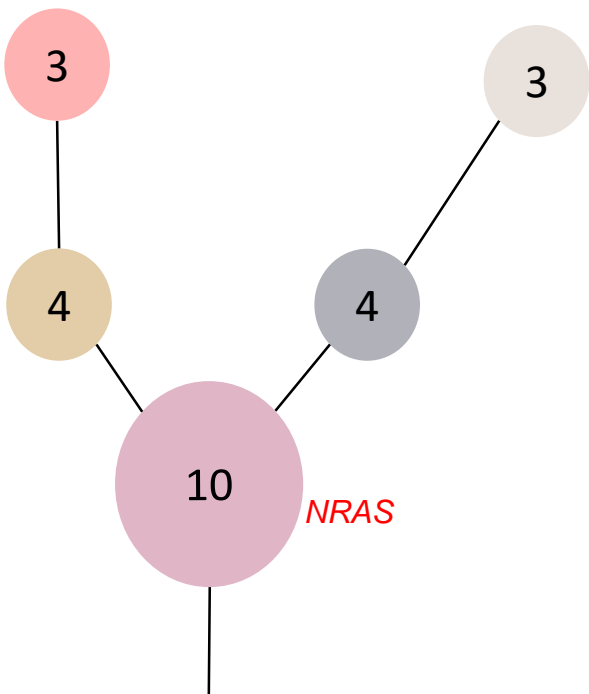
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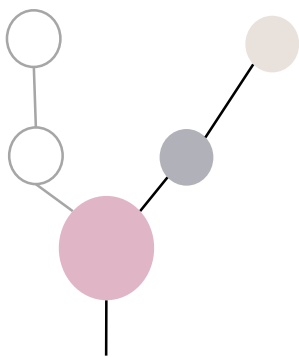
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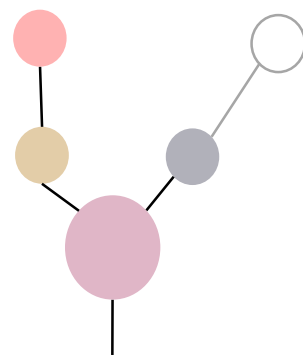




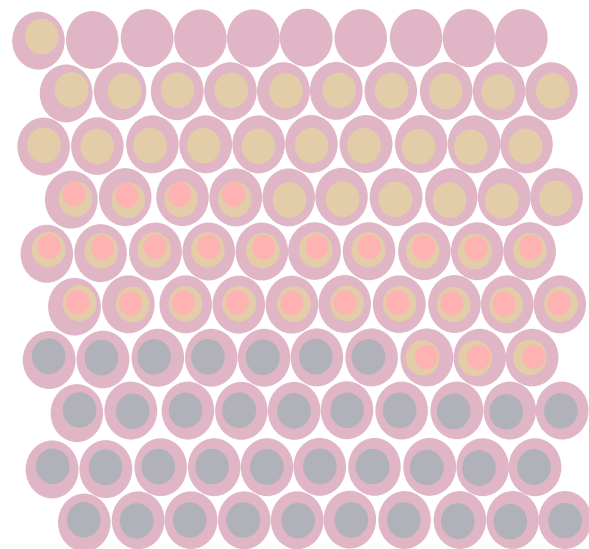
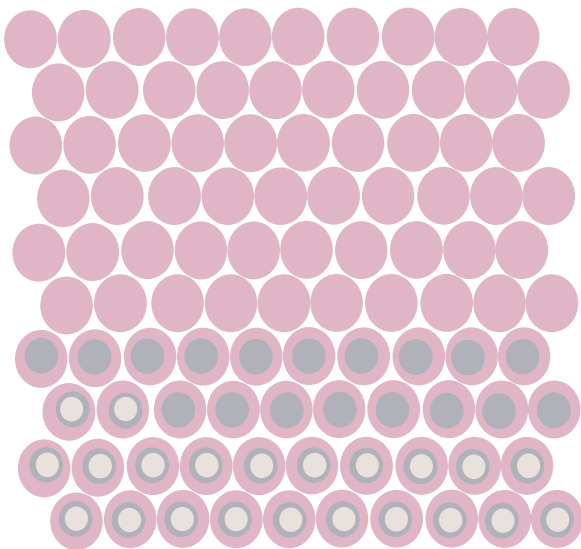
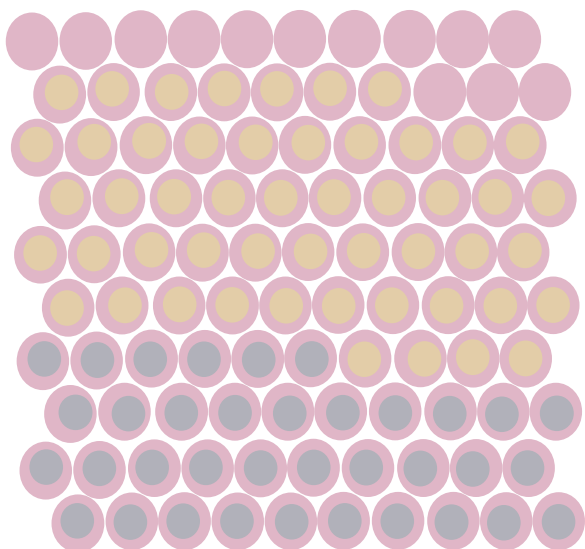
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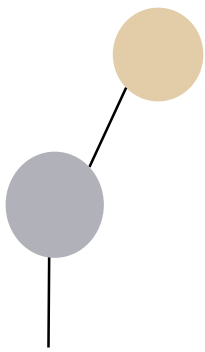
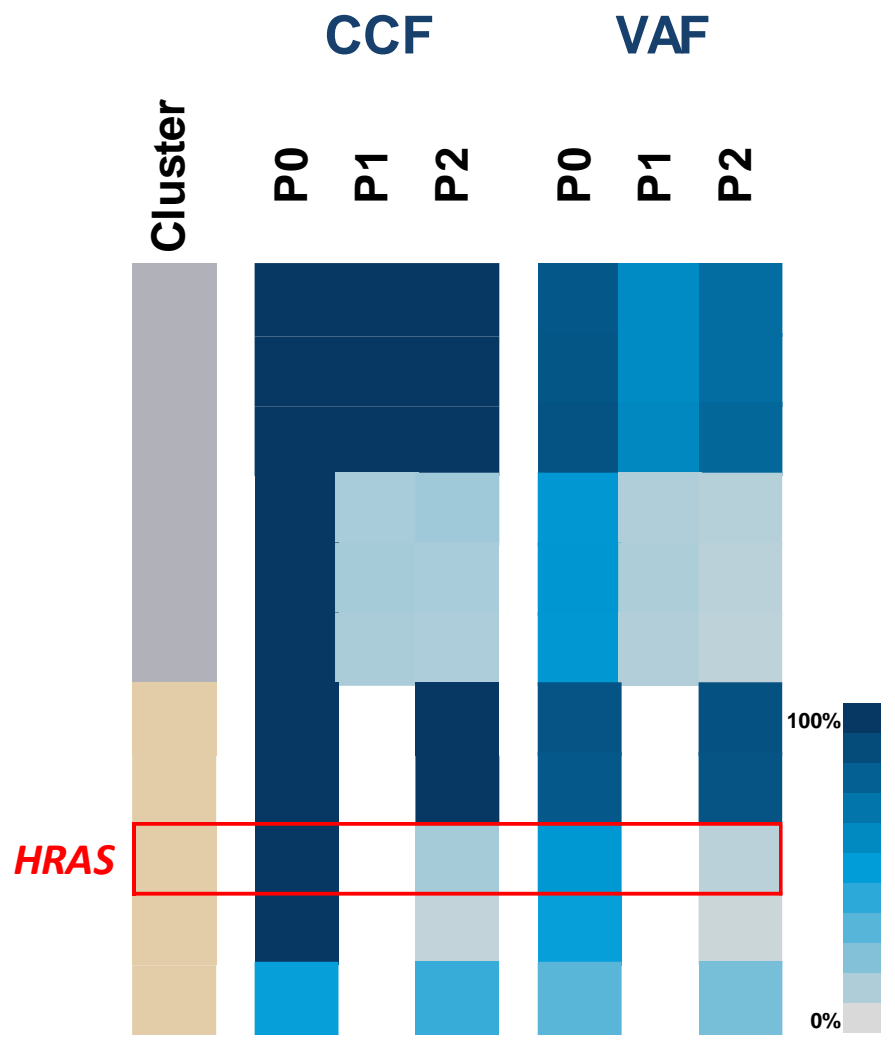
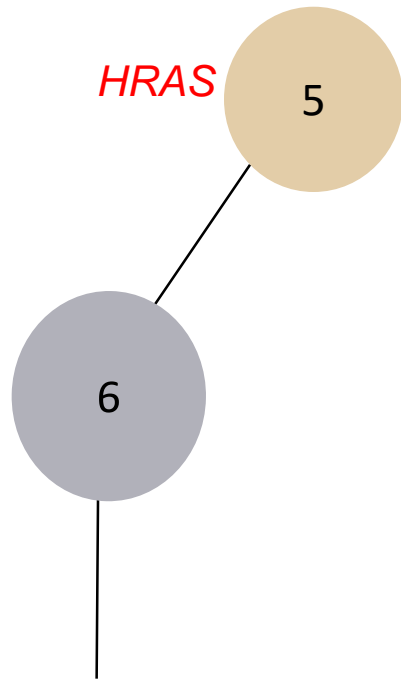


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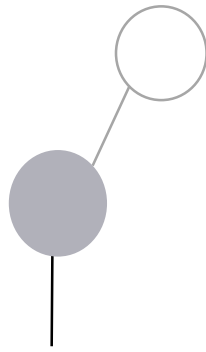


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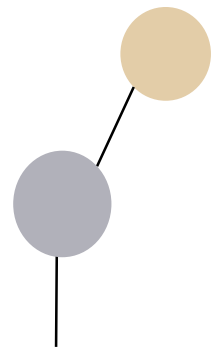




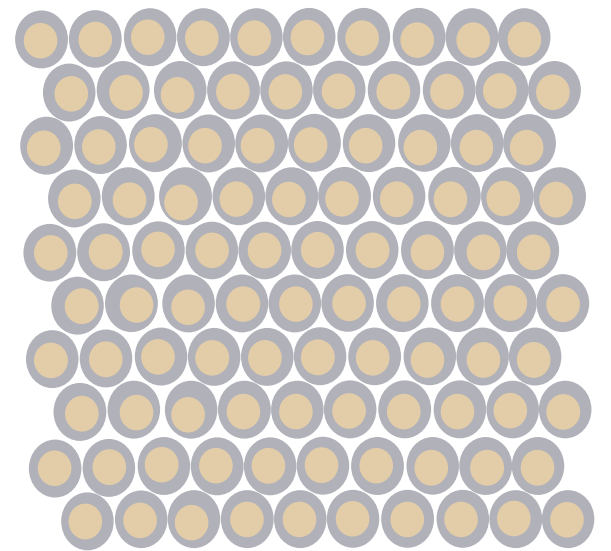
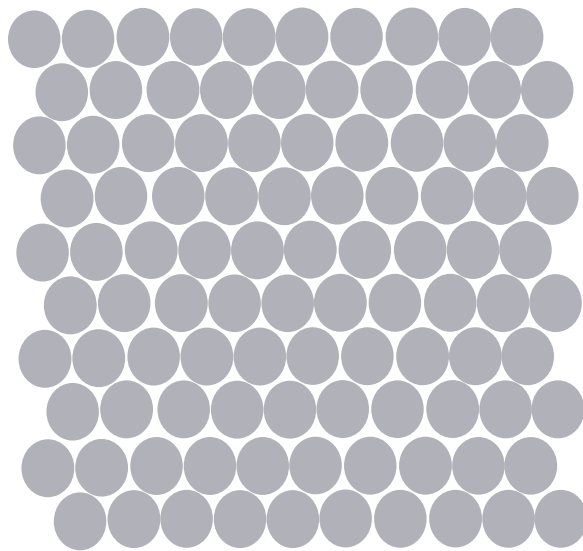
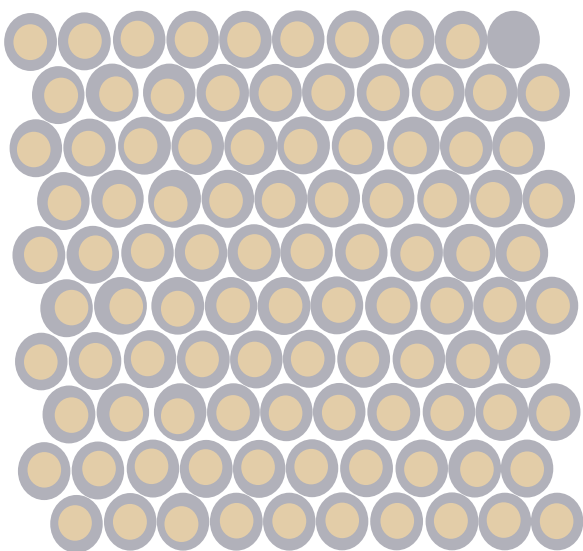
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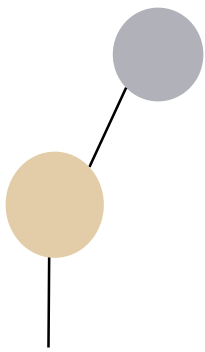
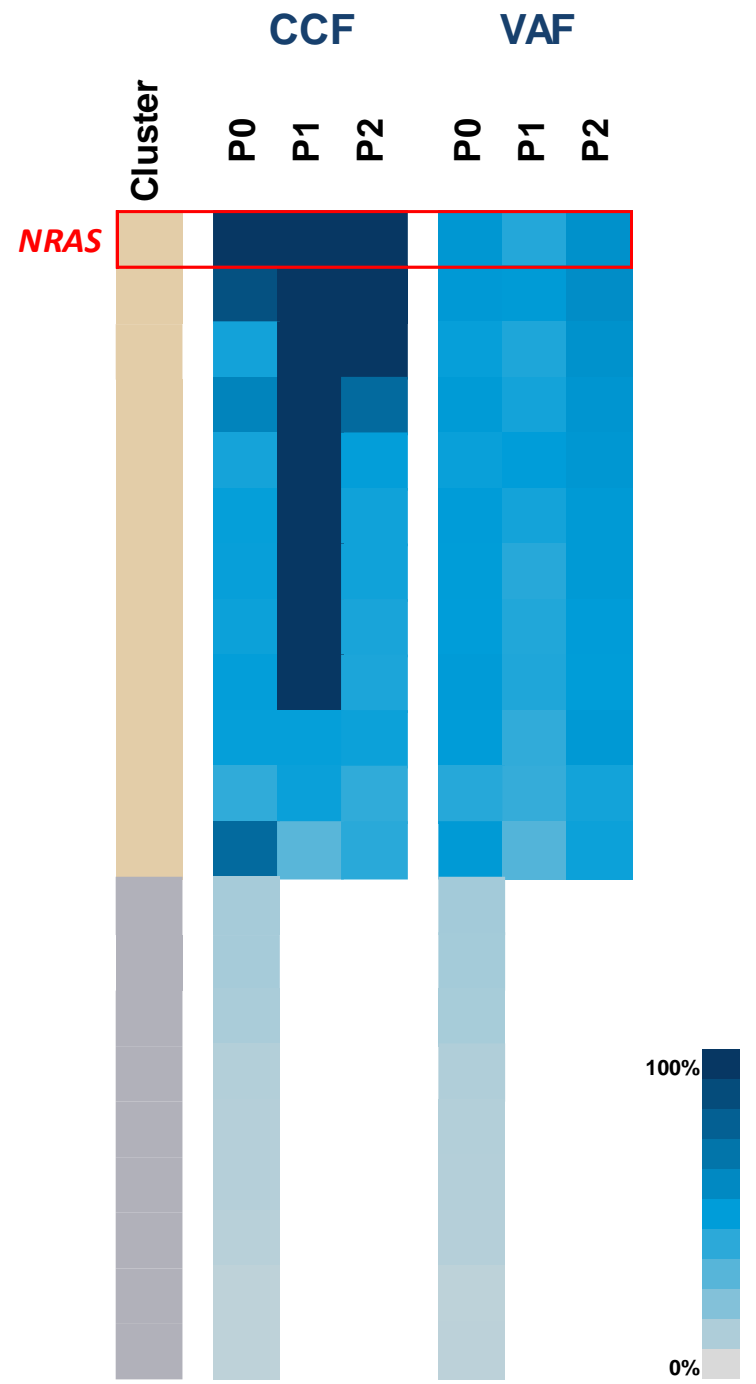
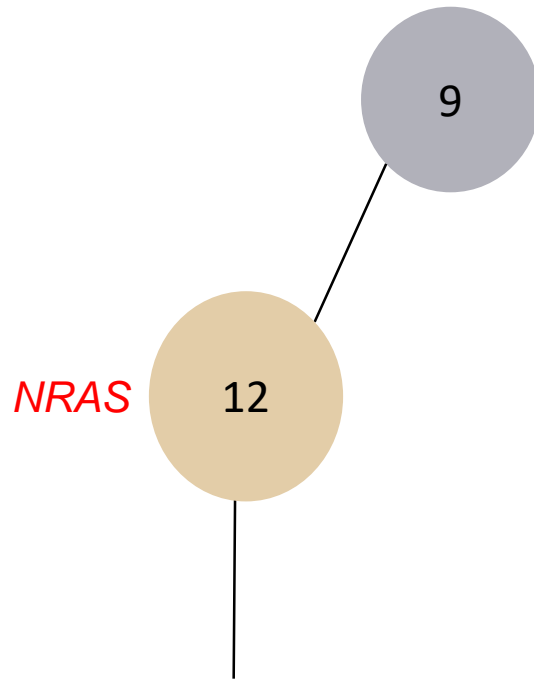


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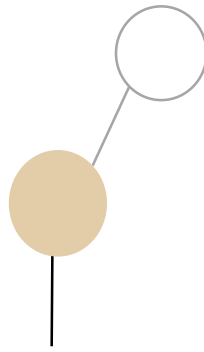


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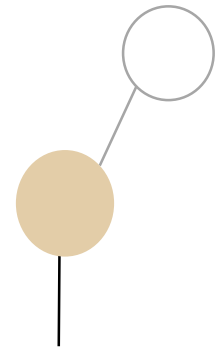




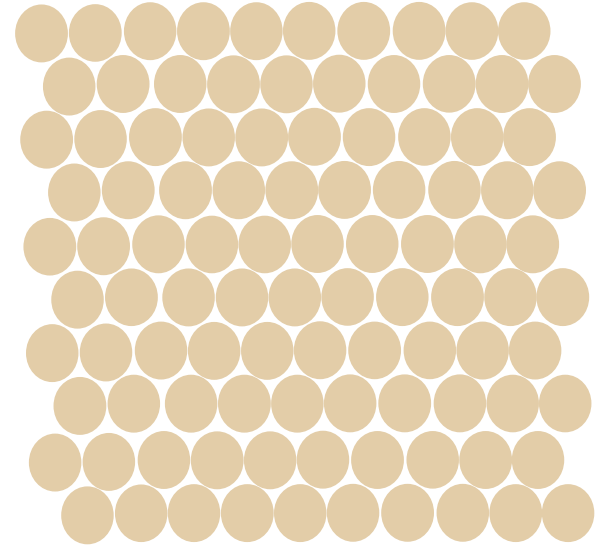
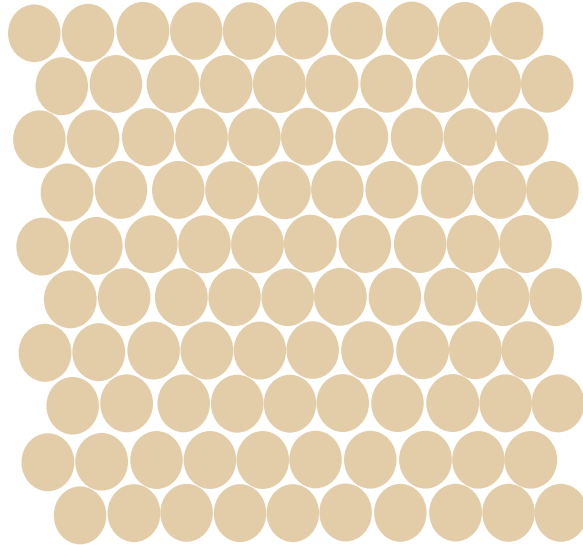
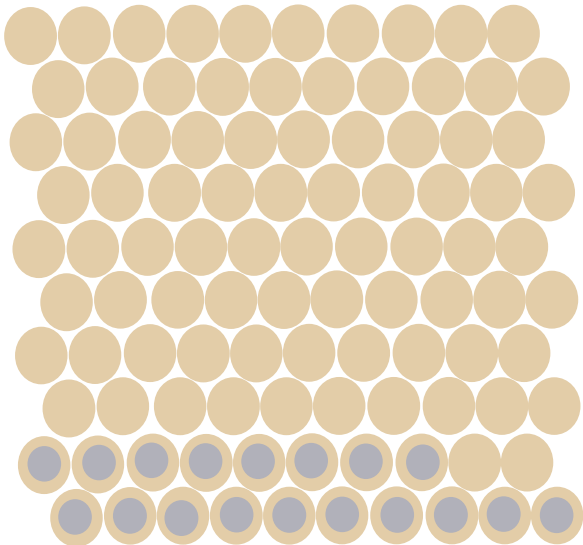
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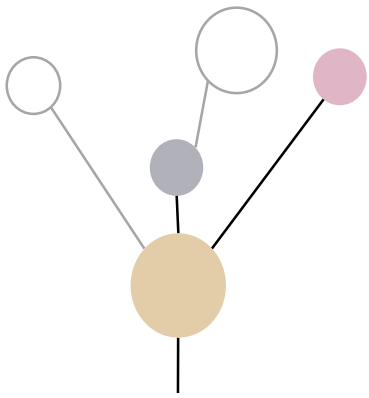
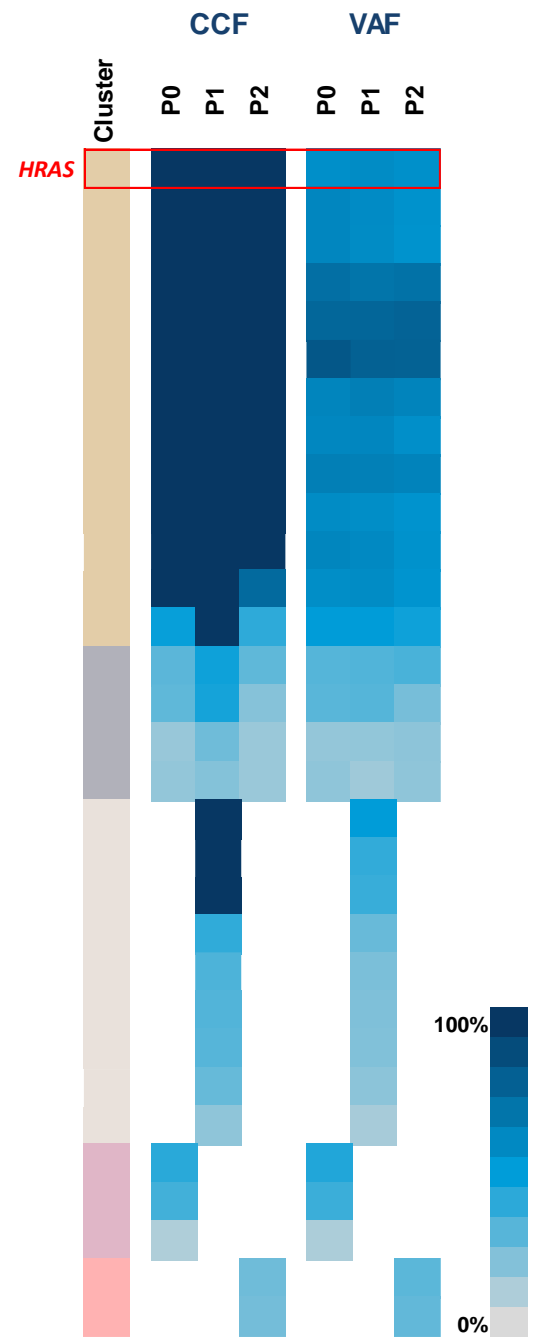
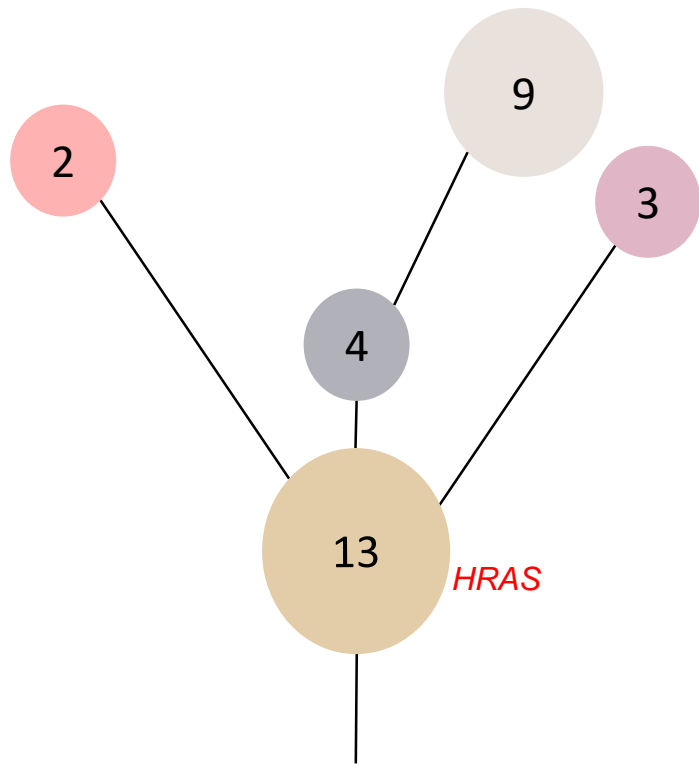


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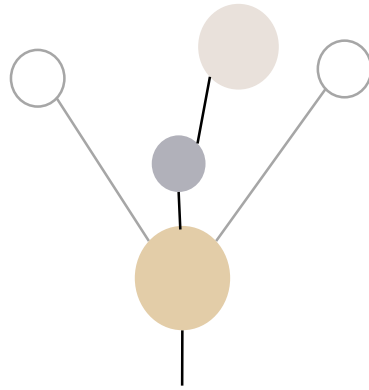


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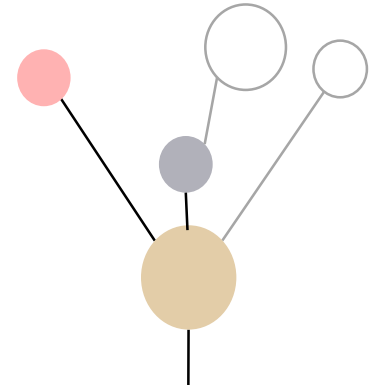




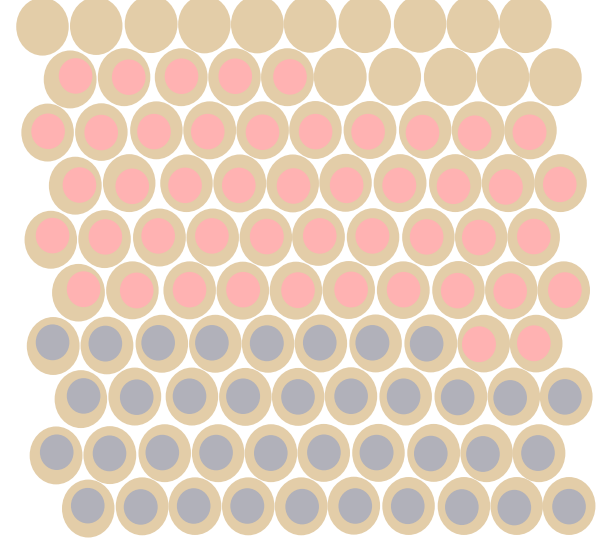
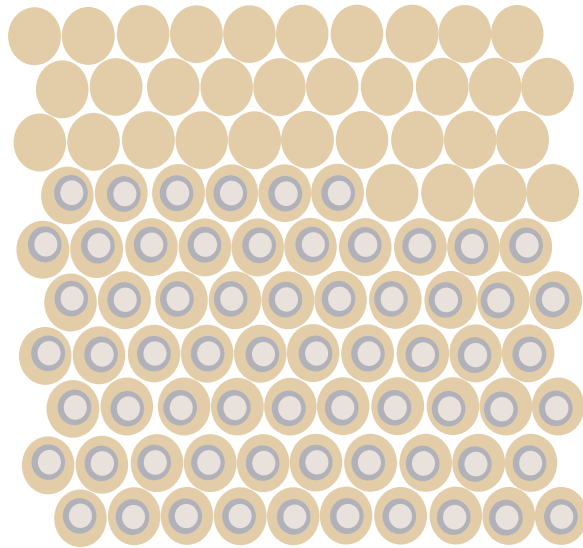
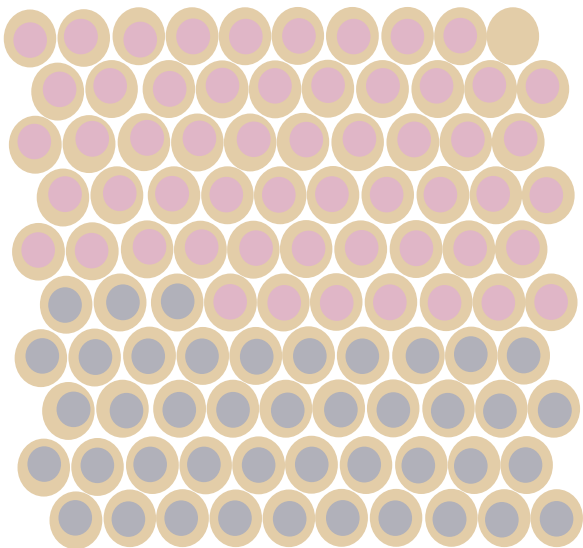
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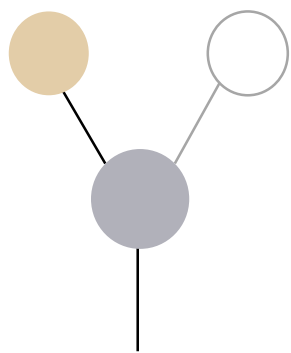
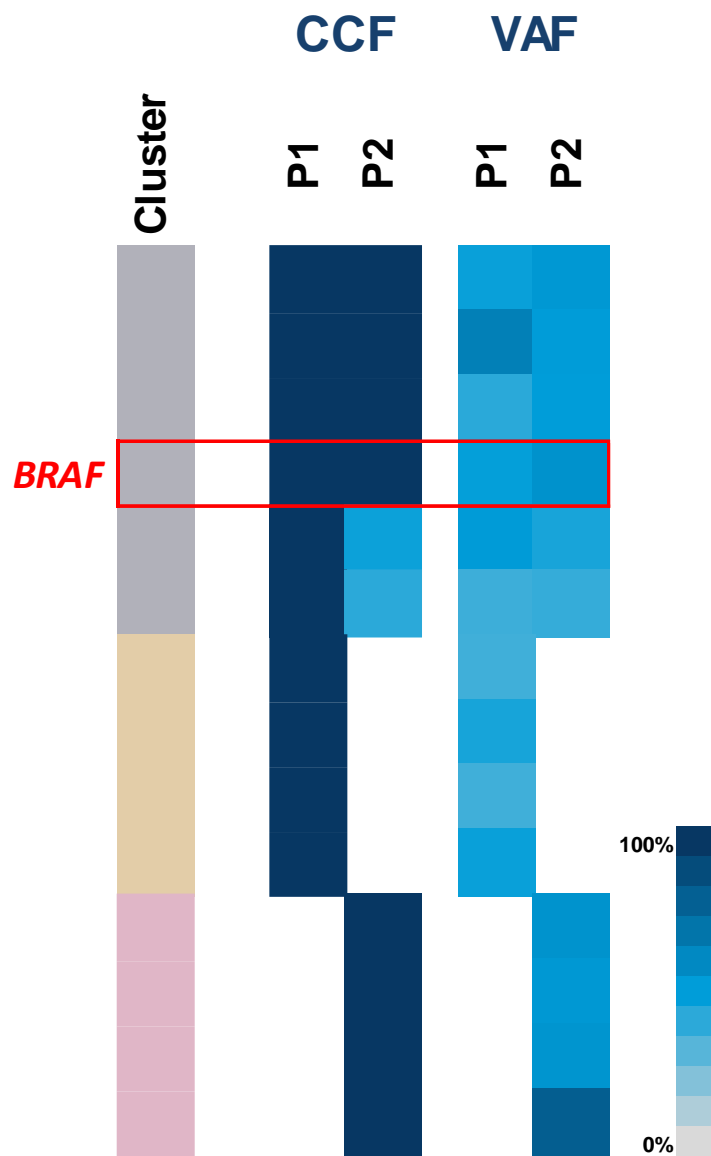
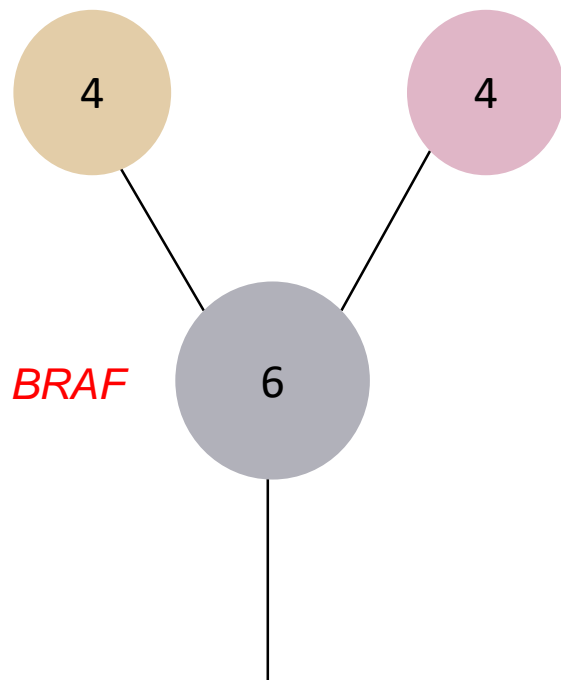


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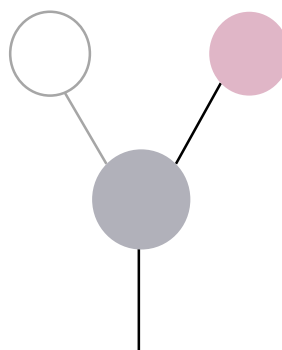
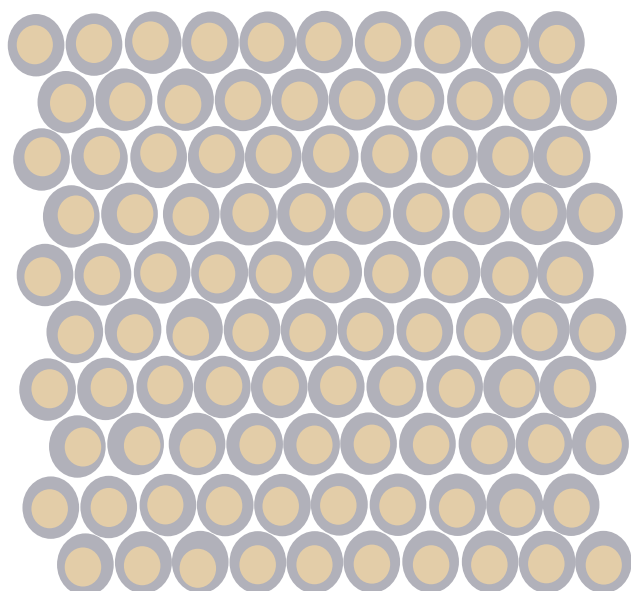


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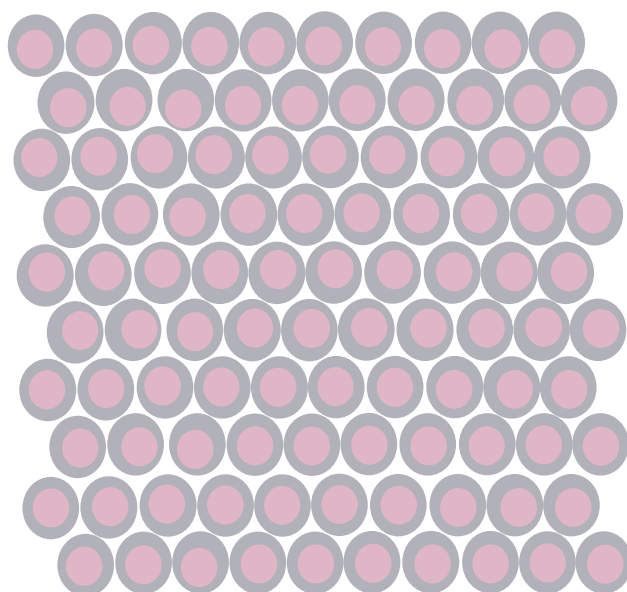


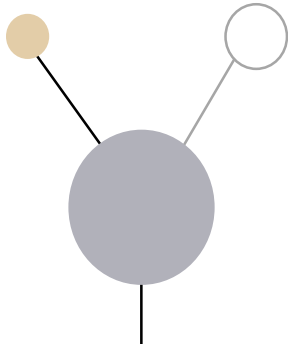
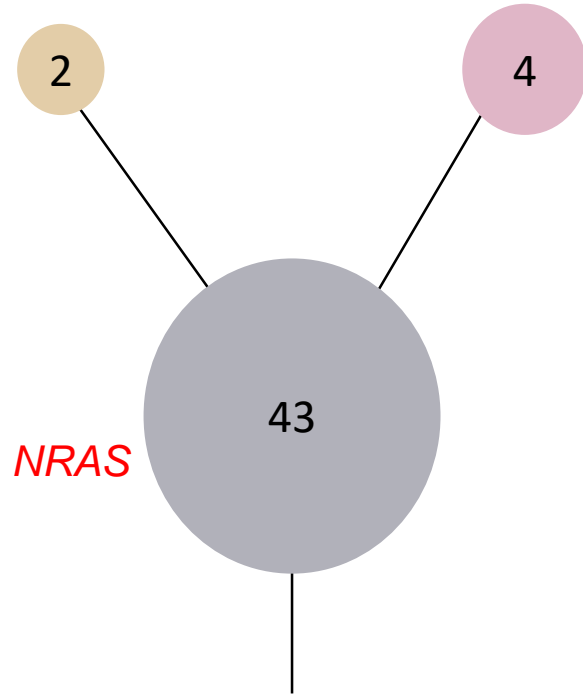


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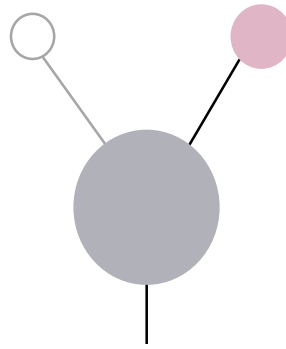


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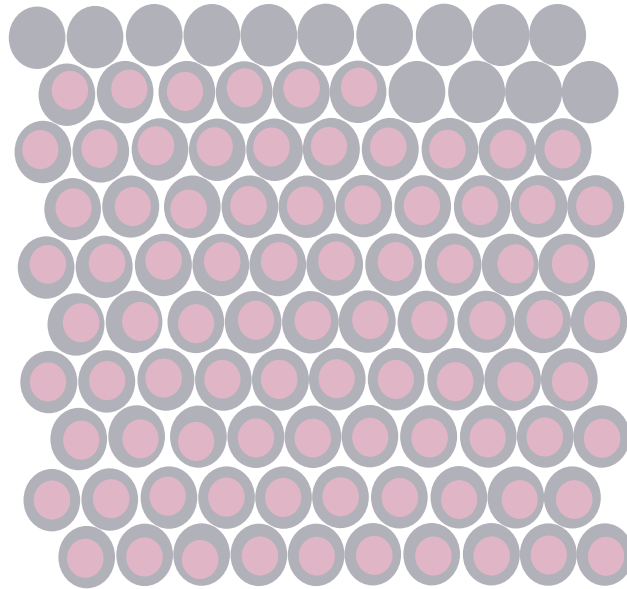
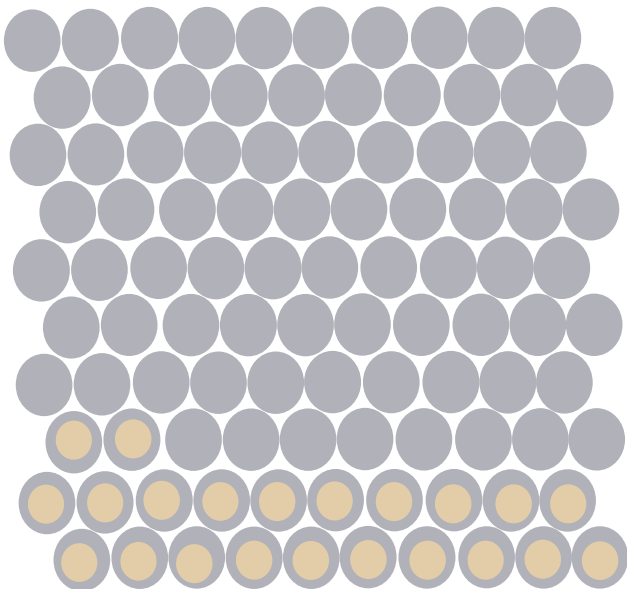


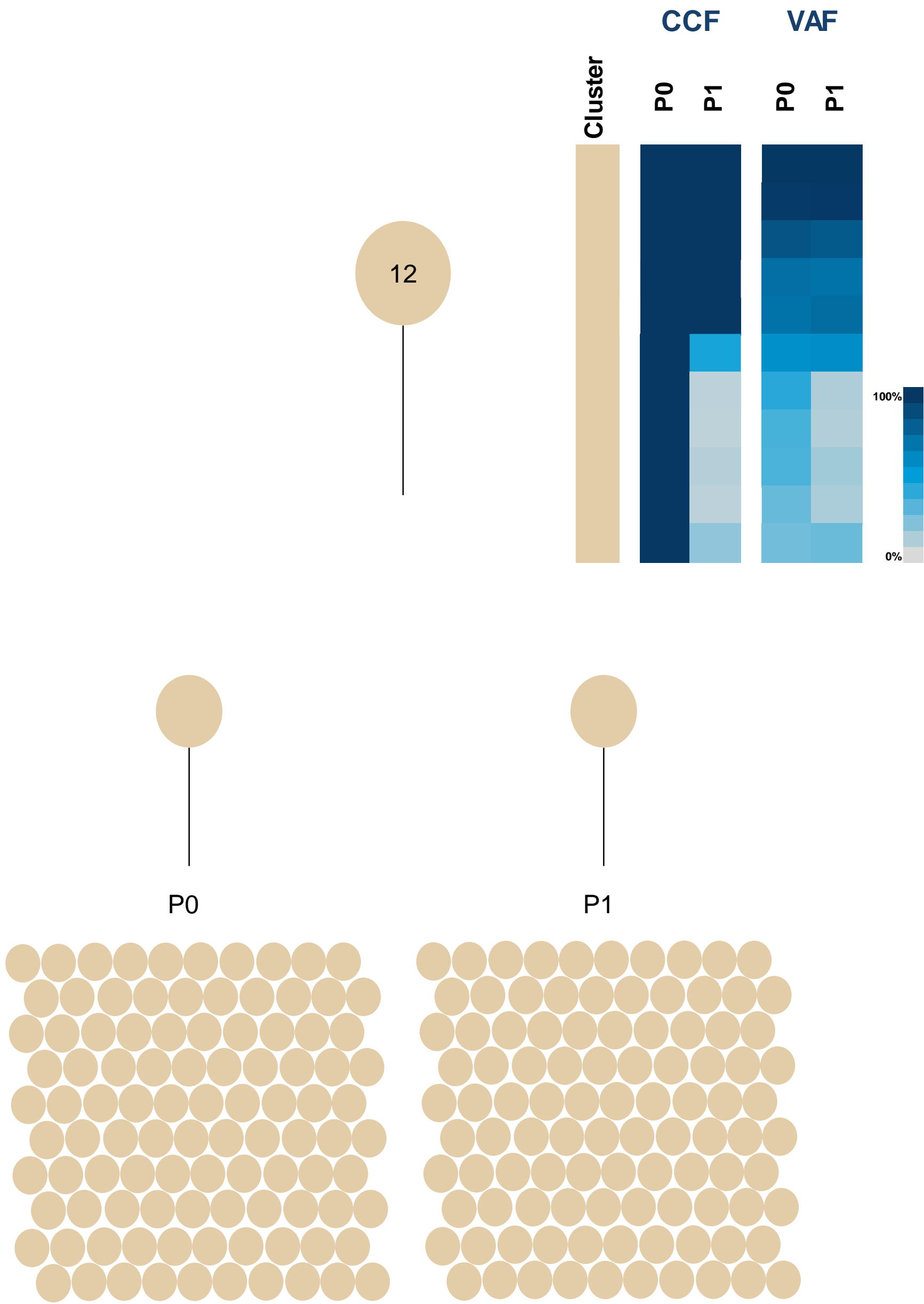


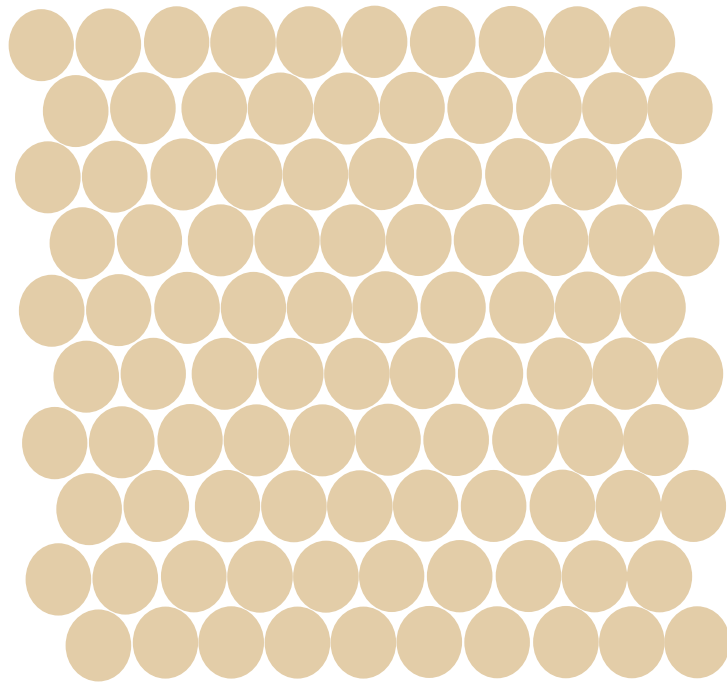
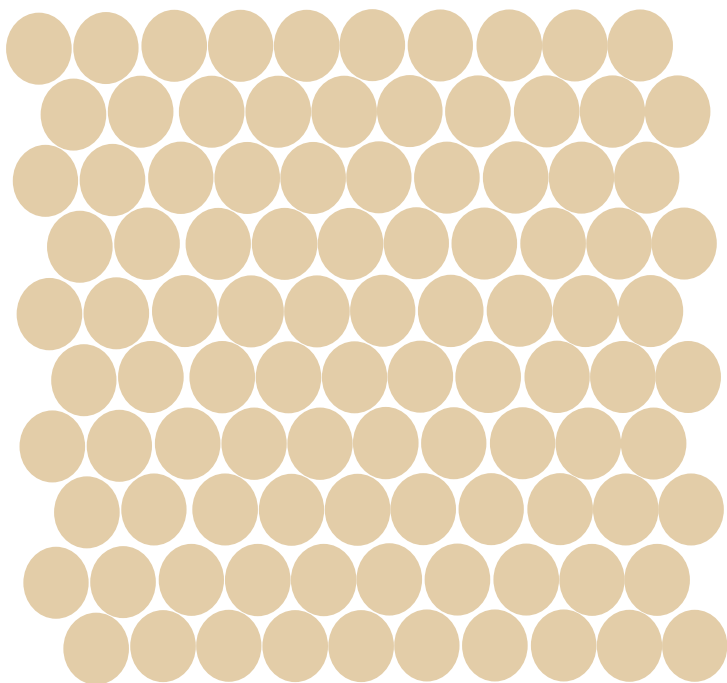
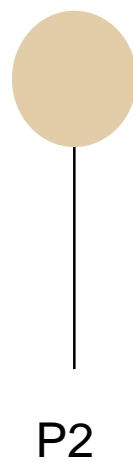
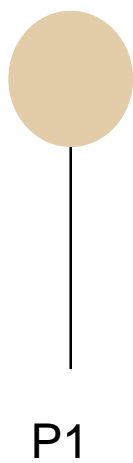
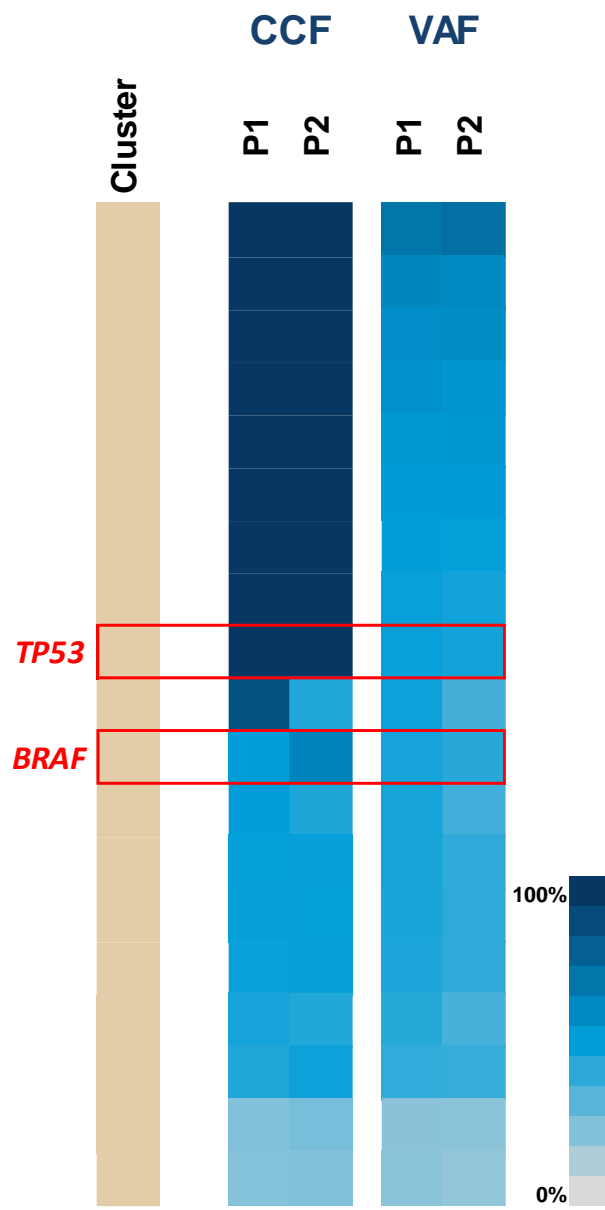
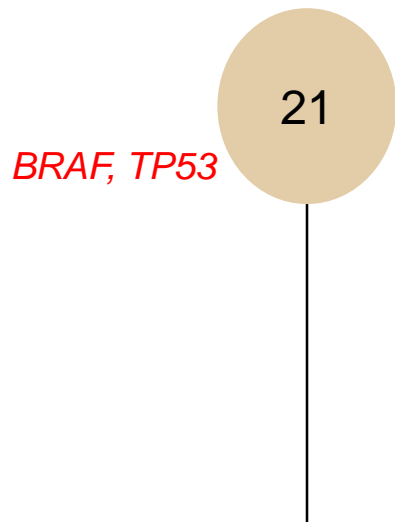
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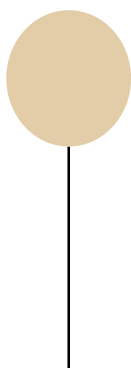
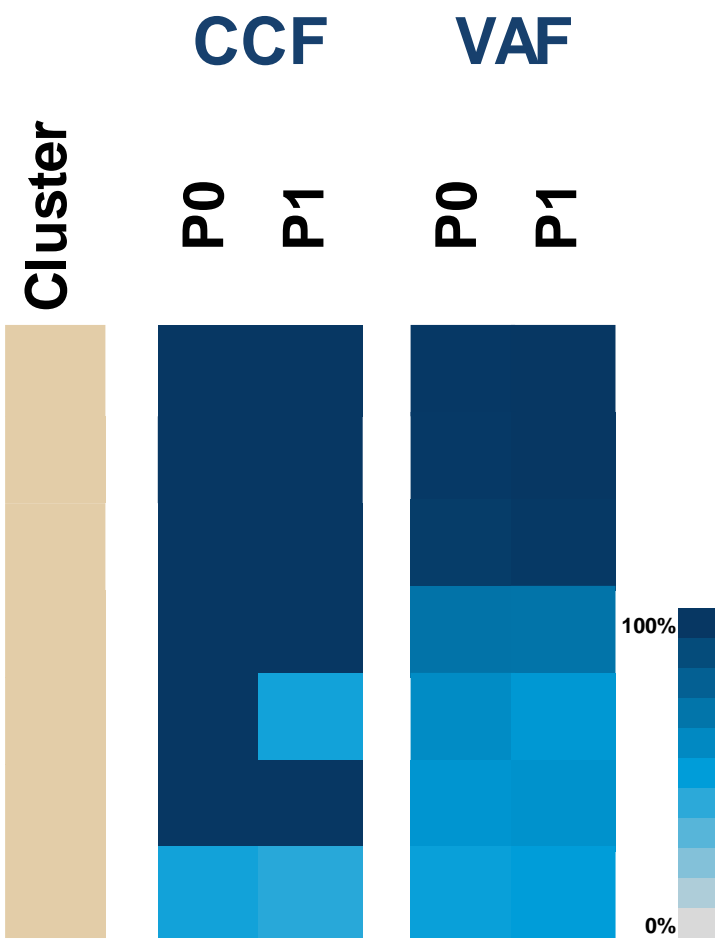
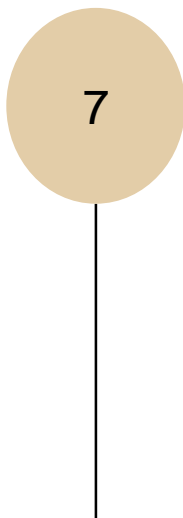


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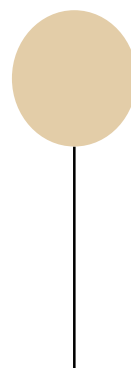
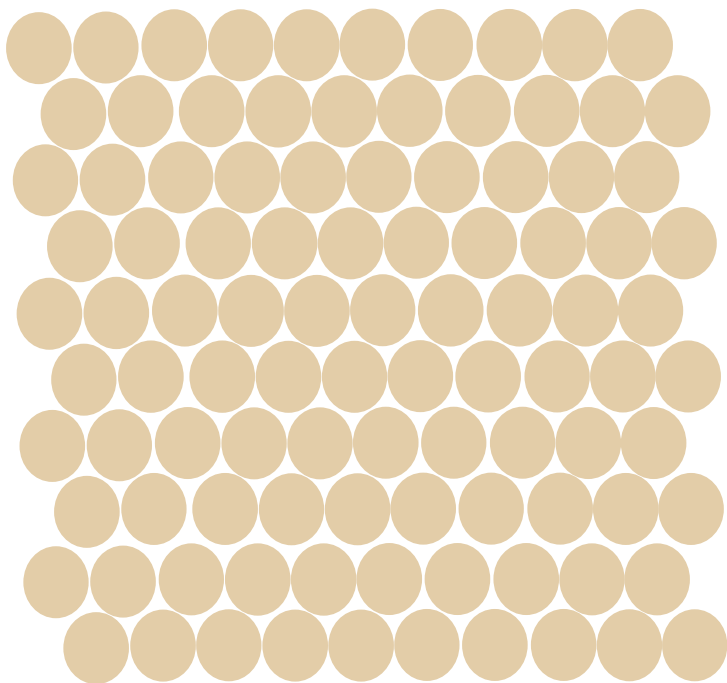








P0



P1

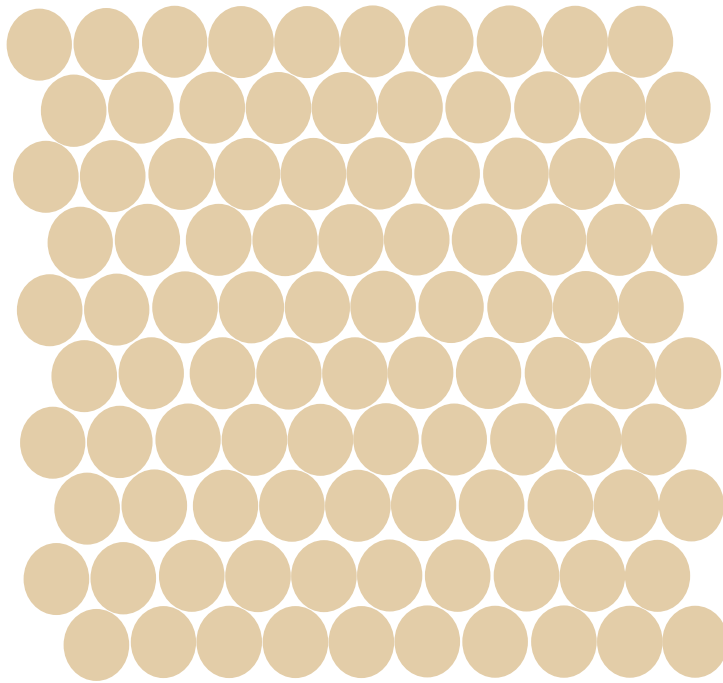


Figure S3: Phylogenetic trees. Phylogenetic trees for 77 PTC tumors. For each sample only the optimal trees derived using LICHeE (Lineage Inference for Cancer Heterogeneity and Evolution) have been presented. The right-side panel shows a colored bar representing all mutation clusters, with corresponding cancer cell fractions (CCF) and variant allele frequency (VAF) values as a heatmap, where darker colors indicate higher values. Driver genes are highlighted in red. The middle top pane shows the complete phylogenetic tree as constructed based on mutation clusters, and where relevant, primary and relapse phylogenetic trees have been shown separately in a black box. Different colored nodes represent distinct clones, with the number of mutations contributing to the cluster displayed inside each node. Below are the phylogenetic trees shown for each region, where clusters not found in a given region have been represented as grey empty nodes. “P”, represents regions from primary tumors; “R”, represents the tissues from . Beneath each regional phylogenetic tree, a grid of a 100 representative cells shows the mutational clusters present via coinciding cluster colors. In relevant samples, the left-side panel shows copy number aberrations (“Amp”, amplification) of cancer driver genes and corresponding cluster. Relapse cases (A) are denoted in green, whereas (B) Non-relapse cases are denoted in black.

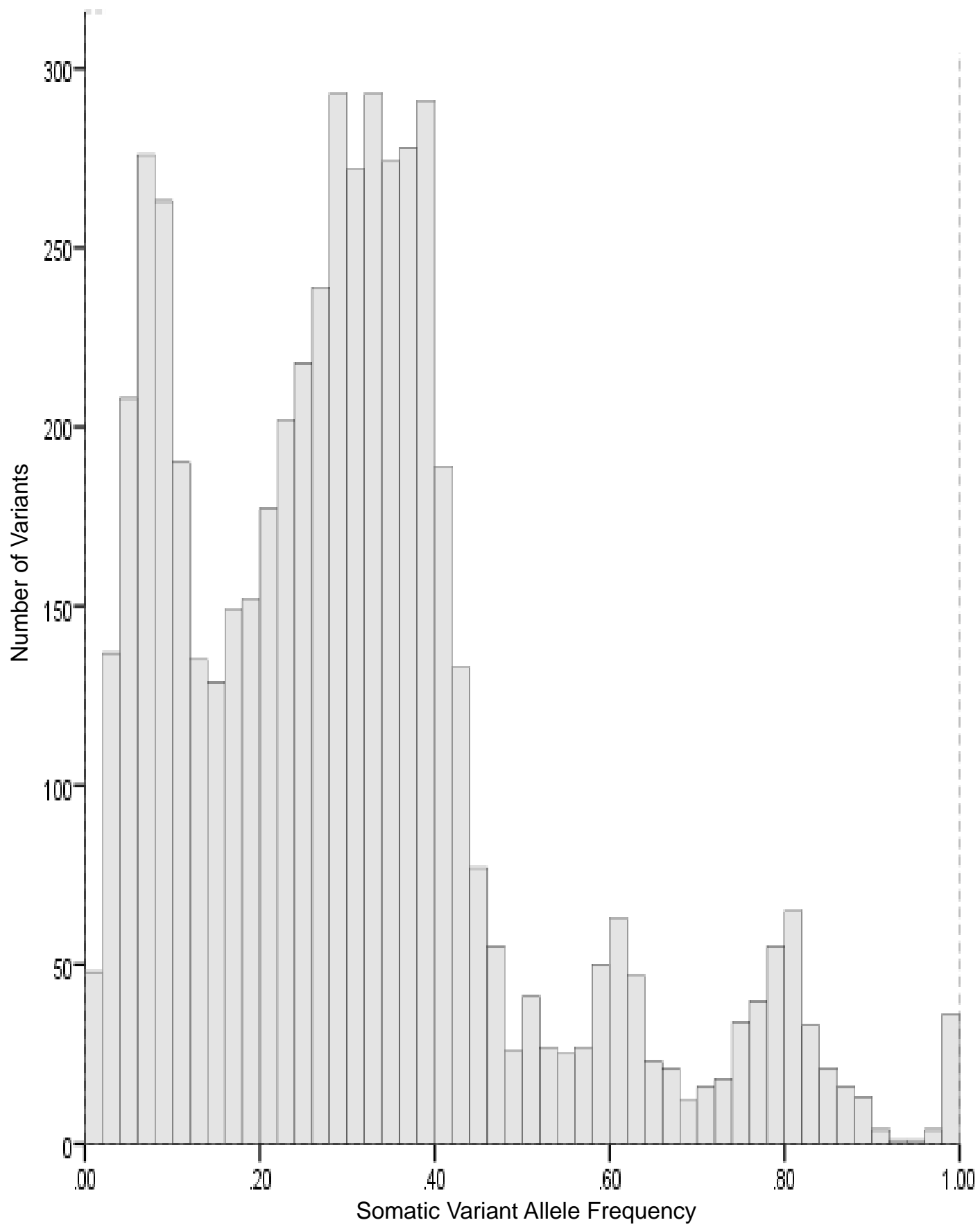


Figure S4: Variant allele frequency (VAF) with the number of somatic mutations.

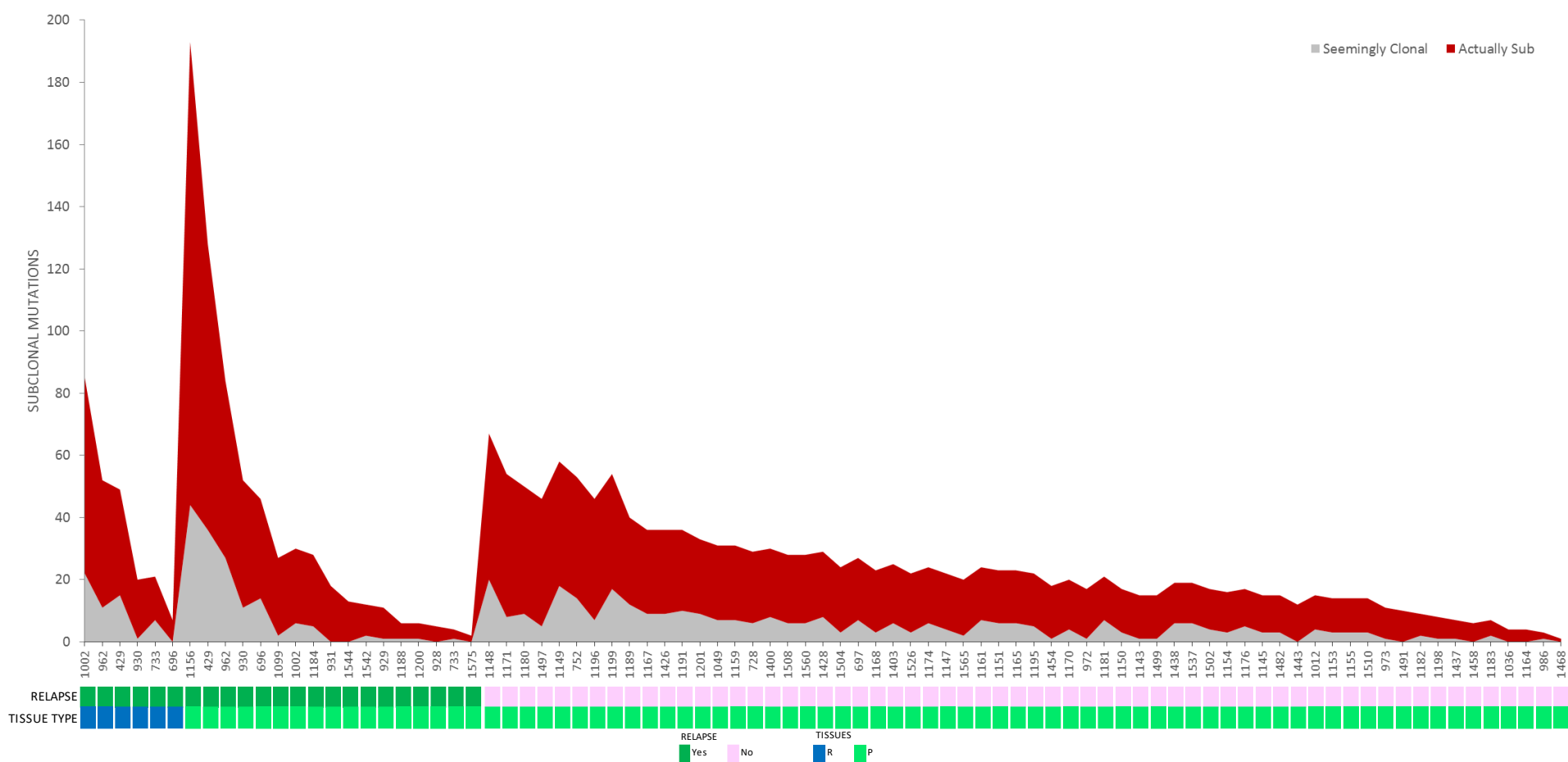


Figure S5: Illusion of Clonality. Barplot depicts all subclonal mutations, and whether these exhibit an illusion of clonality; whereby if the mutation was mostly clonal, but appeared subclonal in at least one tissue, overall the mutation would be considered subclonal

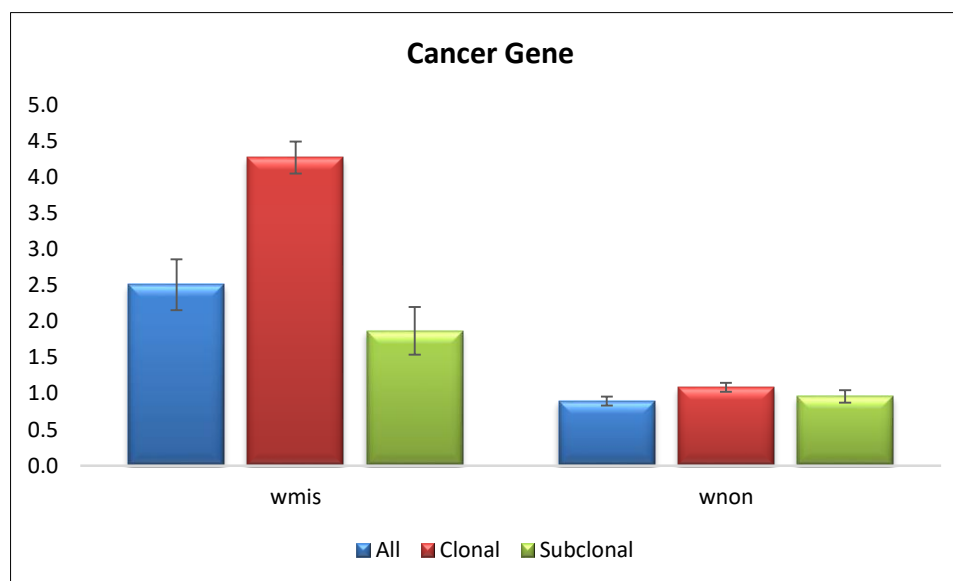
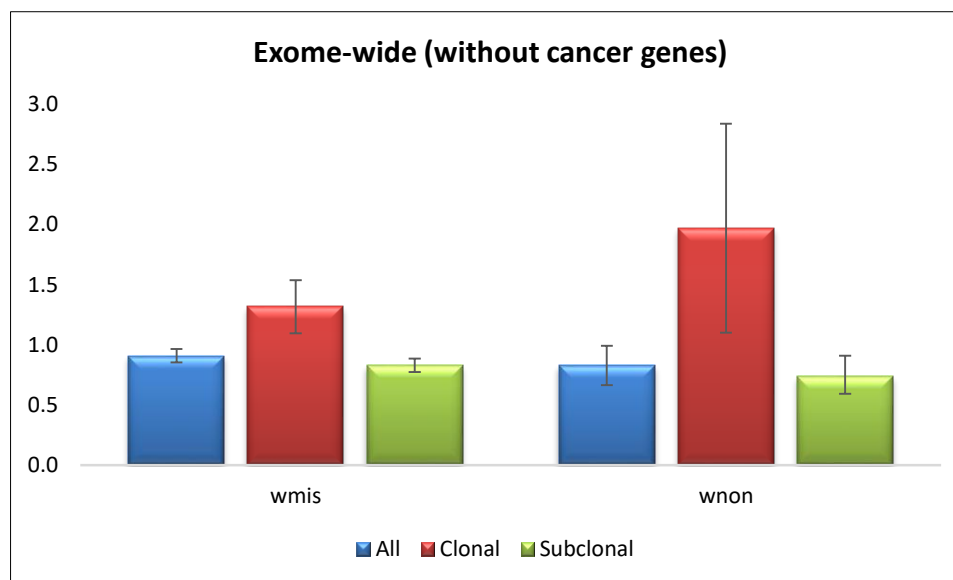
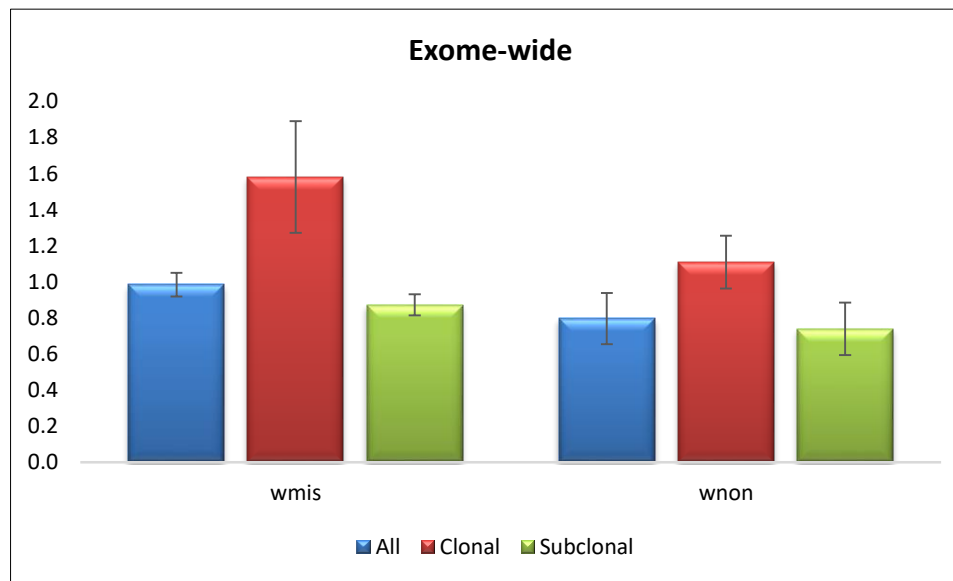


Figure S6: Plot showing dN/dS ratio. dN/dS ratio calculated as exome wide, exome wide without cancer genes and for cancer genes

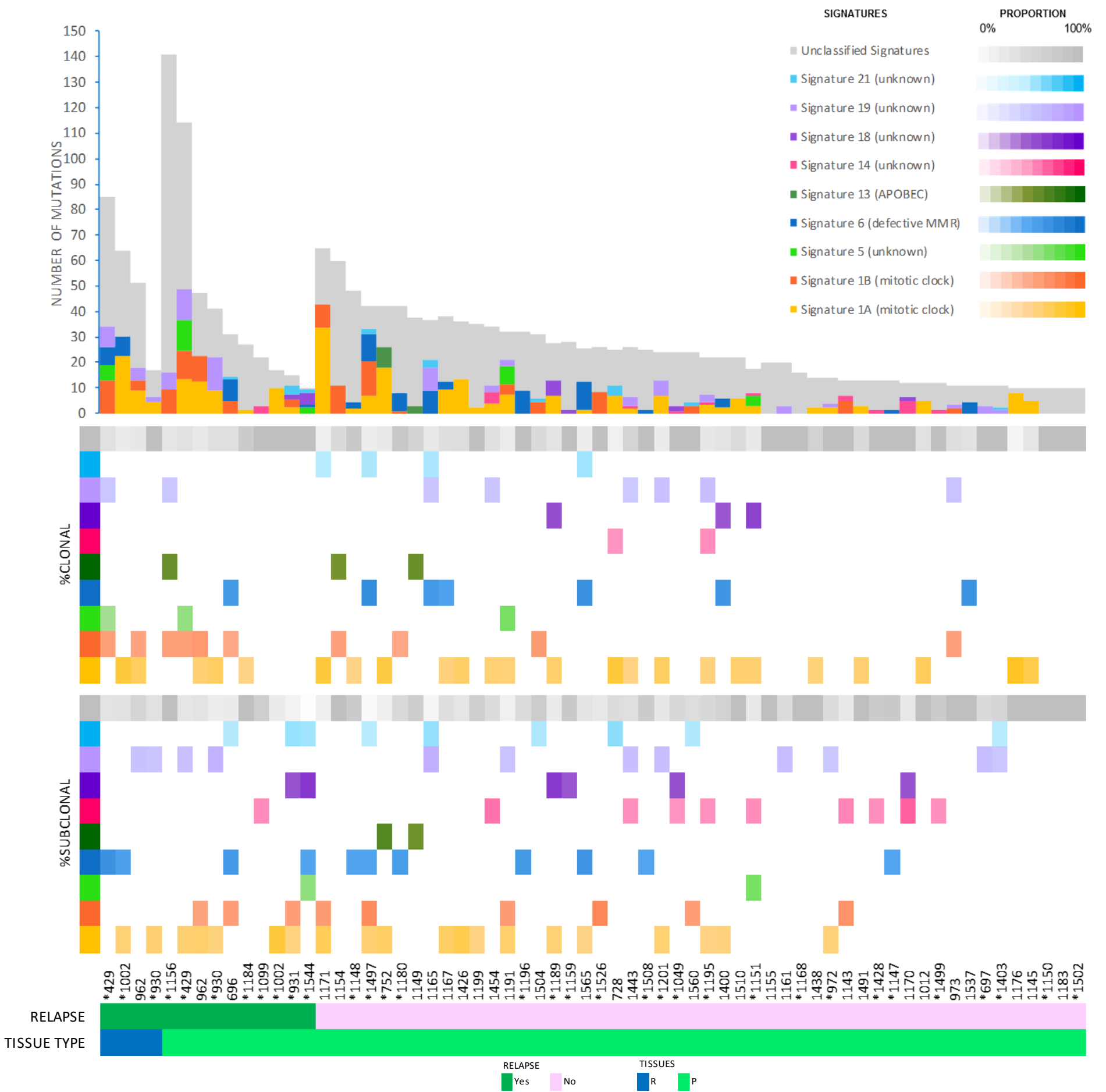
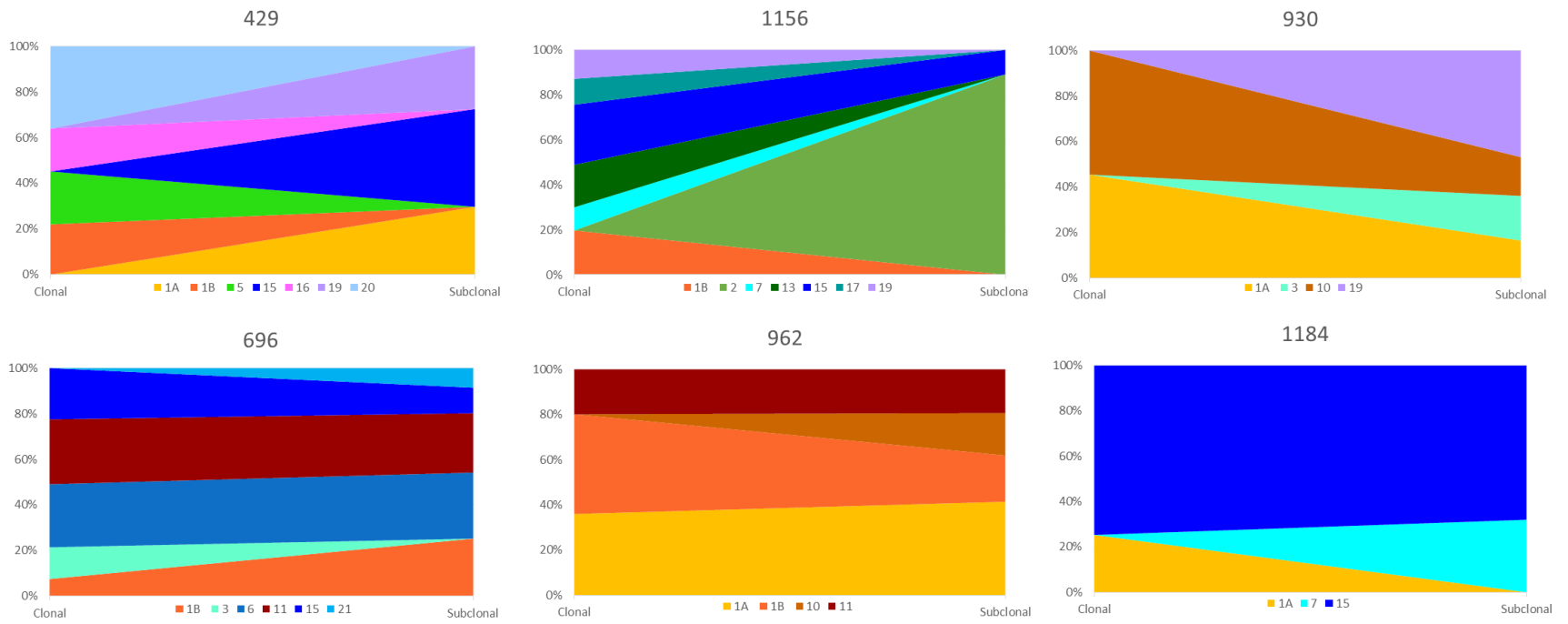
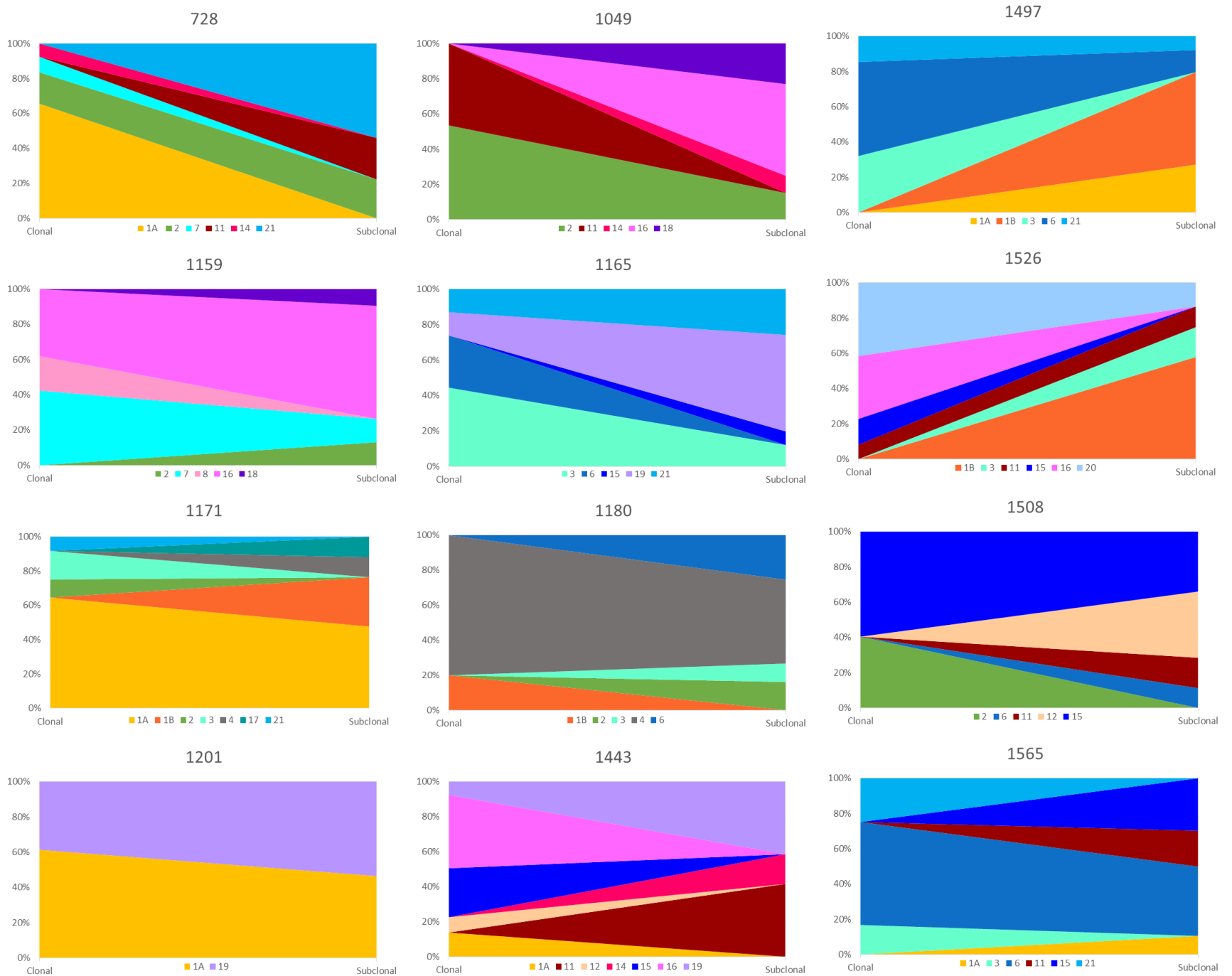


Figure S7: Mutational Signatures in PTC Cohort and Role in PTC Evolution. Significant mutational signatures identified in PTC cohort, split according to , relapse, tissue type (R=Relapsed tissue; P=Primary tissue) and proportion of clonality (more intense color represents higher proportion). Asterisk (*) represents samples with high number of subclonal mutations (median, 41%).

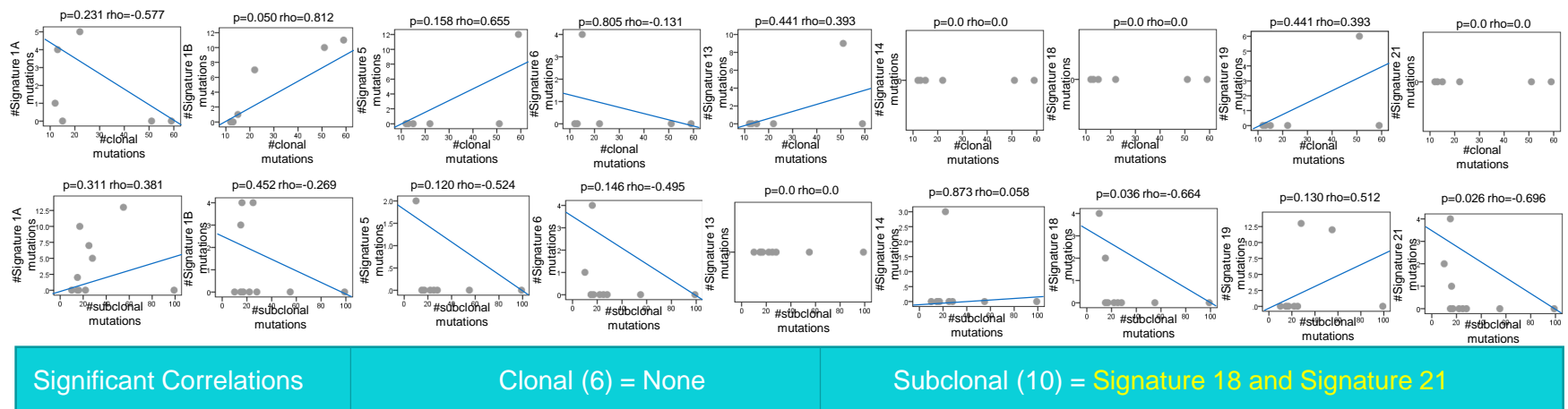
A Primary PTC with Relapse



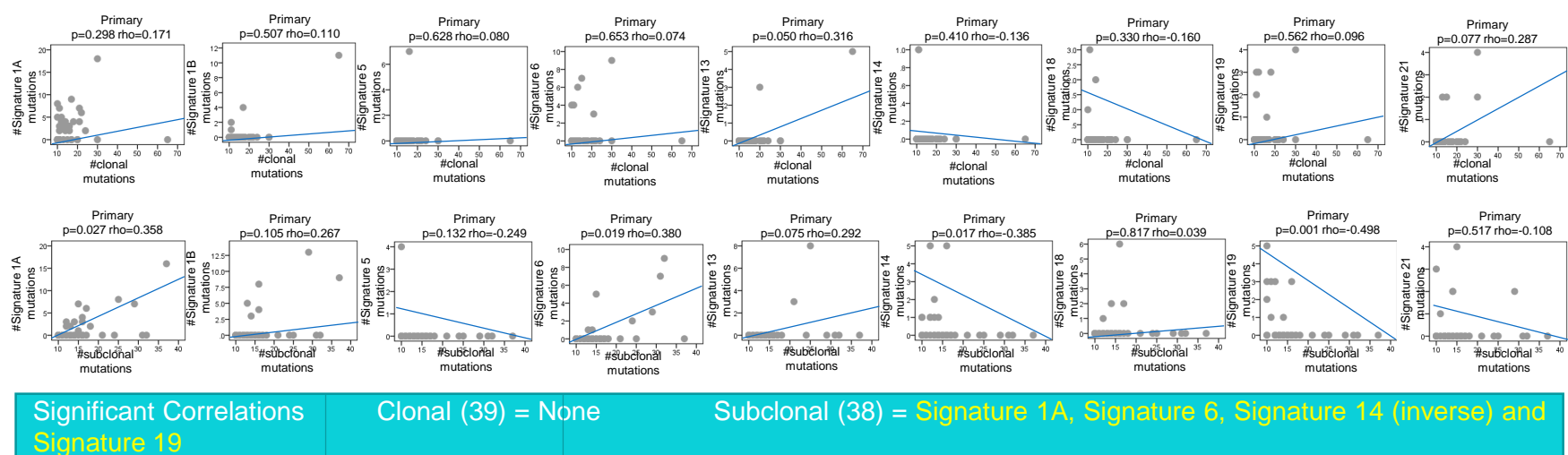
B Primary PTC without Relapse



A Primary PTC with Relapse



B Primary PTC without Relapse



C Overall Primary

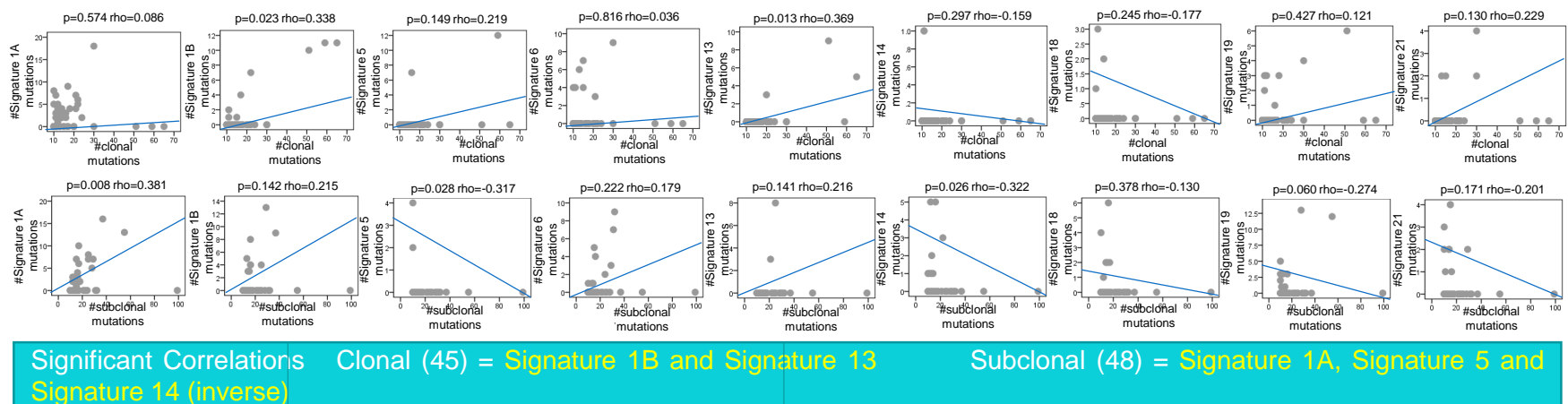


Figure S9 : Correlation of prevalence of mutational signatures in primary PTC tumors with relapse (A), primary PTC tumors (B) and in all primary PTC tissues, regardless of relapse (C). Significance from Spearman's rank correlation is indicated. A summary of the significant correlations are shown below each panel.

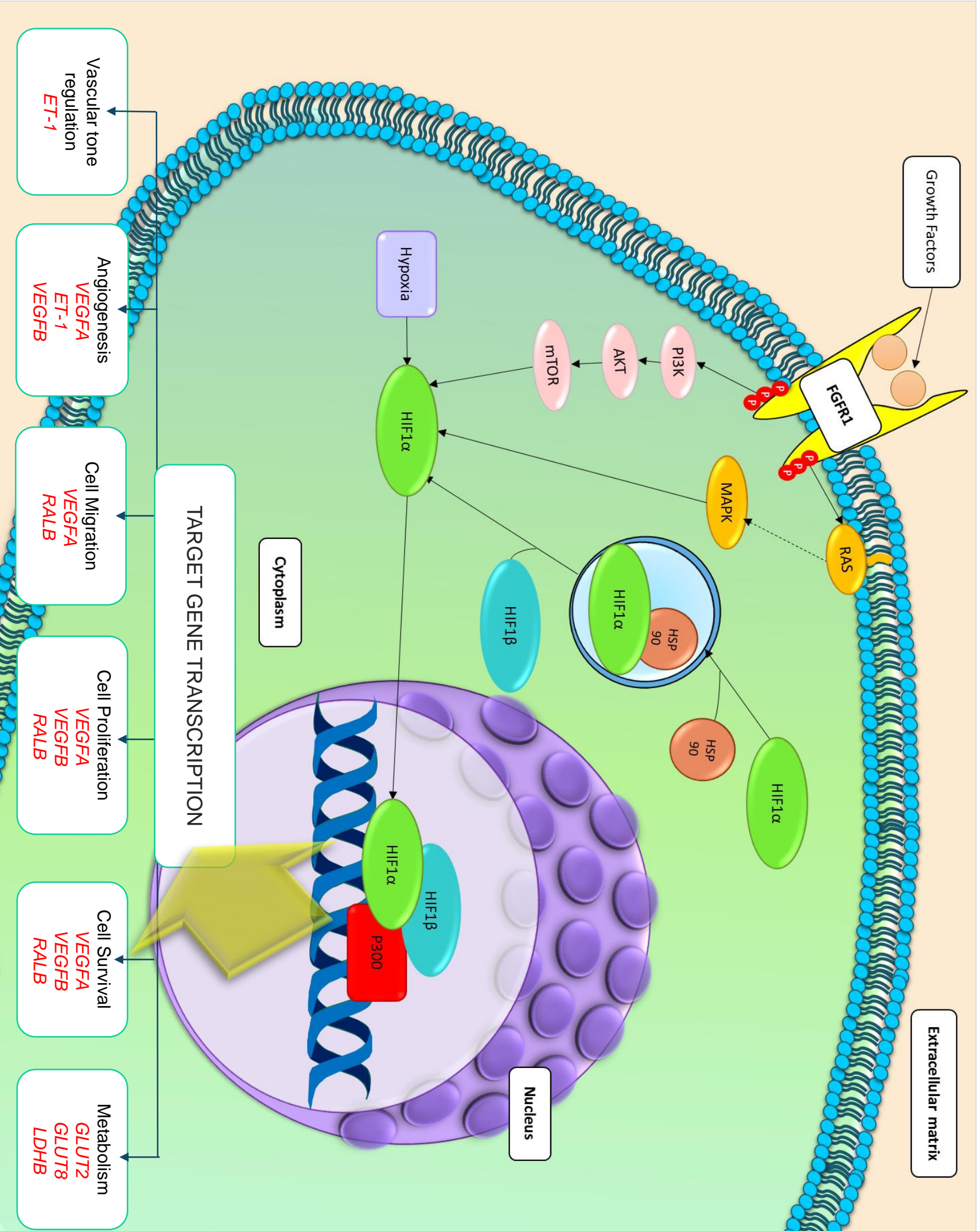


Figure S10: HIF1α pathway in PTC cancer progression.

Schematic of HIF1α positive regulatory genes and their effects on PTC progression. HIF1α signaling transduction causing downstream target gene transcription (summarized in the grey panel below) contributes to tumor progression via cell survival, proliferation and migration; metabolism; angiogenesis and vascular tone regulation. *FGFR1*, fibroblast growth factor receptor-1; P, phosphorylated; *PI3K* (*PIK3CA*, *PIK3CG*), phosphoinositide 3-kinase; *AKT*, AKT serine/threonine kinase; *mTOR*, mechanistic target of rapamycin kinase; *RAS* (*HRAS*), *RAS* proto-oncogene, GTPase; *MAPK* (*MAPK4*, *MAPK9*), mitogen-activated protein kinase; *HIF1α*, hypoxia-inducible factor 1-alpha; *HIF1β*, hypoxia-inducible factor 1-beta; *HSP90* (*HSP90AA1*), heat shock protein 90; *p300* (*EP300*), histone acetyltransferase *p300*; *ET-1* (*EDN1*), endothelin 1; *VEGF* (*VEGFA*, *VEGFB*), vascular endothelial growth factor; *GLUT* (*SCL2A2/GLUT2*; *SCL2A8/GLUT8*), solute carrier family 2 facilitated glucose transporter; *LDH* (*LDHB*), lactate dehydrogenase.

Table S1. Summary of clinical and pathological characteristics of the PTC cohort (n=79)

Clinico-pathological characteristics	Number of cases, n(%)
Median age at diagnosis (range) in years	33 (25-42)
Gender	
Male	15 (19.0)
Female	64 (81.0)
Histological subtype	
Classical variant	42 (53.2)
Follicular variant	17 (21.5)
Tall Cell variant	11 (13.9)
Other variants	9 (11.4)
Extra-thyroidal extention	
Present	29 (36.7)
Absent	50 (63.3)
Lymphovascular invasion	
Present	28 (41.2)
Absent	40 (58.8)
Margin involvement	
Present	28 (38.9)
Absent	44 (61.1)
pT	
T1	19 (24.1)
T2	21 (26.6)
T3	37 (46.8)
T4	2 (2.5)
pN	
N0	39 (50.6)
N1	38 (49.4)
pM	
M0	75 (94.9)
M1	4 (5.1)
Stage	
I	71 (89.9)
II	8 (10.1)

Table S5: Multivariate analysis for Mutation –Disease-free survival (17 events among 79 patients)

Factor	Adjusted hazard ratio (95% CI)	p-value
Age	0.988 (0.937-1.041)	0.642
Gender	0.587 (0.180-1.916)	0.377
Stage	0.298 (0.074-1.199)	0.088
Extra thyroidal Extension	1.585 (0.552-4.549)	0.392
Tumor size	1.258 (0.947-1.670)	0.113
Mutation	3.623 (1.096-11.973)	0.035

Table S6: Association of clinico-pathological characteristics with subclonal mutations in PTC (n=79)

	Total		High Subclonal mutations		Low subclonal mutations		p value
	No.	%	No.	%	No.	%	
No. of patients	79		38	48.1	41	51.9	
Age (Yrs)							
≤ 45	69	87.3	35	50.7	34	49.3	0.214
> 45	10	12.7	3	30.0	7	70.0	
Sex							
Female	64	81.0	32	50.0	32	50.0	0.484
Male	15	19.0	6	40.0	9	60.0	
Extrathyroidal extension							
Absent	50	63.3	25	50.0	25	50.0	0.657
Present	29	36.7	13	44.8	16	55.2	
Surgical Margins							
Absent	44	61.1	22	50.0	22	50.0	1.000
Present	28	38.9	14	50.0	14	50.0	
pT							
T1	19	24.1	12	63.2	7	36.8	0.458
T2	21	26.6	10	47.6	11	52.4	
T3	37	46.8	15	40.5	22	59.5	
T4	2	2.5	1	50.0	1	50.0	
pN							
pN0	39	50.6	17	43.6	22	56.4	0.427
pN1	38	49.4	20	52.6	18	47.4	
pM							
pM0	75	94.9	34	45.3	41	54.7	0.014
pM1	4	5.1	4	100.0	0	0.0	
Stage							
I	71	89.9	34	47.9	37	52.1	0.910
II	8	10.1	4	50.0	4	50.0	
Histology Type							
Classical variant	42	53.2	22	52.4	20	47.6	0.642
Follicular Variant	17	21.5	6	35.3	11	64.7	
Tall Cell Variant	11	13.9	6	54.5	5	45.5	
Other variants	9	11.4	4	44.4	5	55.6	
Recurrence							
Yes	17	21.5	13	76.5	4	23.5	0.005
No	62	78.5	25	40.3	37	59.7	
HIF-1α IHC							
High	52	66.7	29	55.8	23	44.3	0.076
Low	26	33.3	9	34.6	17	65.4	
Disease-free survival				60.6		92.5	0.010

Table S9: Association of clinico-pathological characteristics with HIF-1 α expression in PTC

	Total		HIF-1 α High (>20%)		HIF-1 α normal (\leq 20%)		p value
	No.	%	No.	%	No.	%	
No. of patients	1231		843	68.5	388	31.5	
Age (Yrs)							
\leq 45	787	64.3	494	62.8	293	37.2	<0.001
> 45	436	35.7	349	80.0	87	20.0	
Sex							
Female	927	75.8	635	68.5	292	31.5	0.566
Male	296	24.2	208	70.3	88	29.7	
Extrathyroidal extension							
Absent	519	49.2	347	66.9	172	33.1	0.027
Present	535	50.8	391	73.1	144	26.9	
Surgical Margins							
Absent	346	51.7	232	67.0	114	33.0	0.904
Present	323	48.3	218	67.5	105	32.5	
pT							
T1	322	27.1	232	72.0	90	28.0	0.115
T2	248	20.9	162	65.3	86	34.7	
T3	507	42.7	346	68.2	161	31.8	
T4	110	9.3	84	76.4	26	23.6	
pN							
pN0	473	42.7	340	71.9	133	28.1	0.179
pN1	634	57.3	432	68.1	202	31.9	
pM							
pM0	1097	95.1	757	69.0	340	31.0	0.118
pM1	56	4.9	44	78.6	12	21.4	
Stage							
I	822	69.0	528	64.2	294	35.8	<0.001
II	57	4.8	39	68.4	18	31.6	
III	108	9.1	81	75.0	27	25.0	
IV	204	17.1	176	86.3	28	13.7	
Histology Type							
Classical variant	865	70.2	601	69.5	264	30.5	0.158
Follicular Variant	193	15.7	128	66.3	65	33.7	
Tall Cell Variant	97	7.9	70	72.2	27	27.8	
Other variants	76	6.2	44	57.9	32	42.1	
Disease-free survival				73.6		81.3	0.037