

# Supplementary Figures

## Genetic association studies of alterations in protein function expose recessive effects on cancer predisposition

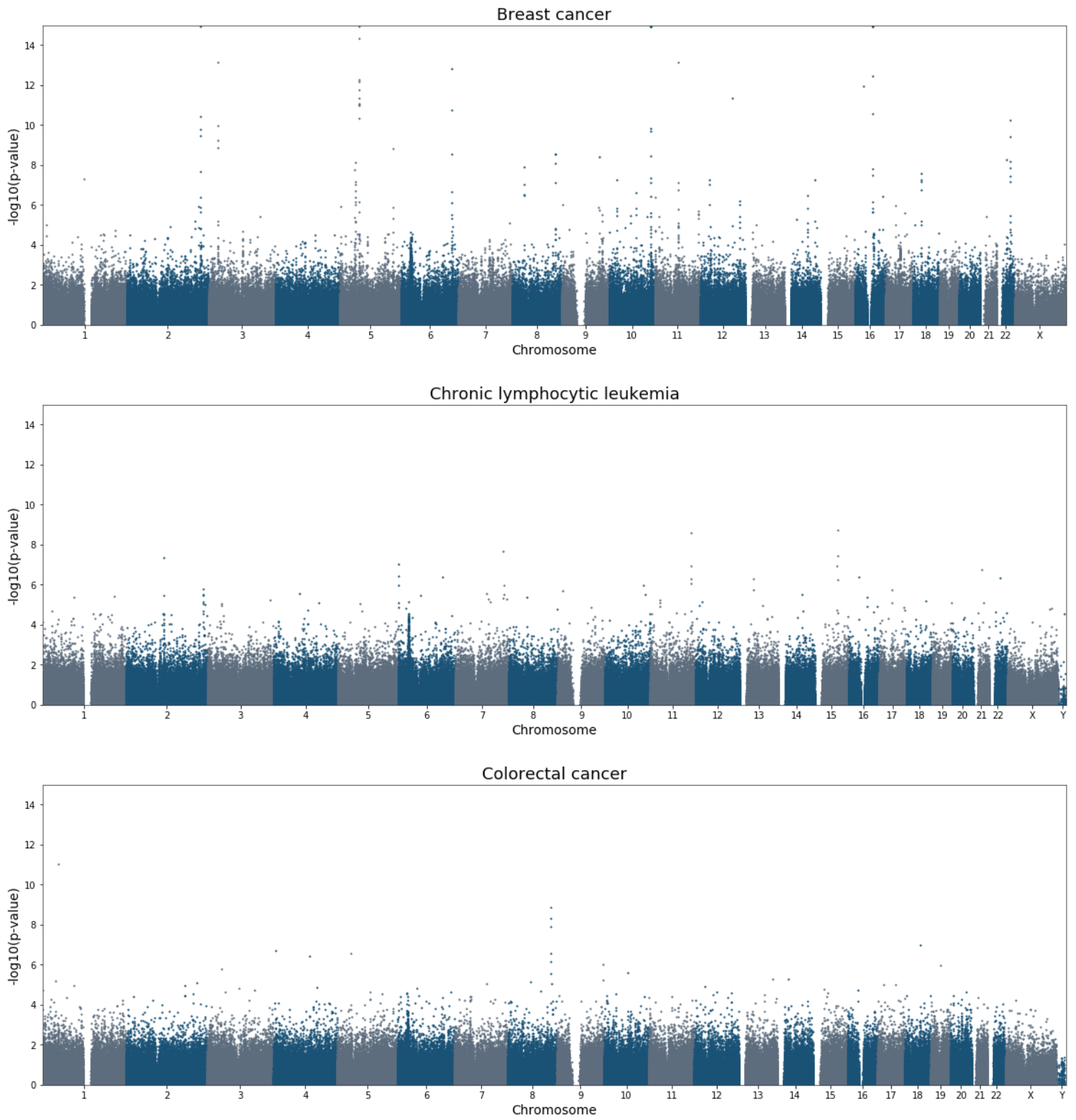
Nadav Brandes, Nathan Linial, Michal Linial

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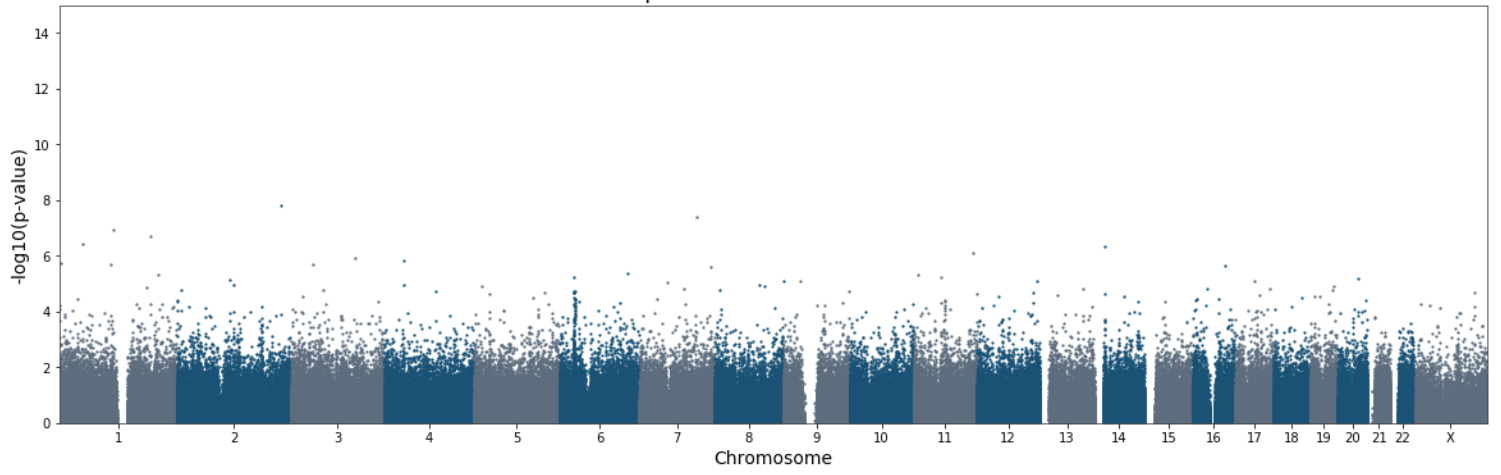
Supplementary Fig. S1: Genome-wide cancer predisposition in all ten cancer-types (an extension of Fig. 4 in the main text; page 2).

Supplementary Fig. S2: Cancer risk across all 110 PWAS-significant genes (an extension of Fig. 6C in the main text; page 6).

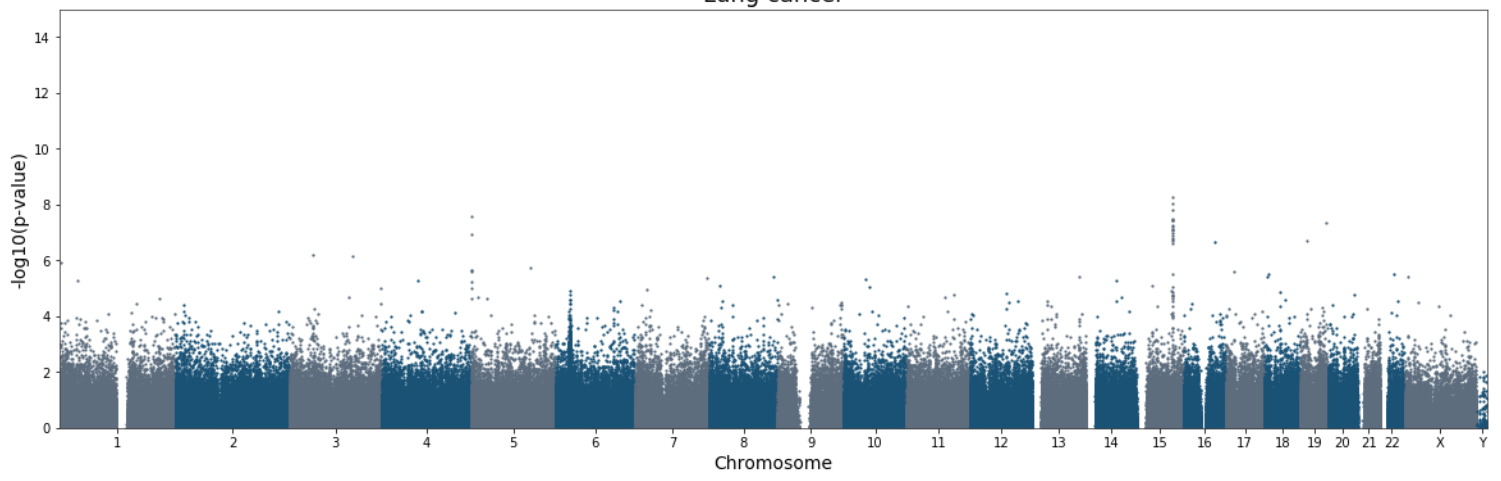
Supplementary Fig. S1: Genome-wide cancer predisposition in all ten cancer-types



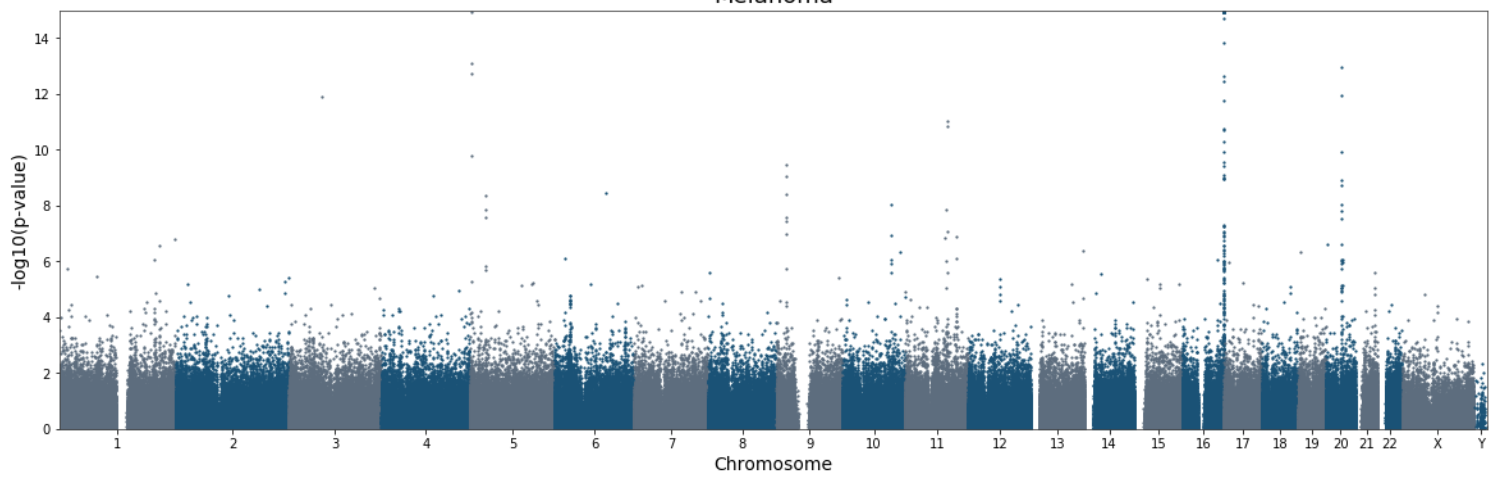
Epithelial ovarian cancer



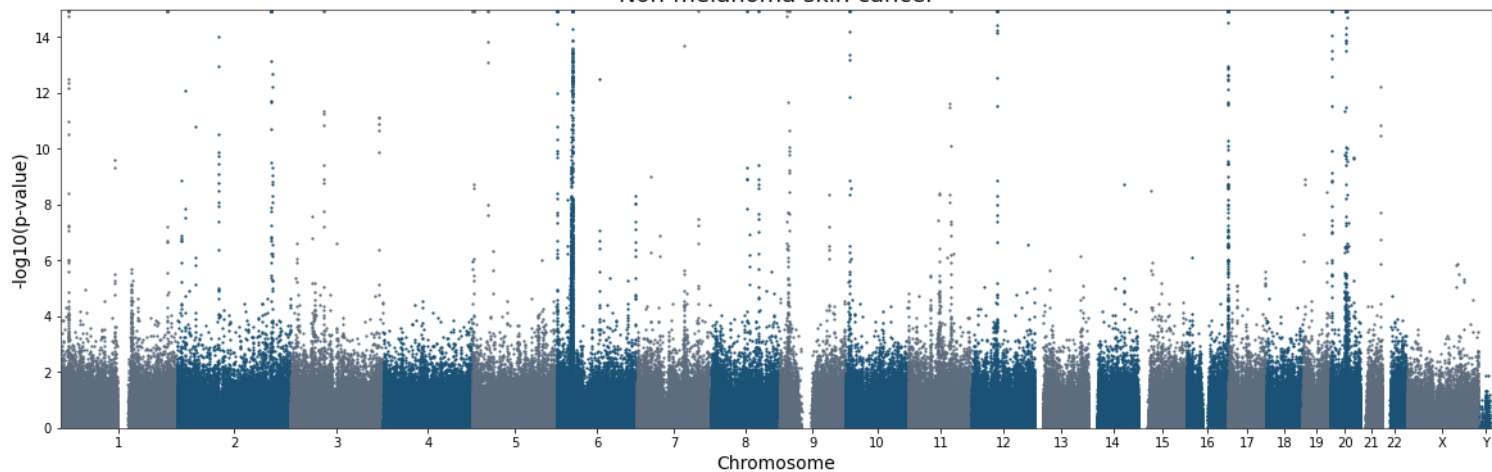
Lung cancer



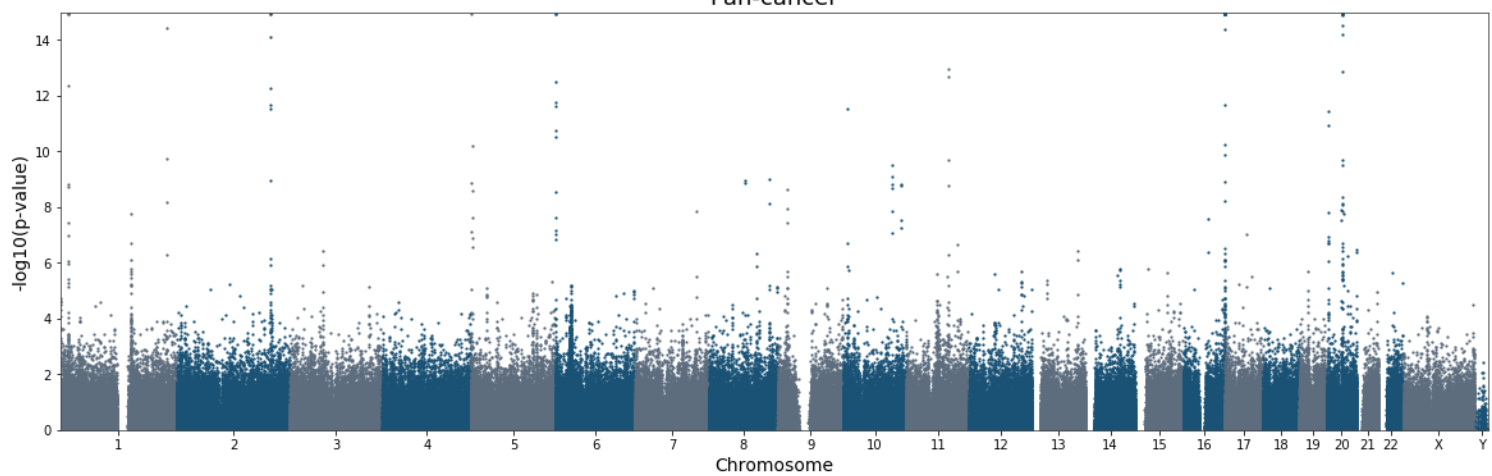
Melanoma



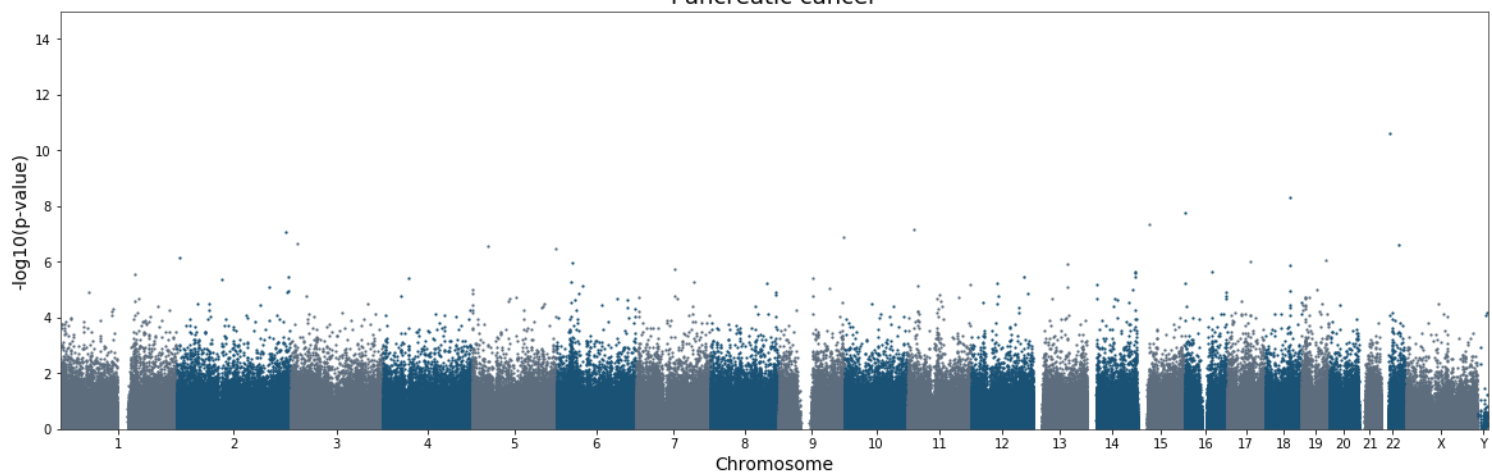
Non-melanoma skin cancer



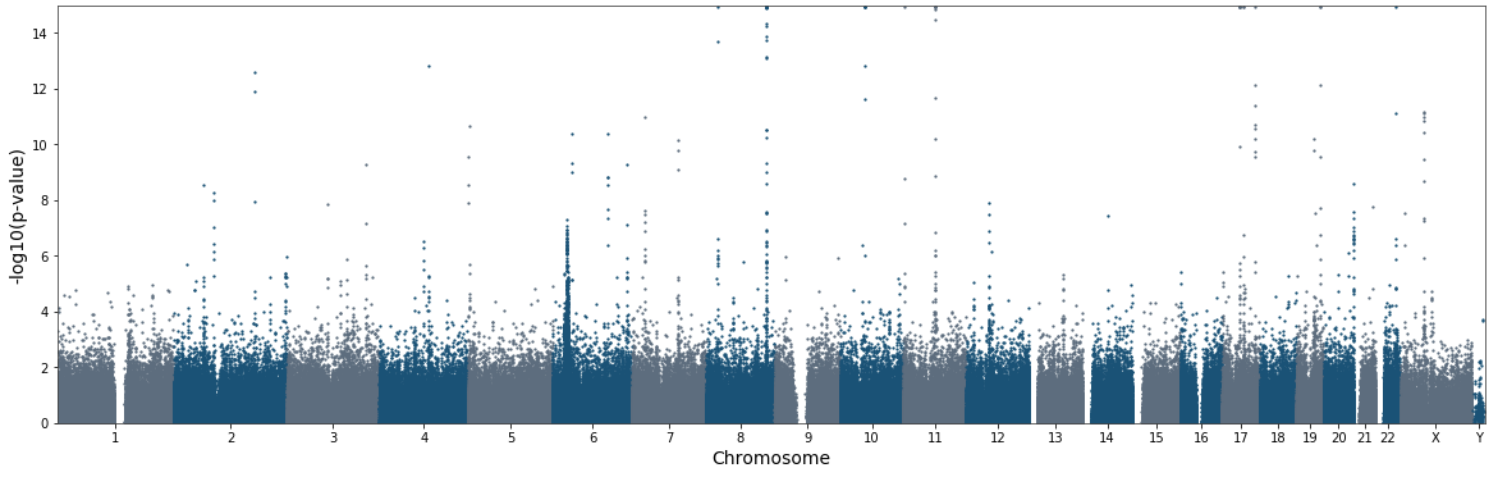
Pan-cancer



Pancreatic cancer

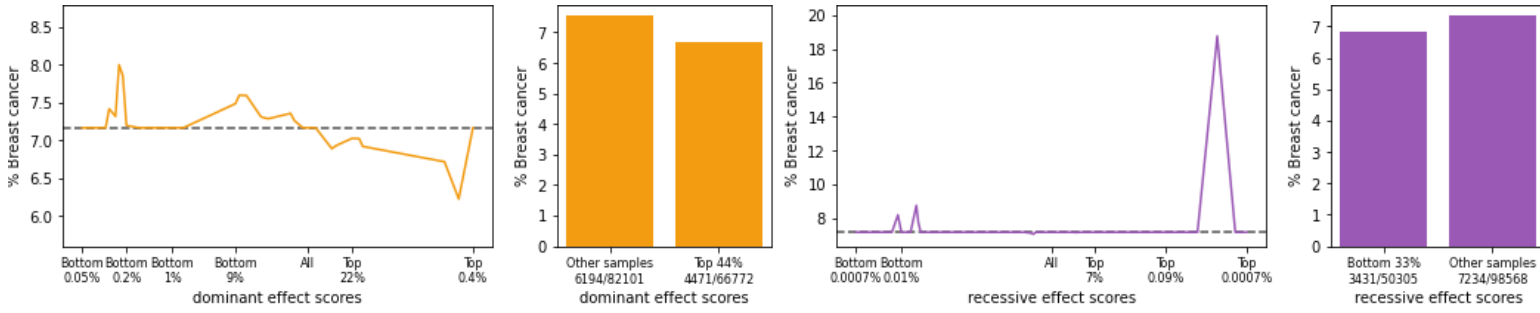


# Prostate cancer

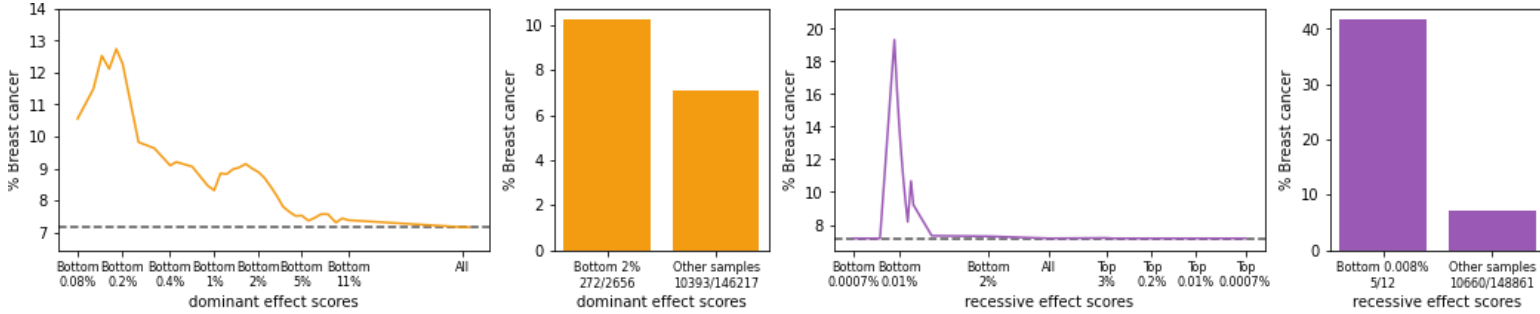


Supplementary Fig. S2: Cancer risk across all 110 PWAS-significant genes

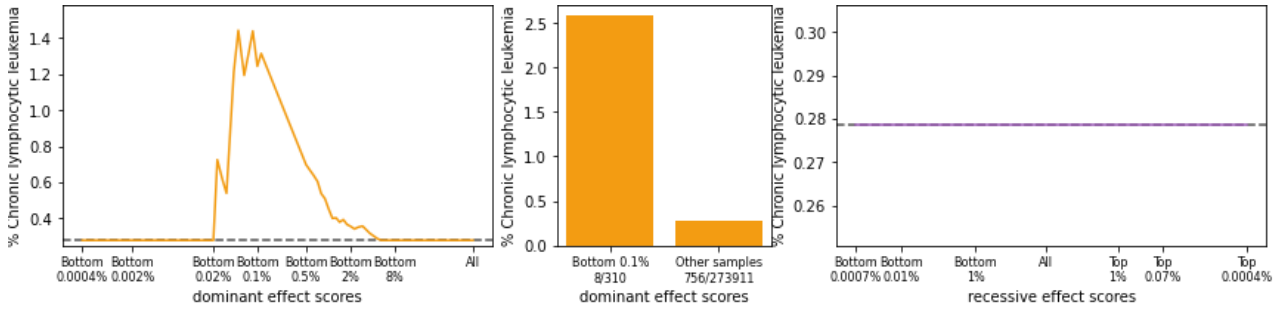
CCDC170 & Breast cancer: PWAS q-value = 5e-05 (Dominant)



CHEK2 & Breast cancer: PWAS q-value = 5e-05 (Dominant)



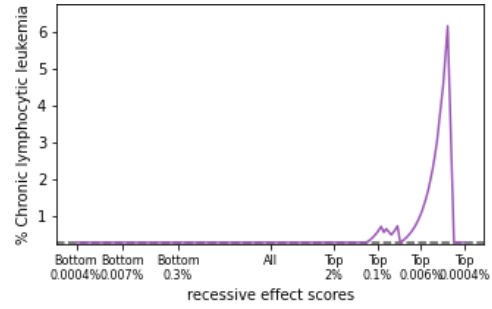
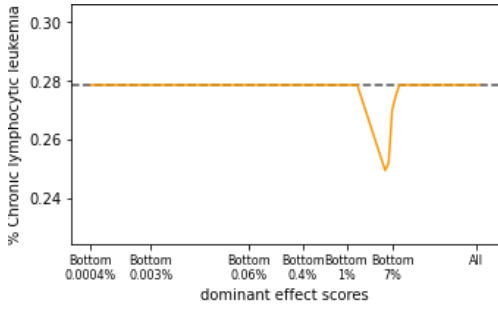
ALDOA & Chronic lymphocytic leukemia: PWAS q-value = 0.007 (Dominant)



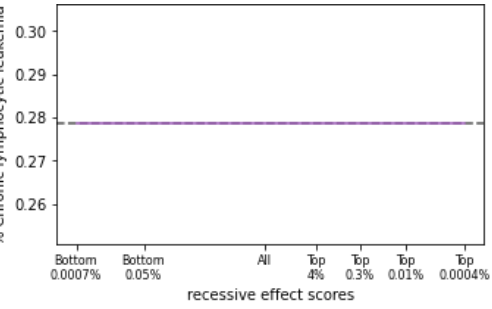
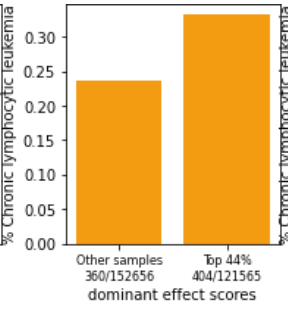
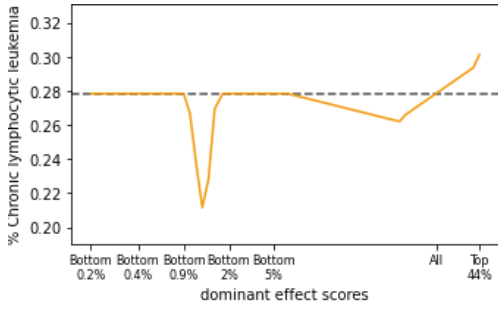
BIRC3 & Chronic lymphocytic leukemia: PWAS q-value = 0.04 (Recessive)



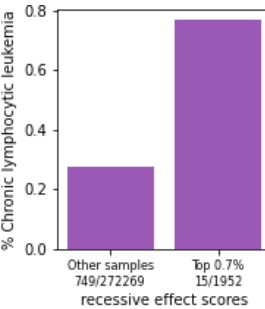
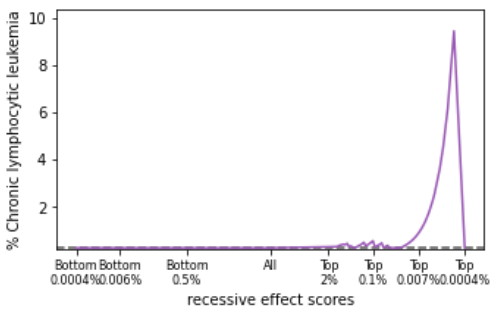
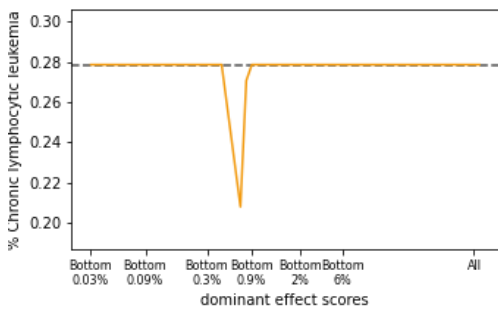
CCT8 & Chronic lymphocytic leukemia: PWAS q-value = 0.02 (Recessive)



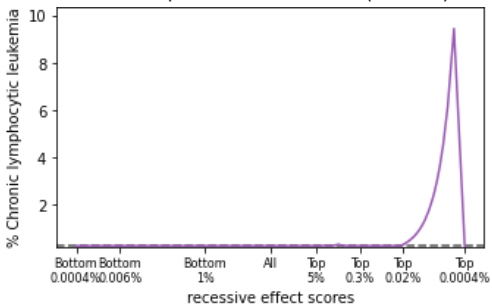
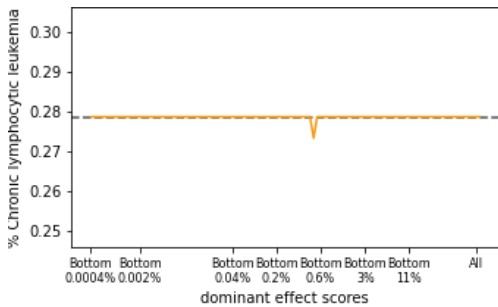
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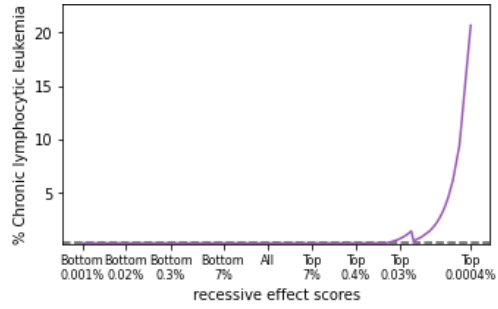
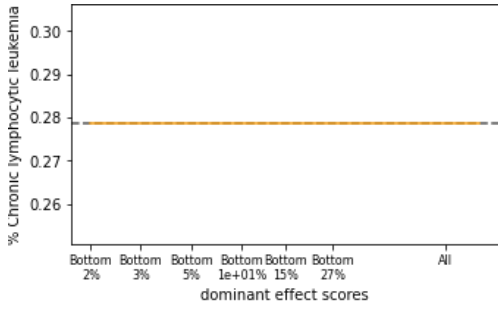
DPT & Chronic lymphocytic leukemia: PWAS q-value = 0.04 (Recessive)



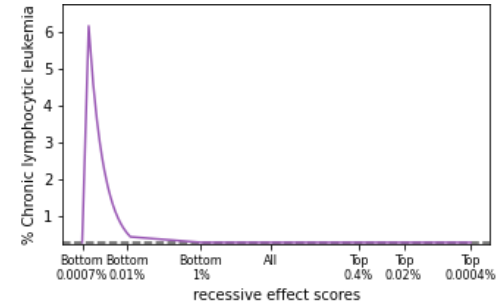
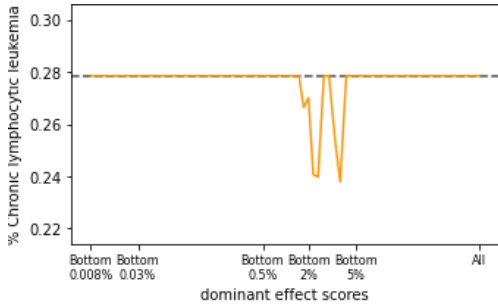
FAM160B1 & Chronic lymphocytic leukemia: PWAS q-value = 0.009 (None)



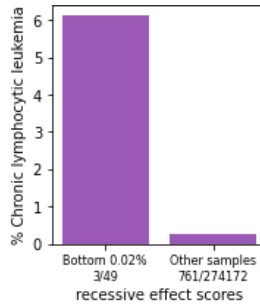
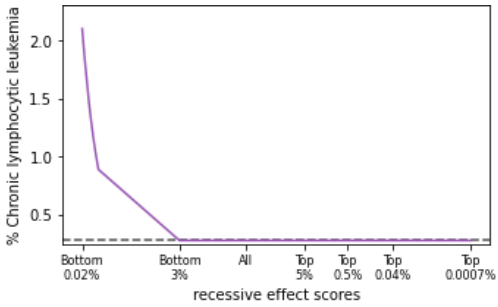
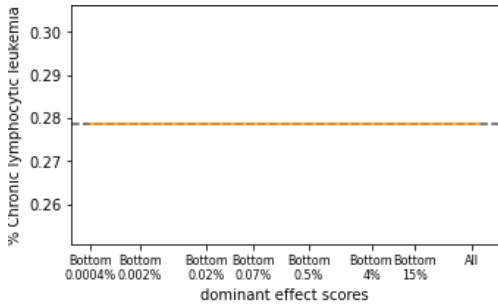
FCGR1A & Chronic lymphocytic leukemia: PWAS q-value = 0.04 (Recessive)



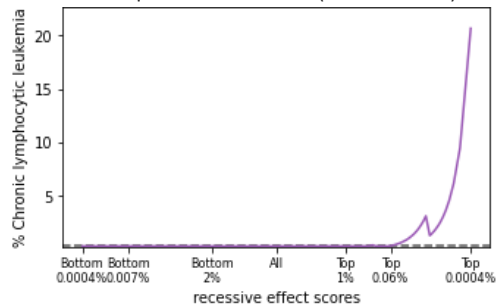
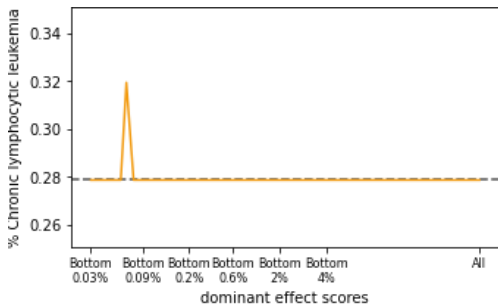
LYZL4 & Chronic lymphocytic leukemia: PWAS q-value = 0.02 (Recessive)



NLRP9 & Chronic lymphocytic leukemia: PWAS q-value = 0.02 (Recessive)

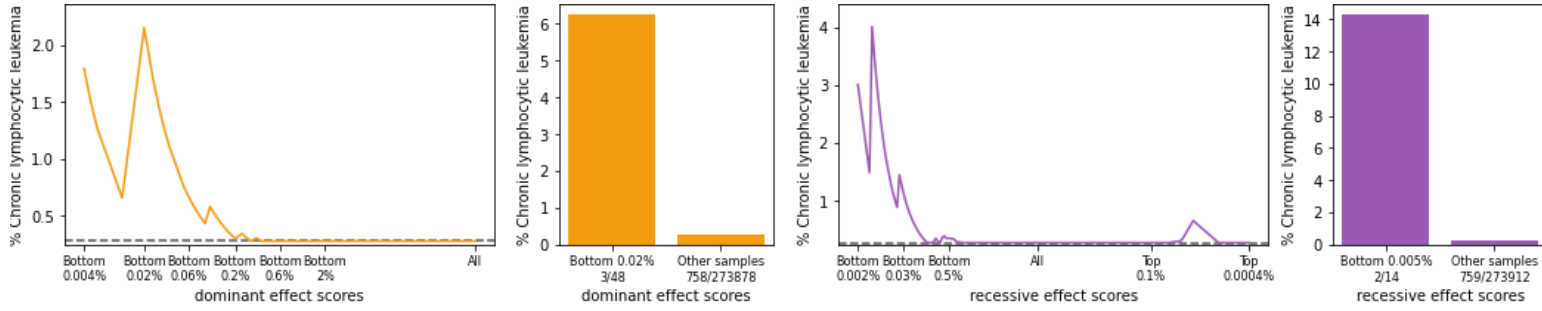


PCDH10 & Chronic lymphocytic leukemia: PWAS q-value = 0.02 (Recessive)

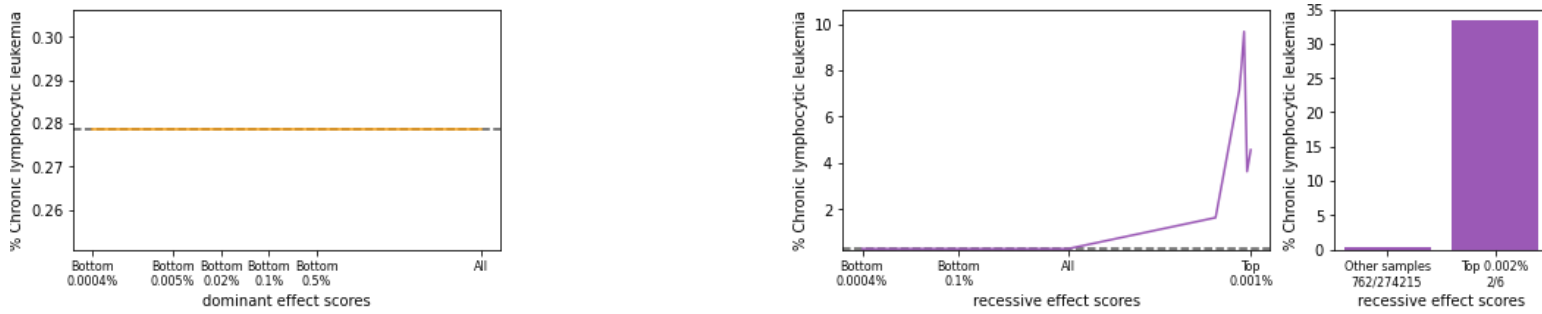




RBMX2 & Chronic lymphocytic leukemia: PWAS q-value = 0.03 (Recessive)



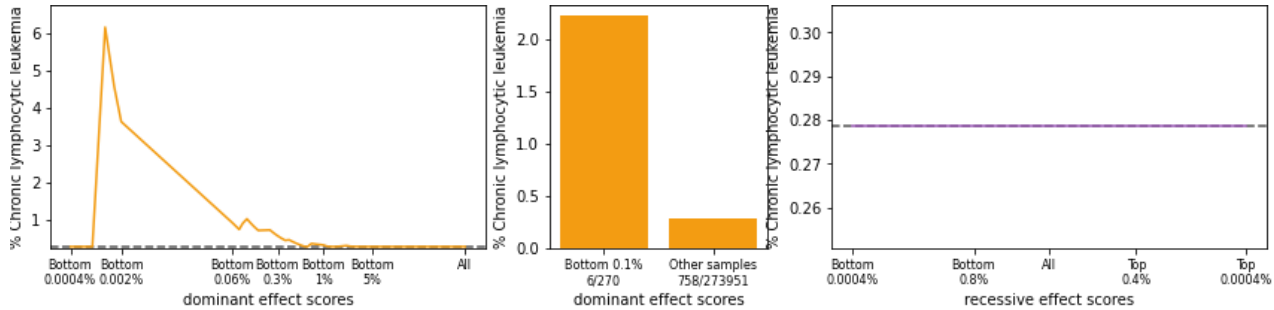
RCHY1 & Chronic lymphocytic leukemia: PWAS q-value = 0.01 (Recessive)



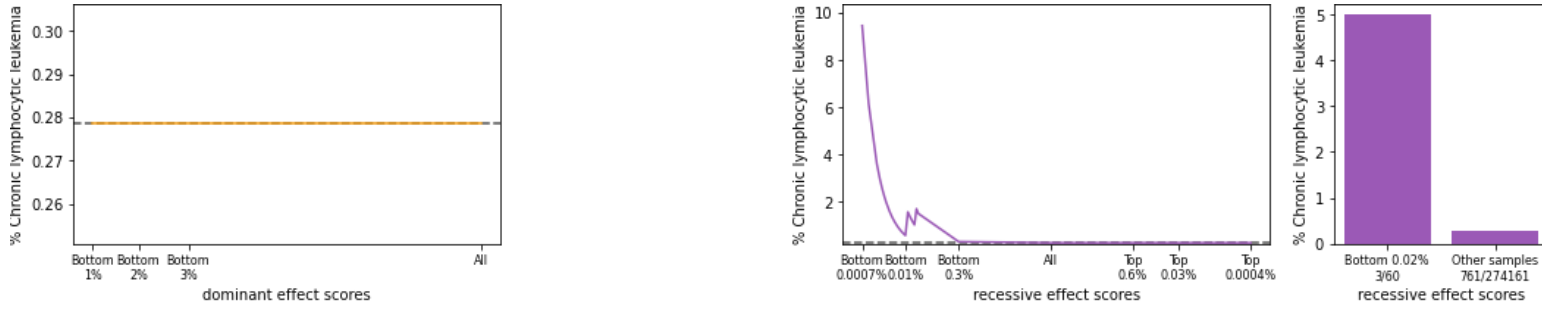
SGSM3 & Chronic lymphocytic leukemia: PWAS q-value = 0.05 (Recessive)



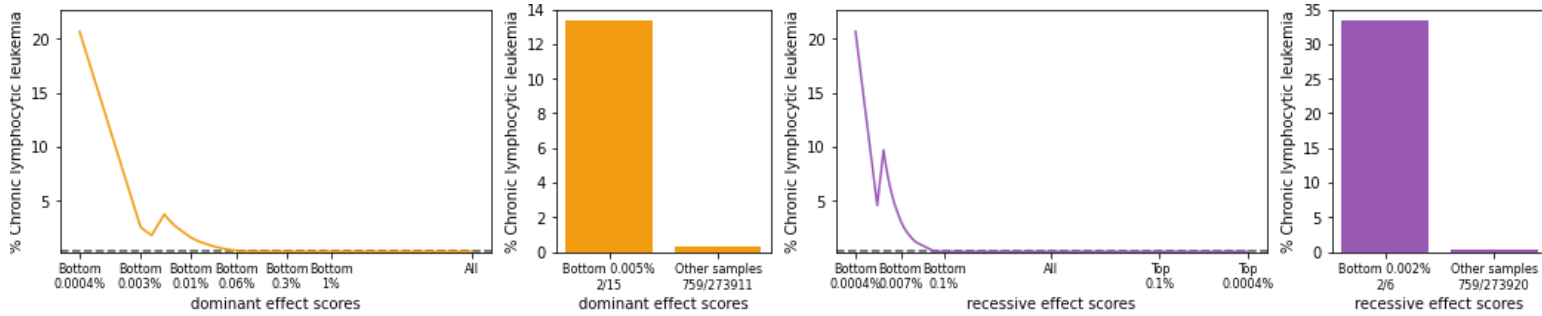
SRSF5 & Chronic lymphocytic leukemia: PWAS q-value = 0.01 (Dominant)



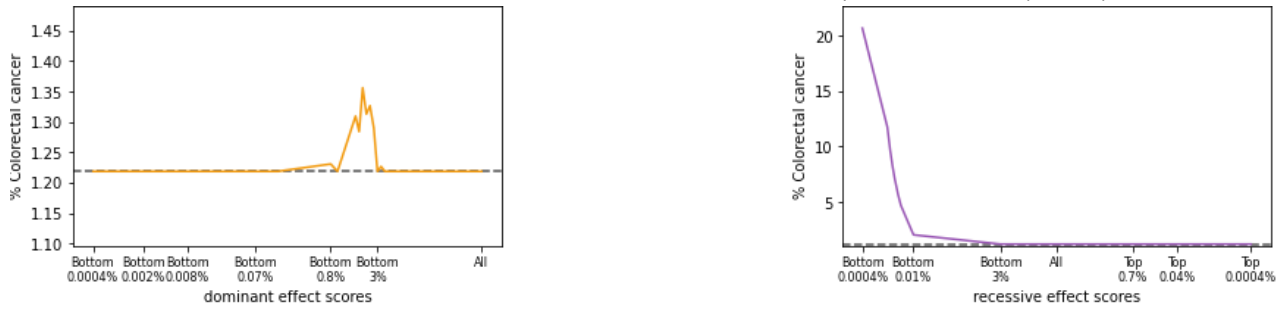
TNFSF18 & Chronic lymphocytic leukemia: PWAS q-value = 0.04 (Recessive)



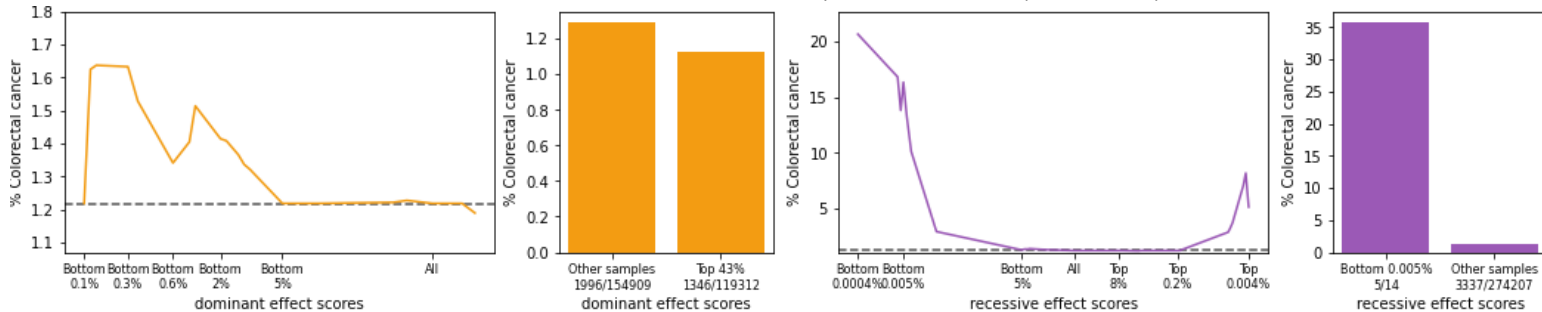
ZNF449 & Chronic lymphocytic leukemia: PWAS q-value = 0.03 (Recessive)



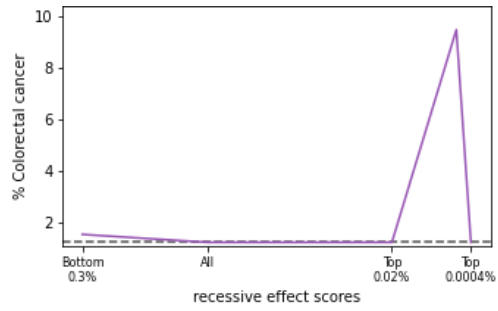
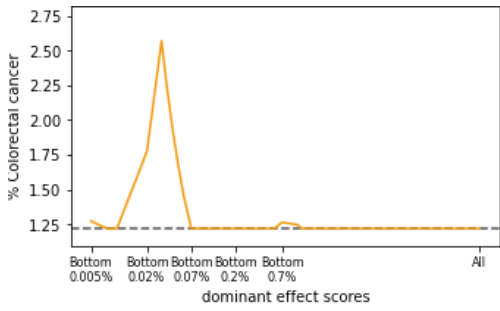
FHL3 & Colorectal cancer: PWAS q-value = 0.03 (None)



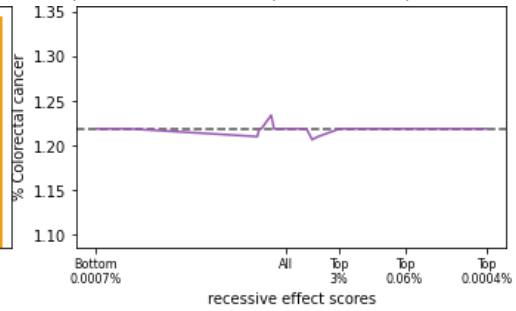
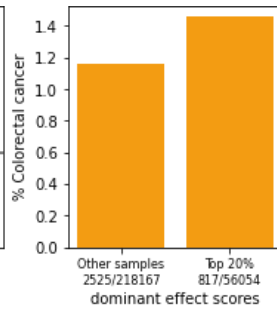
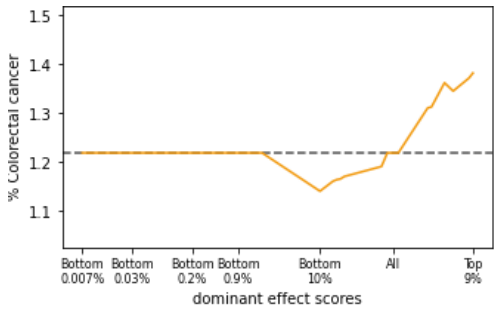
MUTYH & Colorectal cancer: PWAS q-value = 2e-07 (Recessive)



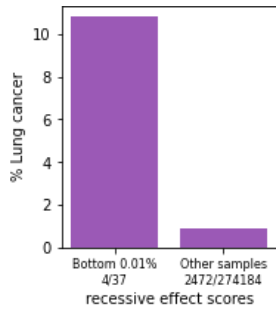
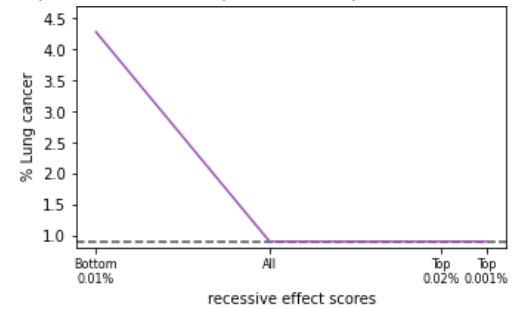
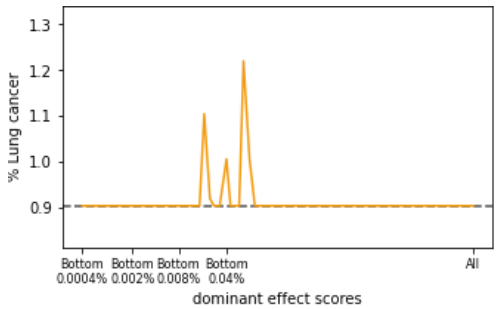
OSTC & Colorectal cancer: PWAS q-value = 0.003 (None)



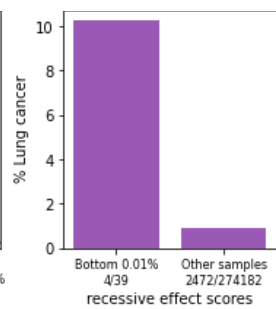
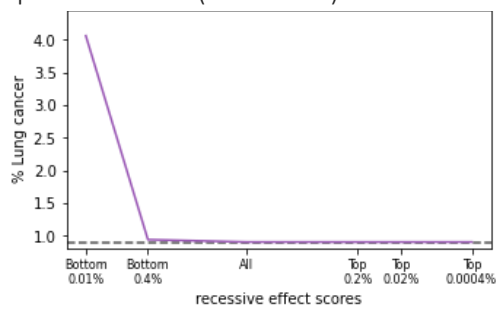
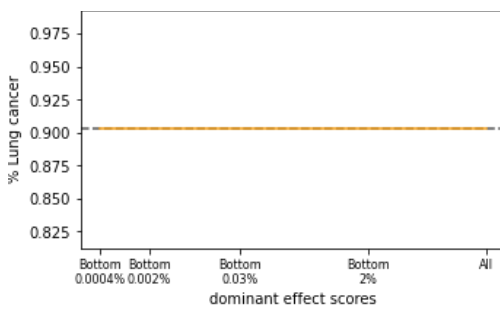
POU5F1B & Colorectal cancer: PWAS q-value = 0.004 (Dominant)



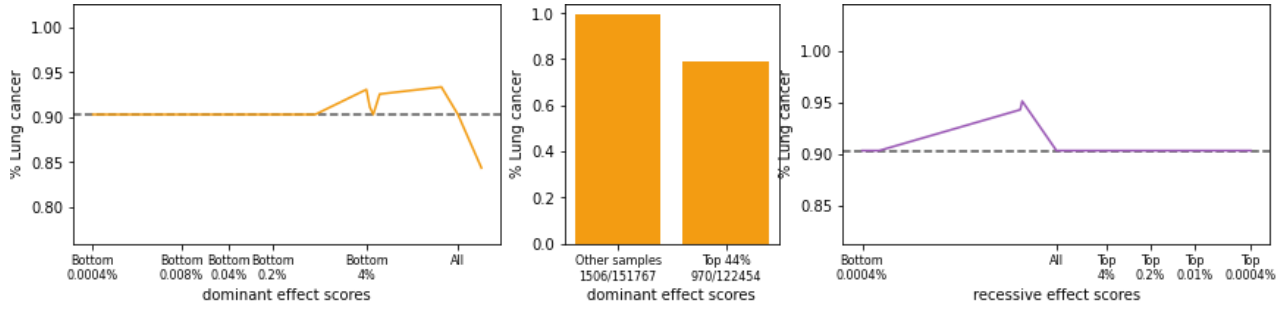
AKIRIN1 & Lung cancer: PWAS q-value = 0.03 (Recessive)



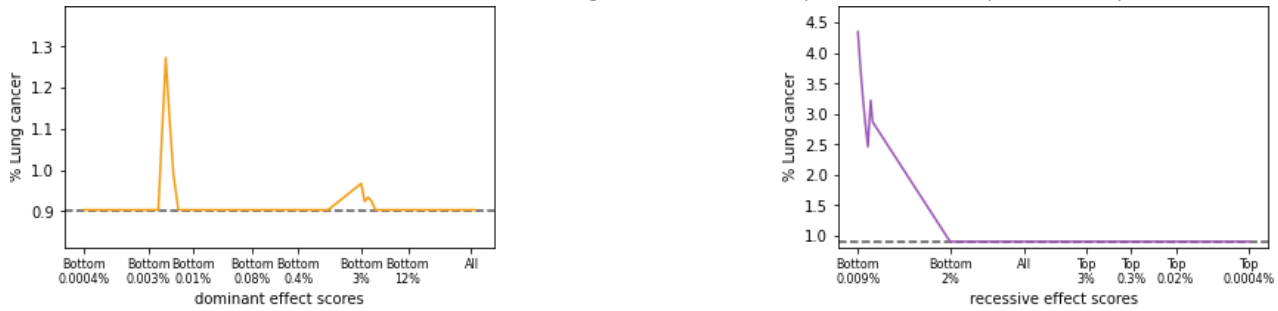
ATPAF2 & Lung cancer: PWAS q-value = 0.02 (Recessive)



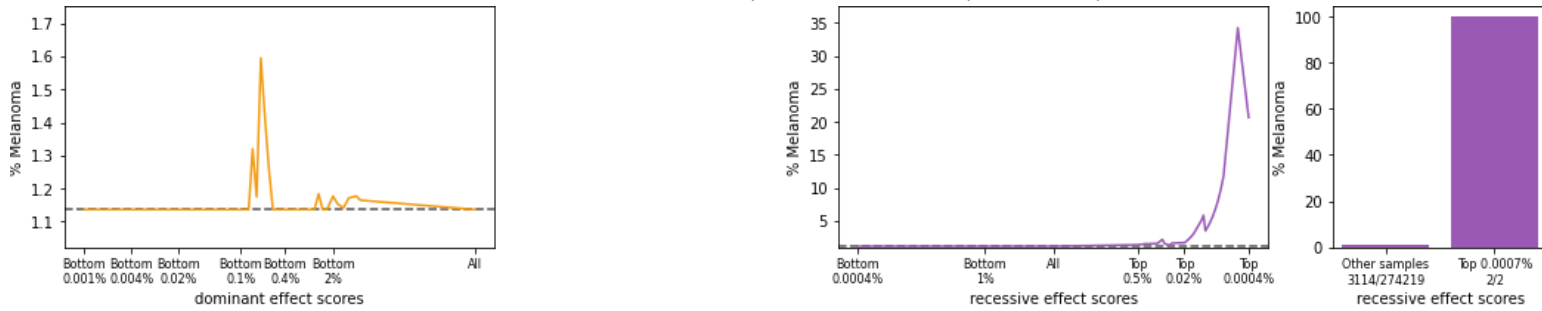
CHRNA5 & Lung cancer: PWAS q-value = 0.003 (Dominant)



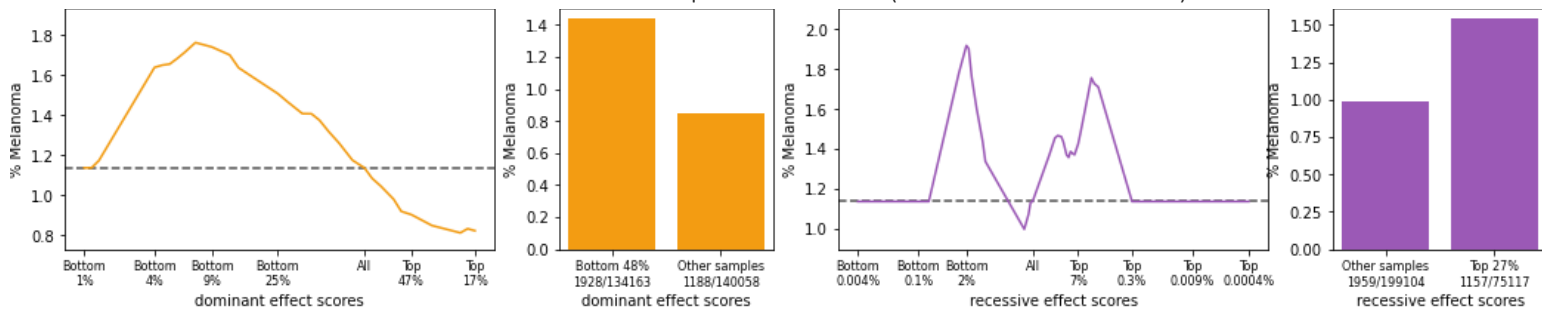
SLC12A6 & Lung cancer: PWAS q-value = 0.04 (Recessive)



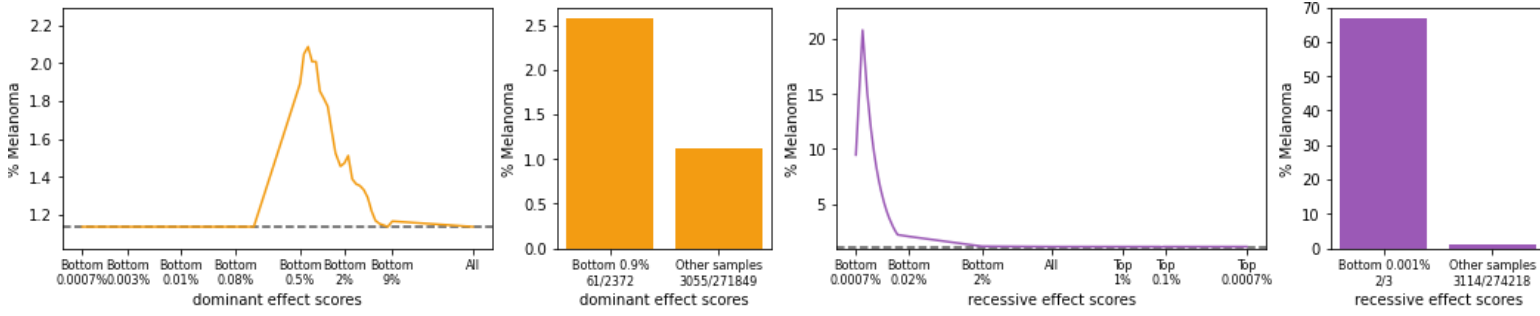
AVP & Melanoma: PWAS q-value = 0.0009 (Recessive)



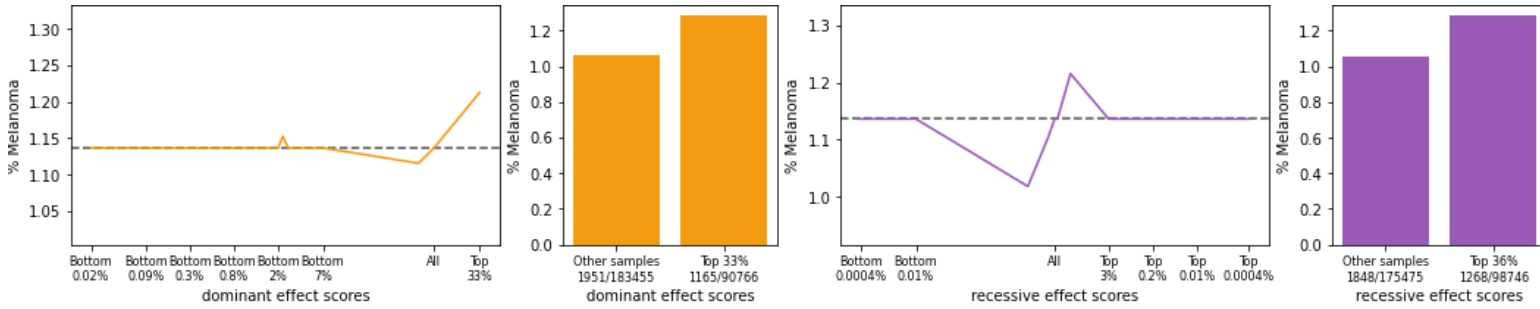
MC1R & Melanoma: PWAS q-value = 2e-53 (Dominant & recessive)



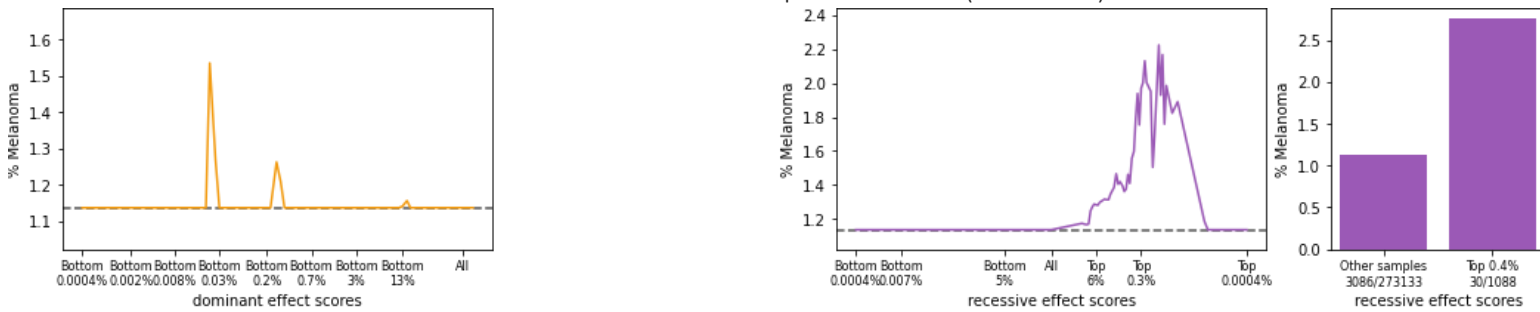
MITF & Melanoma: PWAS q-value = 1e-08 (Dominant & recessive)



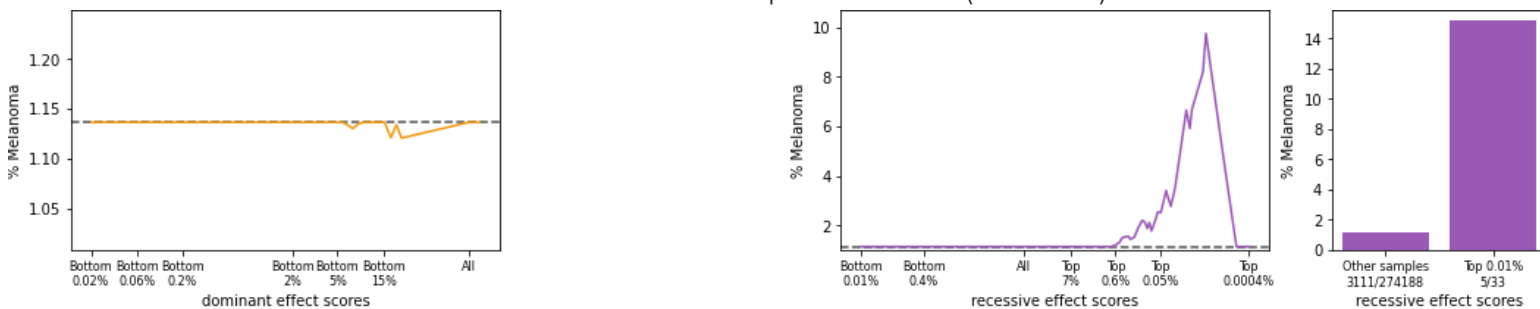
MTAP & Melanoma: PWAS q-value = 0.0001 (Dominant & recessive)



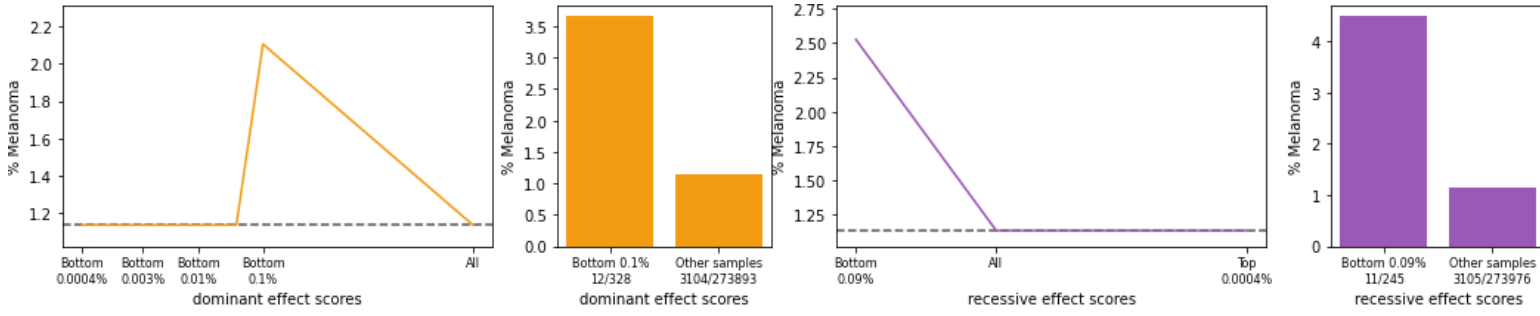
NCOA6 & Melanoma: PWAS q-value = 0.01 (Recessive)



PADI1 & Melanoma: PWAS q-value = 0.004 (Recessive)



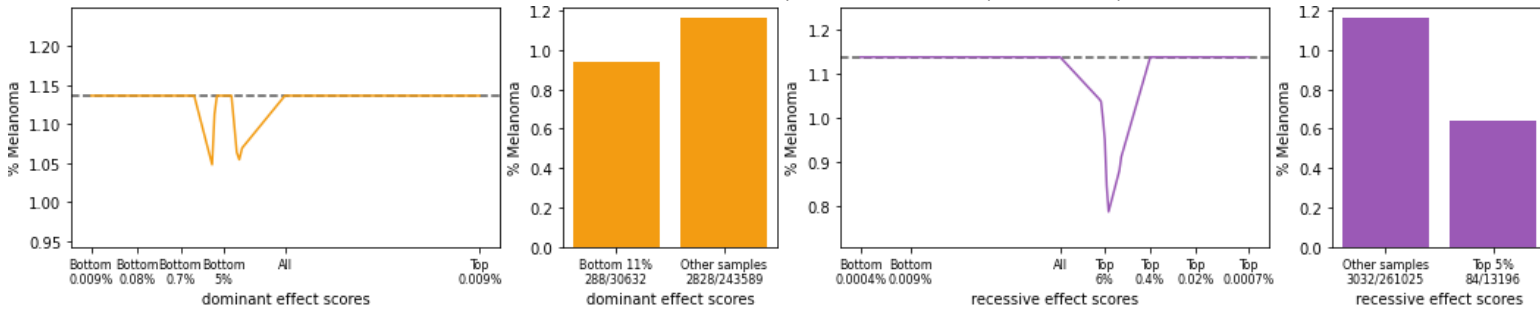
POLR2H & Melanoma: PWAS q-value = 0.01 (Recessive)



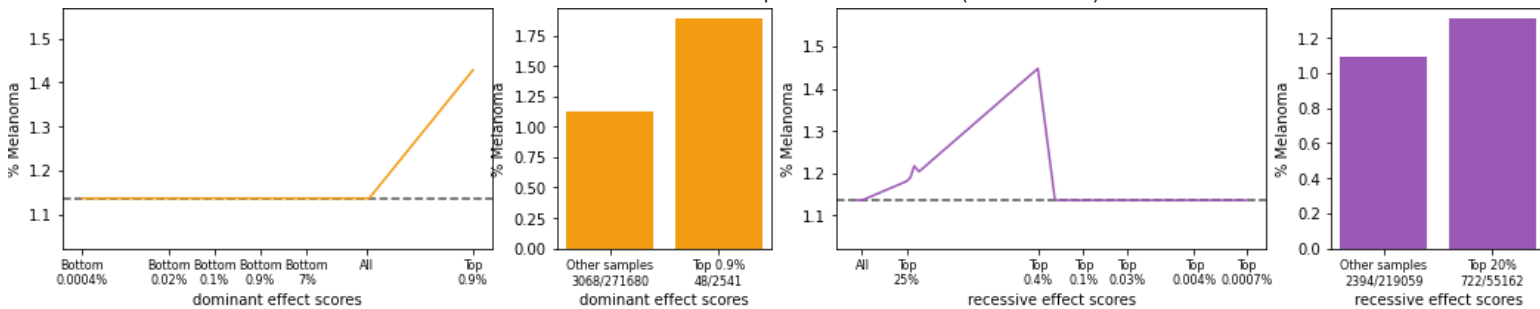
SLC12A9 & Melanoma: PWAS q-value = 0.02 (Recessive)



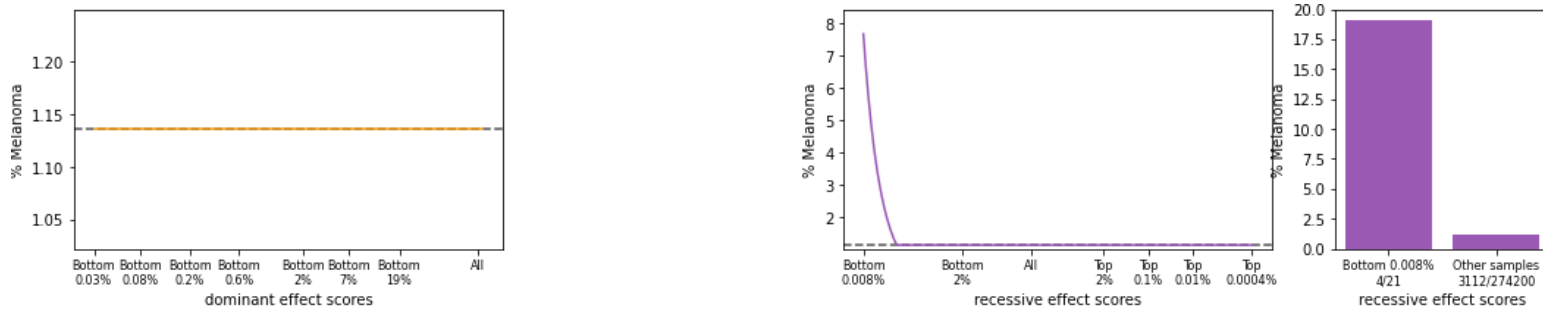
SLC45A2 & Melanoma: PWAS q-value = 8e-05 (Recessive)



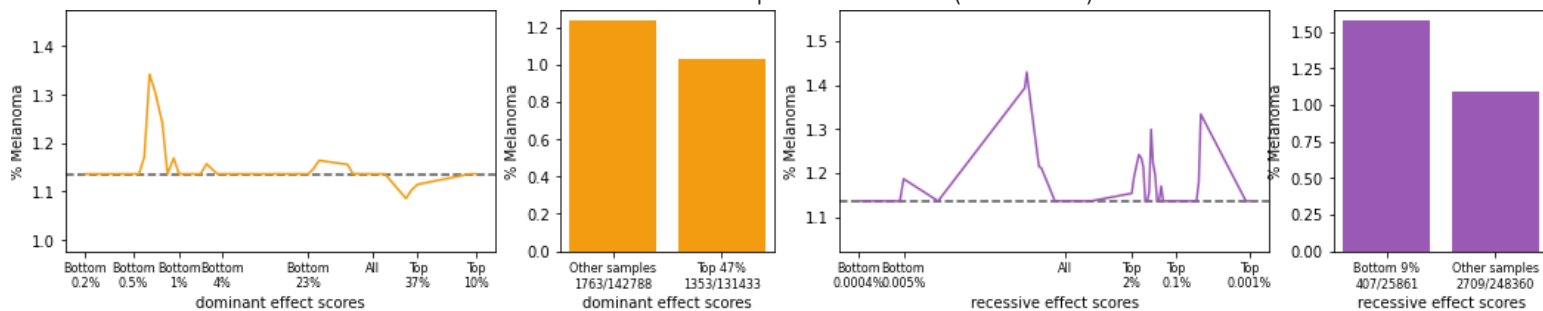
STN1 & Melanoma: PWAS q-value = 0.005 (Recessive)



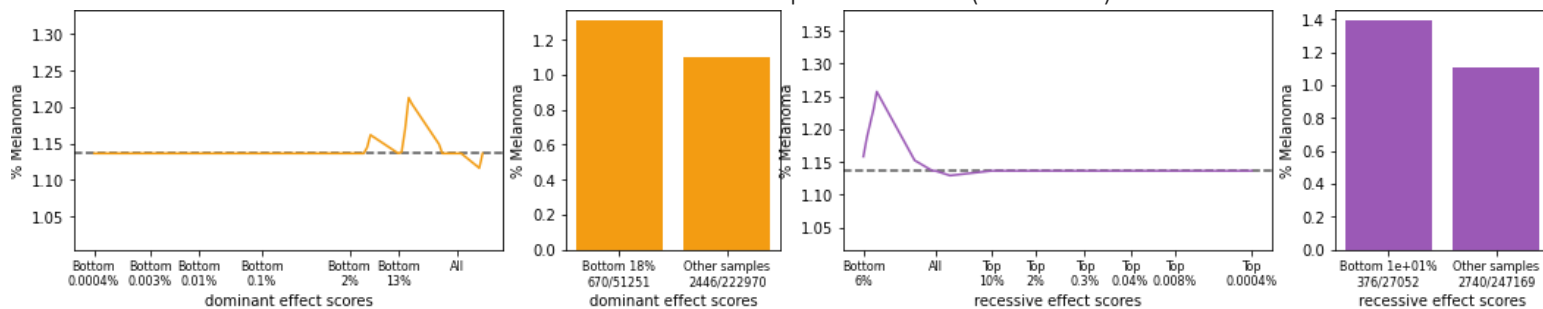
STX8 & Melanoma: PWAS q-value = 0.003 (Recessive)



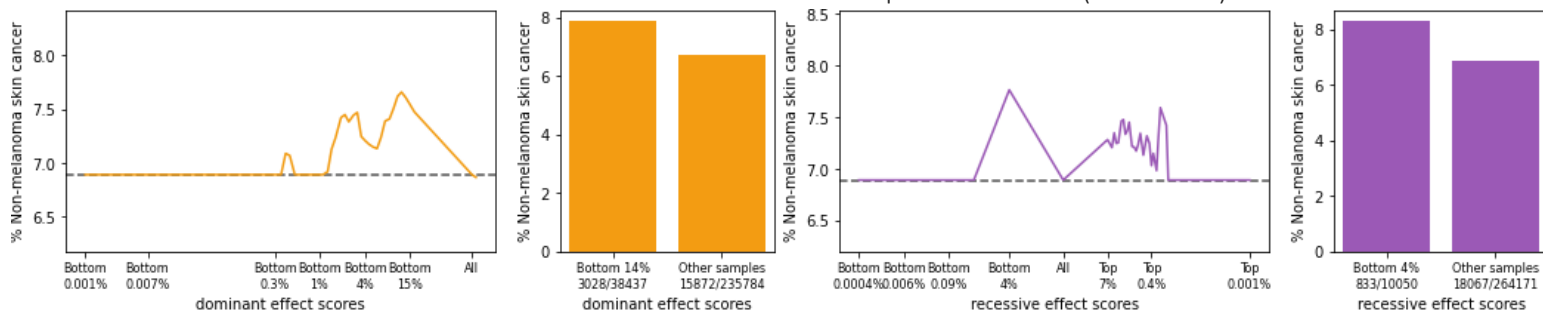
TYR & Melanoma: PWAS q-value = 0.005 (Recessive)



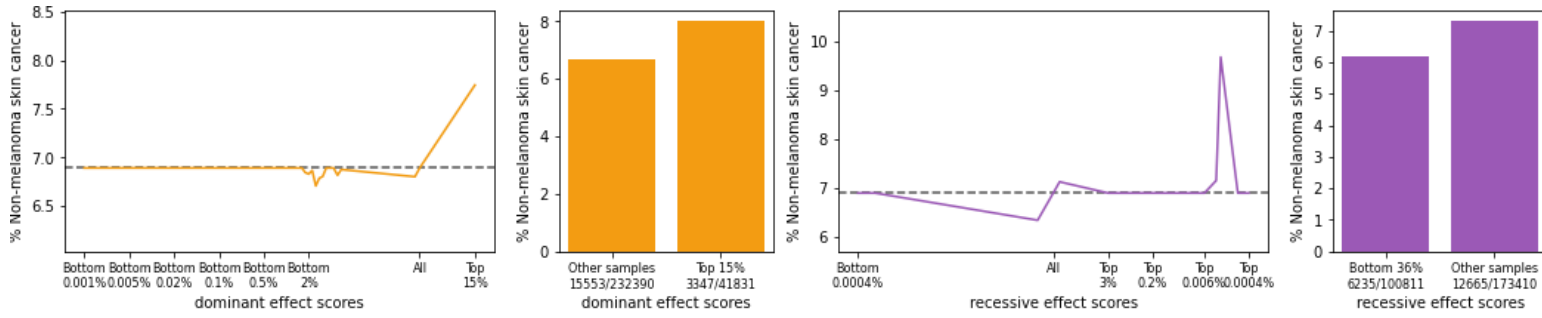
ZNF276 & Melanoma: PWAS q-value = 0.02 (Recessive)



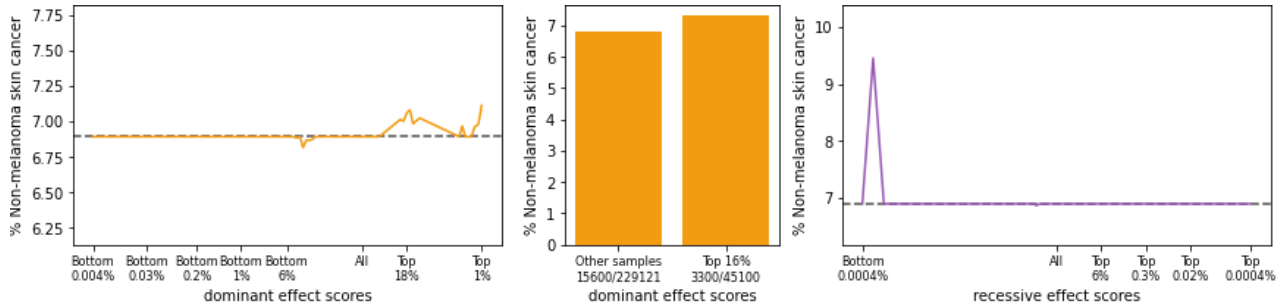
ACTL10 & Non-melanoma skin cancer: PWAS q-value = 0.003 (Dominant)



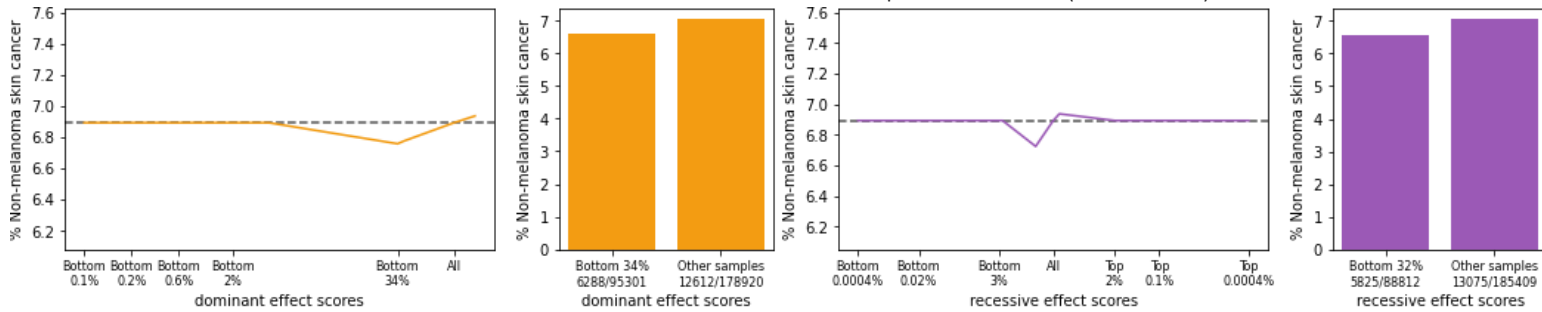
ALS2CR12 & Non-melanoma skin cancer: PWAS q-value = 1e-34 (Dominant & recessive)



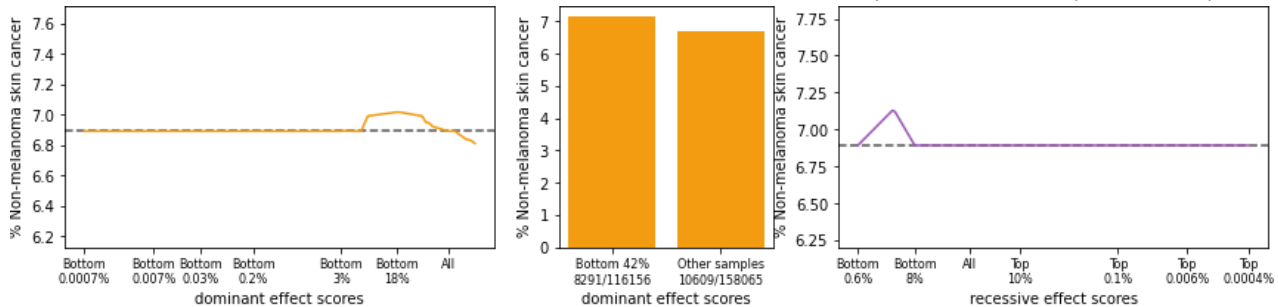
ANKLE1 & Non-melanoma skin cancer: PWAS q-value = 0.05 (Dominant)



BCAS4 & Non-melanoma skin cancer: PWAS q-value = 0.04 (Dominant)

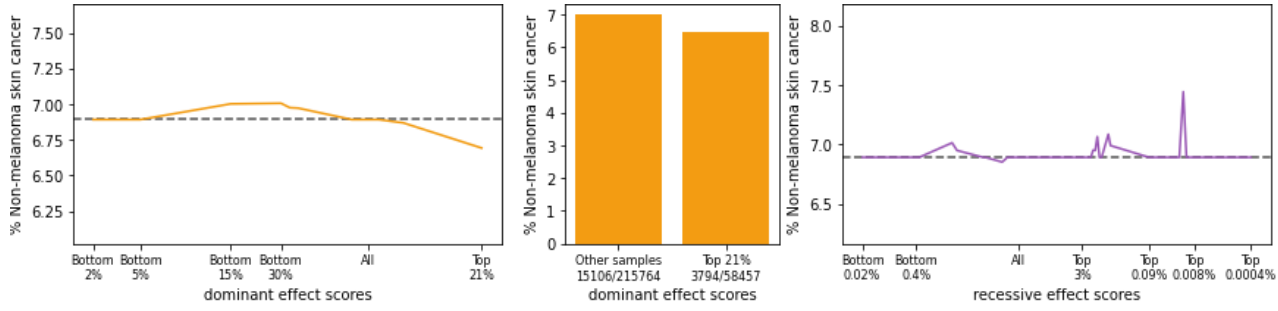


BNIPL & Non-melanoma skin cancer: PWAS q-value = 0.006 (Dominant)

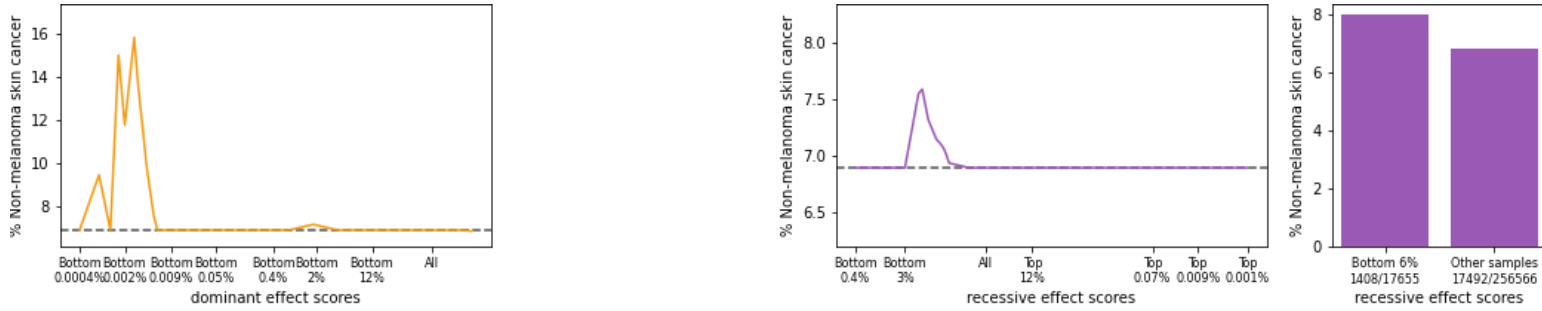




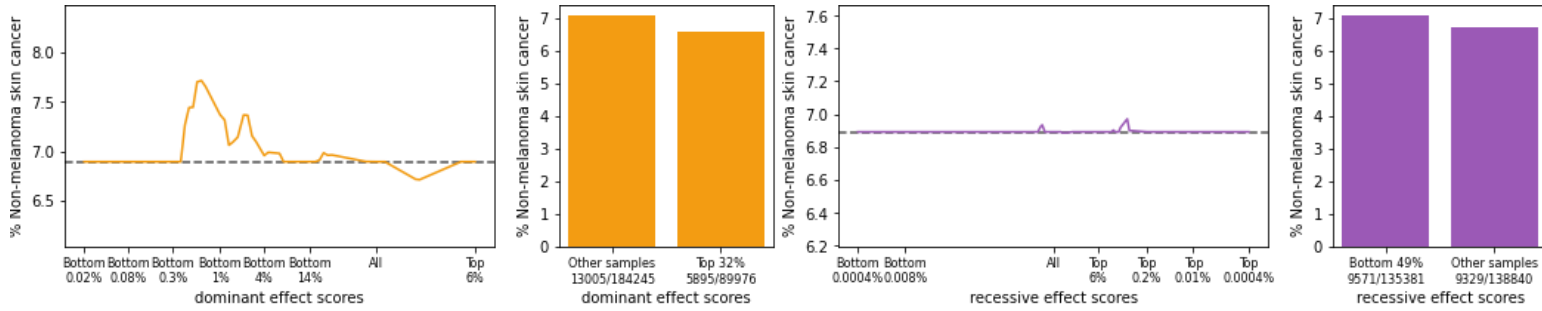
BPIFB3 & Non-melanoma skin cancer: PWAS q-value = 0.008 (Dominant)



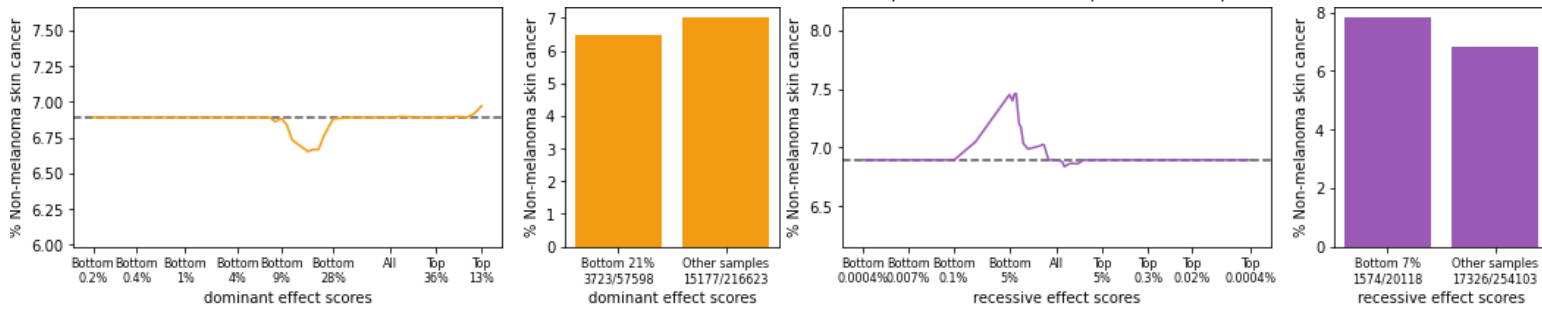
C6orf15 & Non-melanoma skin cancer: PWAS q-value = 0.03 (None)



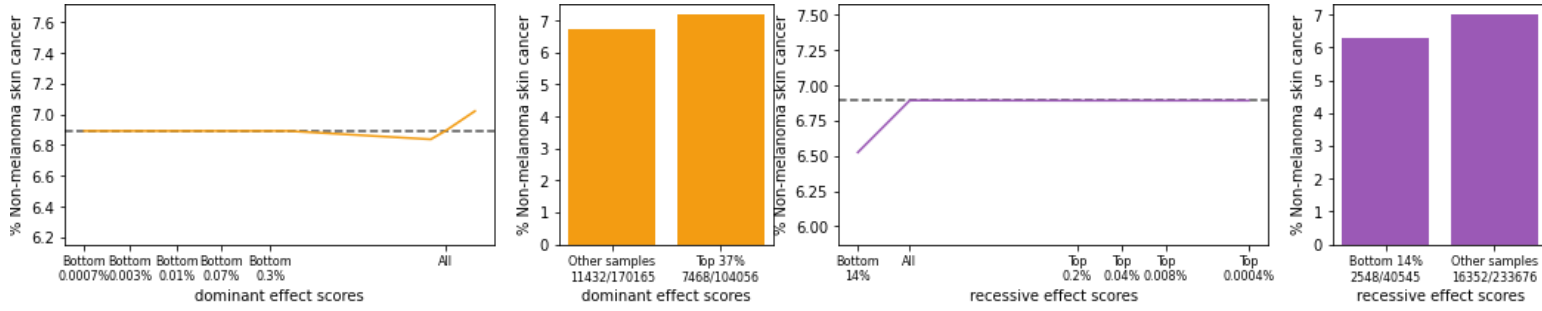
CCDC88B & Non-melanoma skin cancer: PWAS q-value = 0.02 (None)



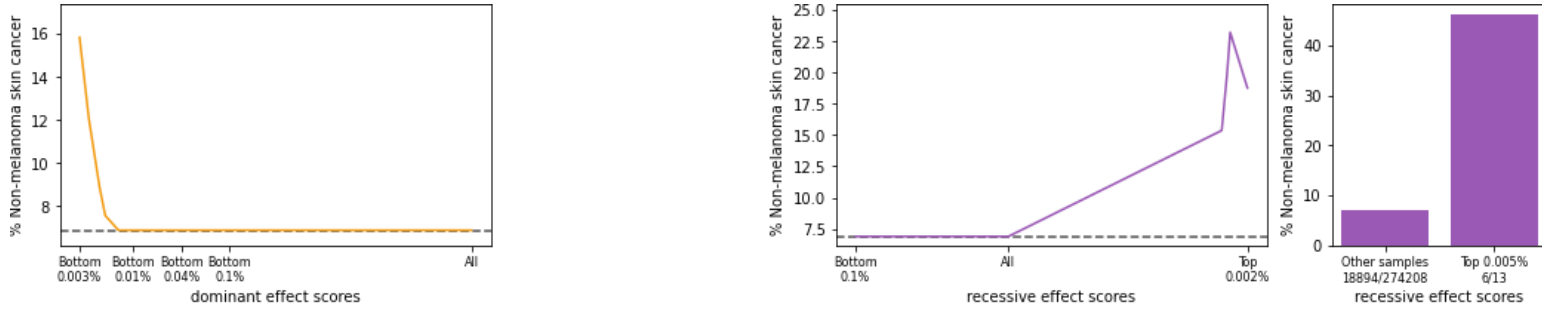
CCHCR1 & Non-melanoma skin cancer: PWAS q-value = 0.001 (Recessive)



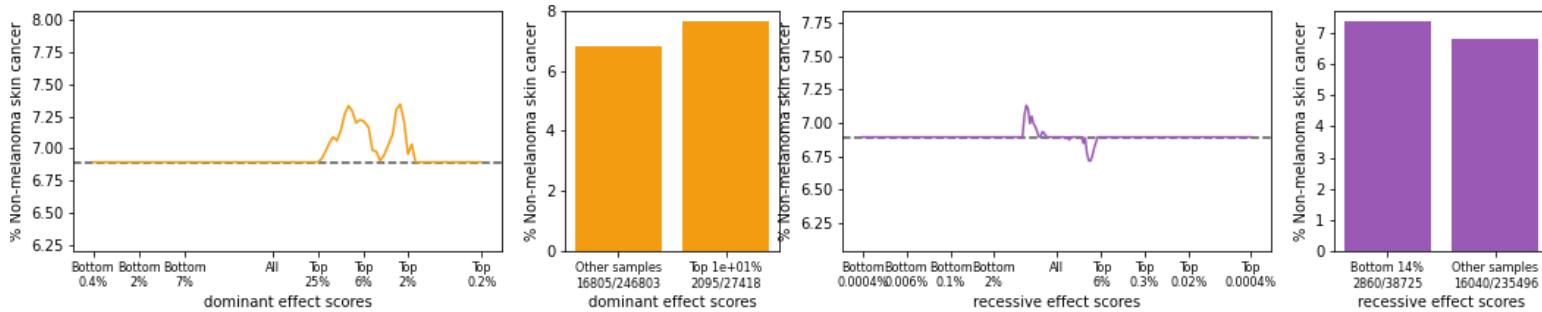
CTLA4 & Non-melanoma skin cancer: PWAS q-value = 4e-06 (Dominant & recessive)



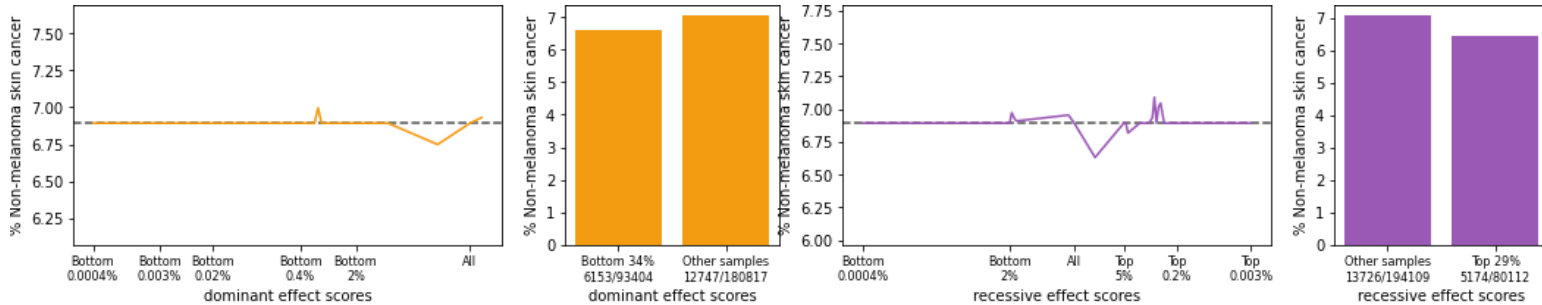
FAM153C & Non-melanoma skin cancer: PWAS q-value = 0.02 (None)



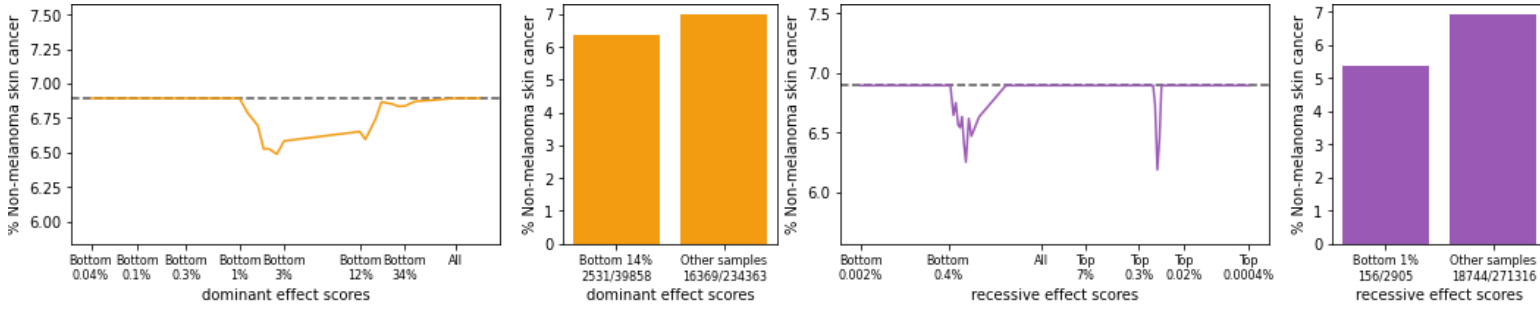
HLA-C & Non-melanoma skin cancer: PWAS q-value = 0.0002 (Dominant)



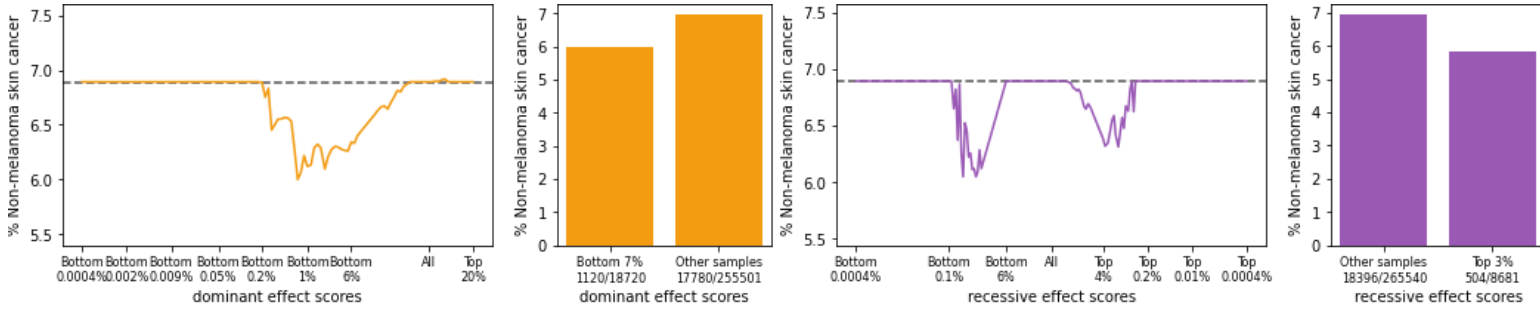
HLA-DPA1 & Non-melanoma skin cancer: PWAS q-value = 6e-05 (Dominant & recessive)



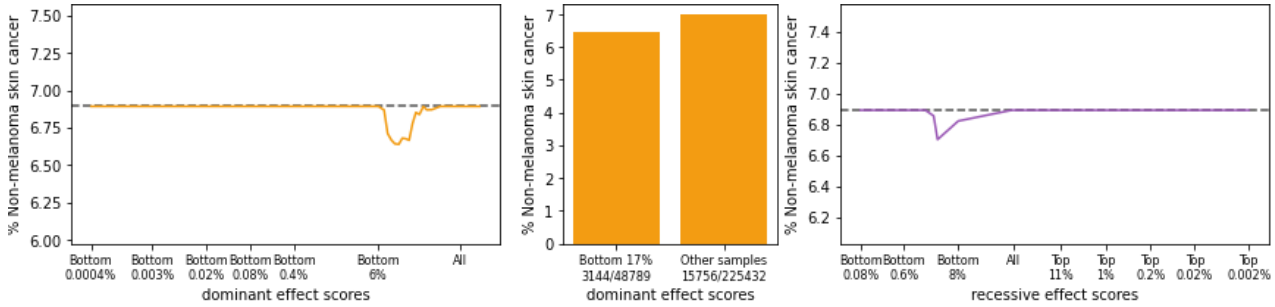
IGKV1-16 & Non-melanoma skin cancer: PWAS q-value = 0.04 (Dominant)



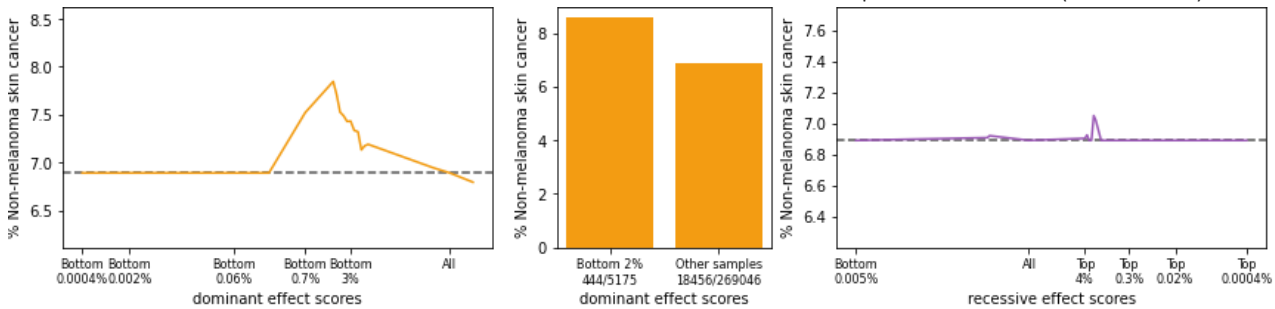
IGKV1-5 & Non-melanoma skin cancer: PWAS q-value = 0.0004 (Dominant)



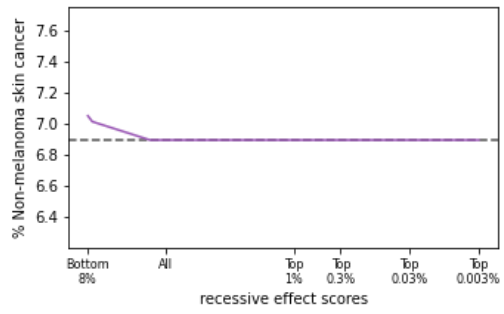
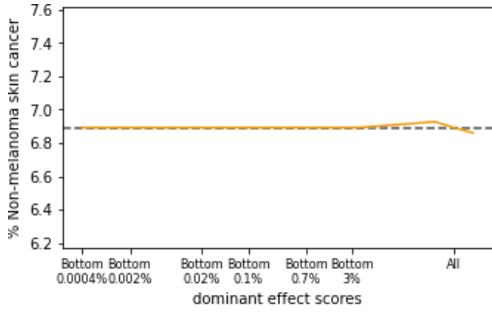
IGKV1D-16 & Non-melanoma skin cancer: PWAS q-value = 0.04 (Dominant)



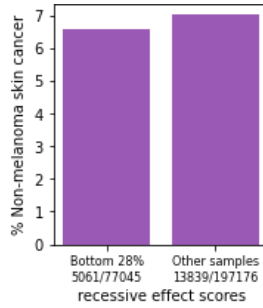
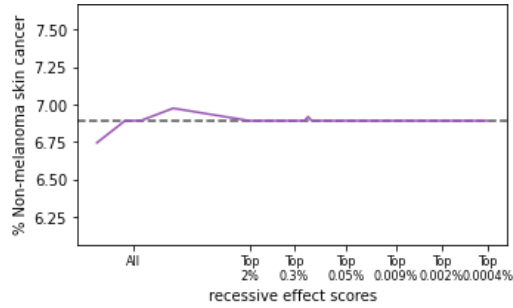
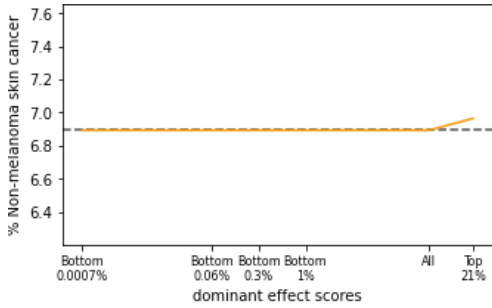
IRF3 & Non-melanoma skin cancer: PWAS q-value = 7e-06 (Dominant)



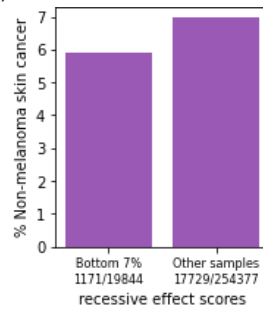
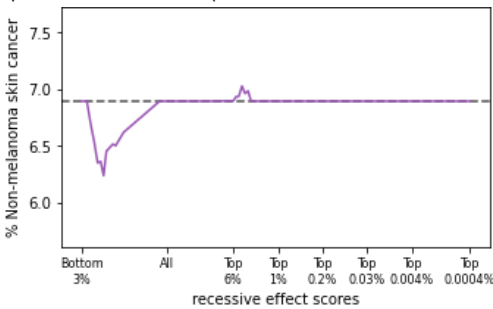
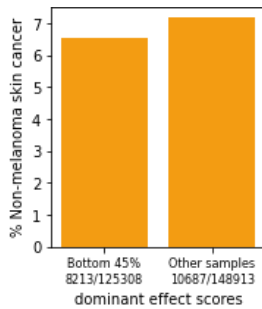
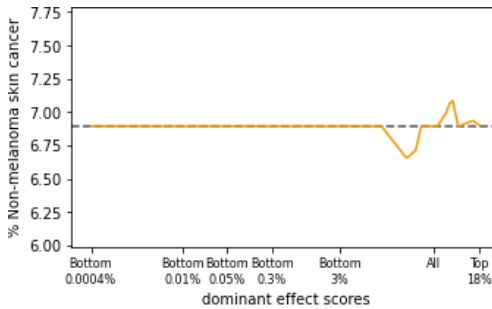
IRF7 & Non-melanoma skin cancer: PWAS q-value = 0.04 (None)



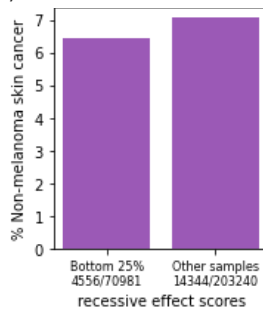
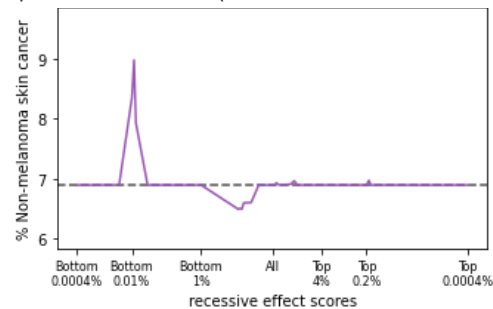
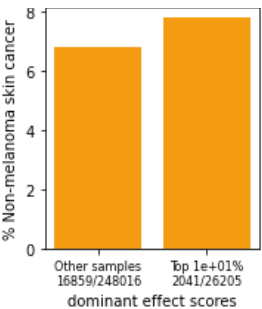
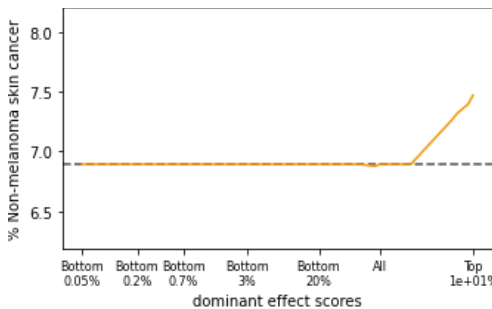
JDP2 & Non-melanoma skin cancer: PWAS q-value = 0.02 (Recessive)



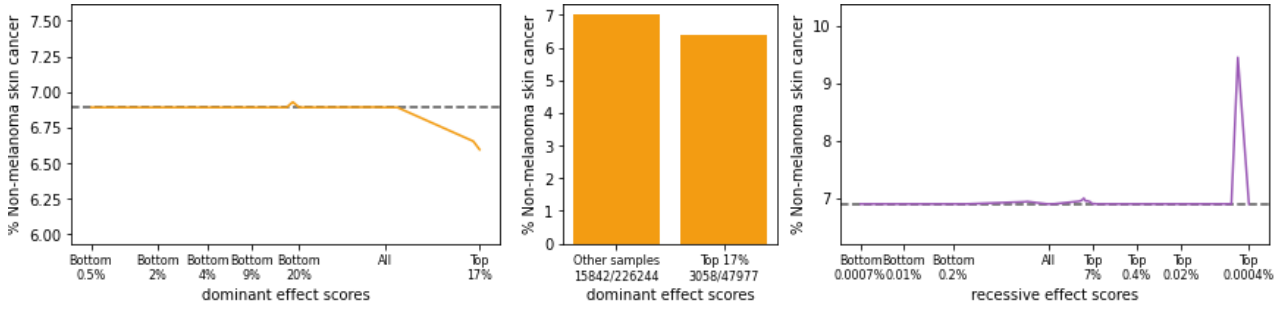
KRT5 & Non-melanoma skin cancer: PWAS q-value = 9e-06 (Dominant & recessive)



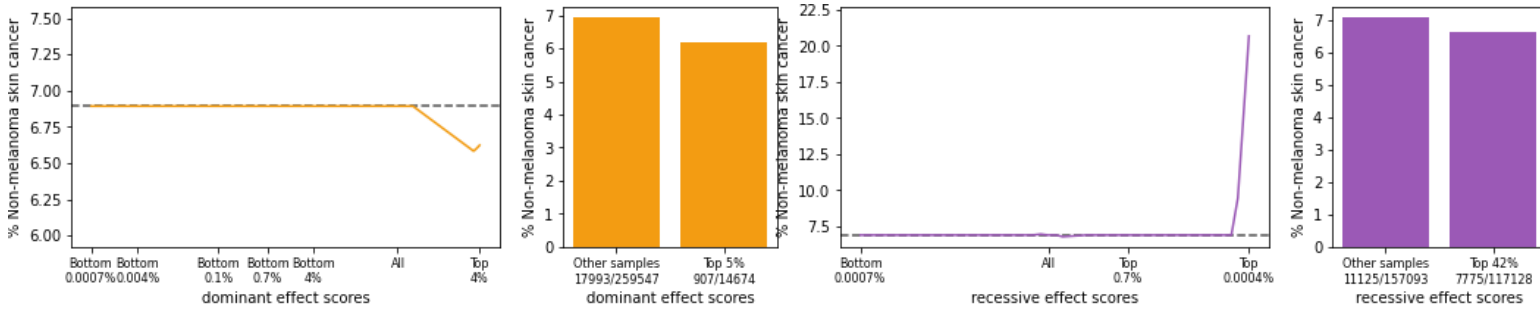
KRT75 & Non-melanoma skin cancer: PWAS q-value = 1e-08 (Dominant & recessive)



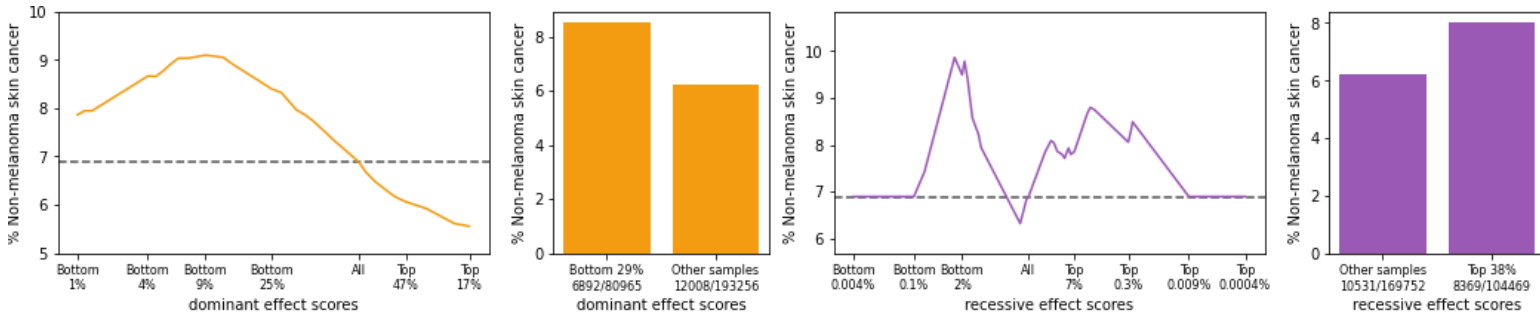
KRT82 & Non-melanoma skin cancer: PWAS q-value = 0.01 (Dominant)



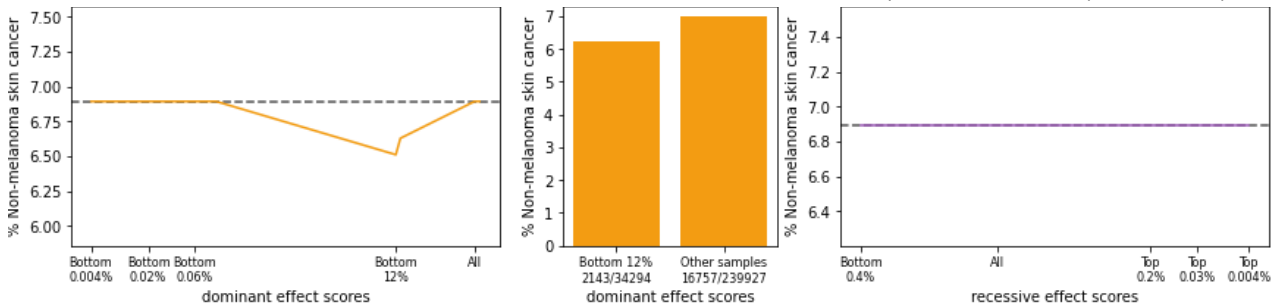
KRT84 & Non-melanoma skin cancer: PWAS q-value = 0.0003 (Recessive)



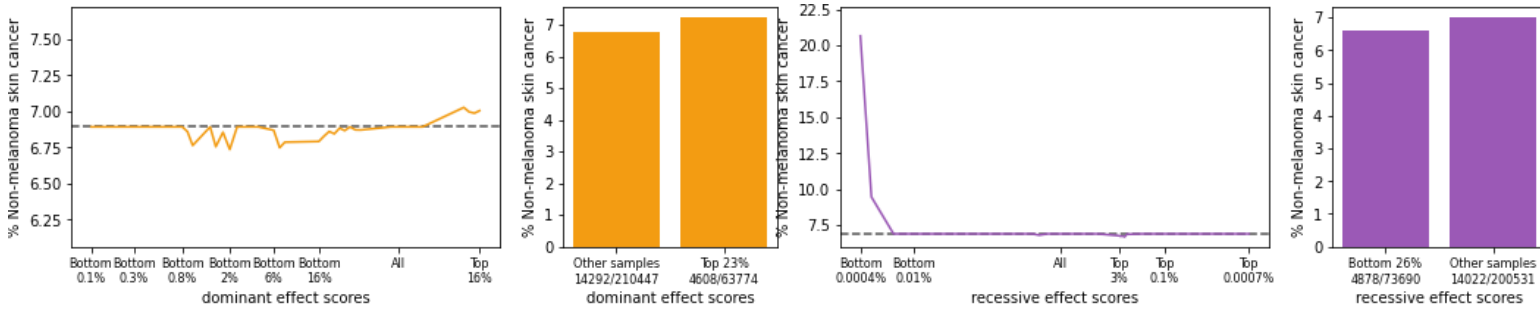
MC1R & Non-melanoma skin cancer: PWAS q-value = 1e-109 (Dominant & recessive)



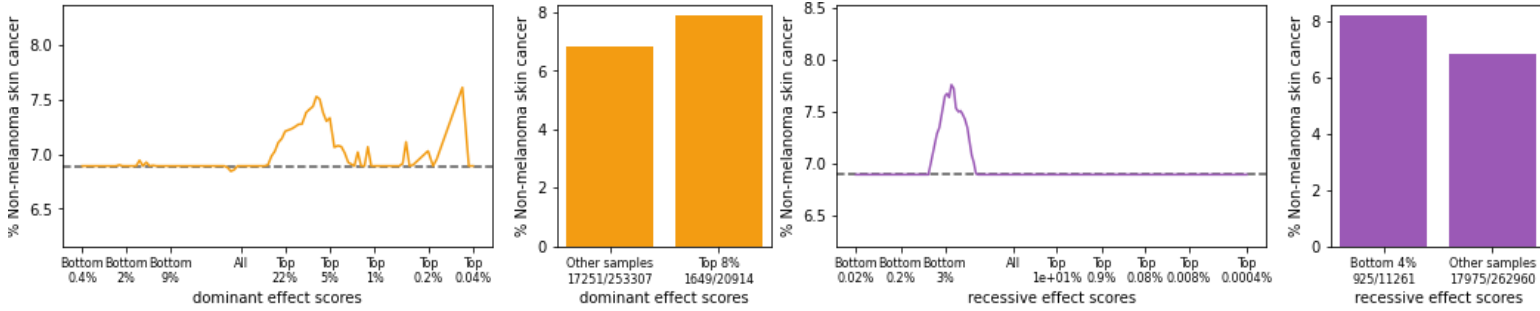
MPIG6B & Non-melanoma skin cancer: PWAS q-value = 0.002 (Dominant)



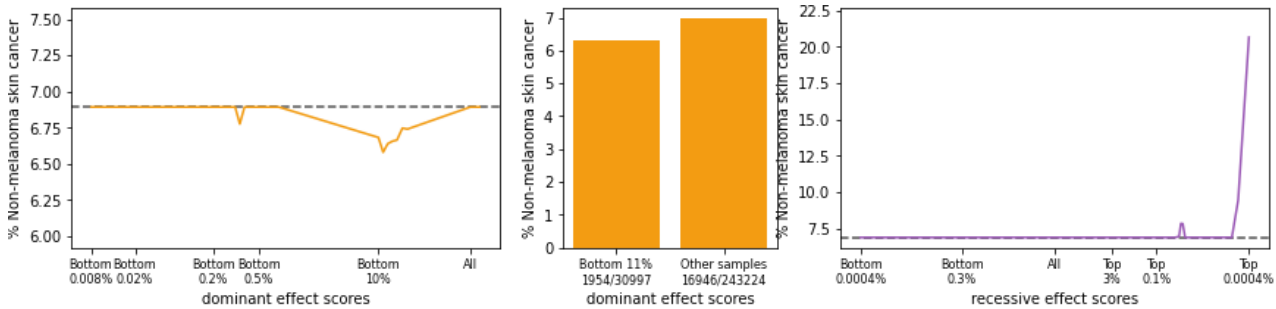
MST1R & Non-melanoma skin cancer: PWAS q-value = 0.05 (None)



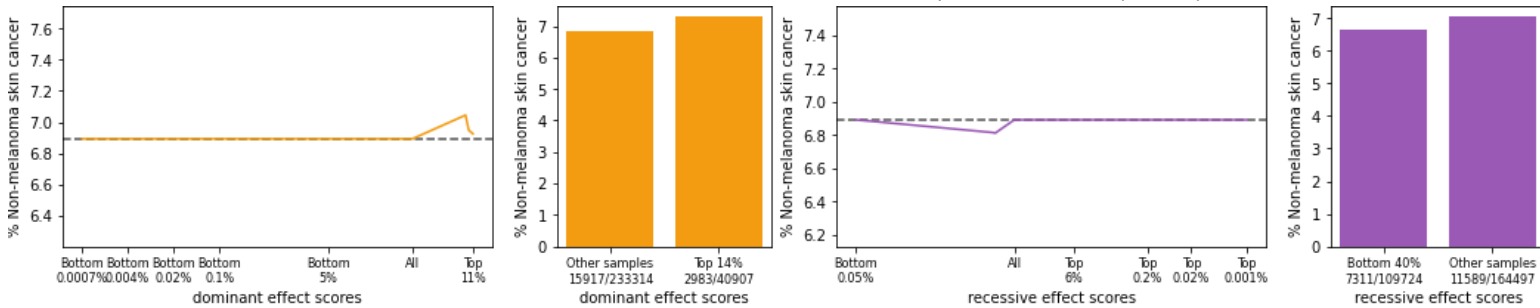
MUC22 & Non-melanoma skin cancer: PWAS q-value = 0.02 (Dominant)



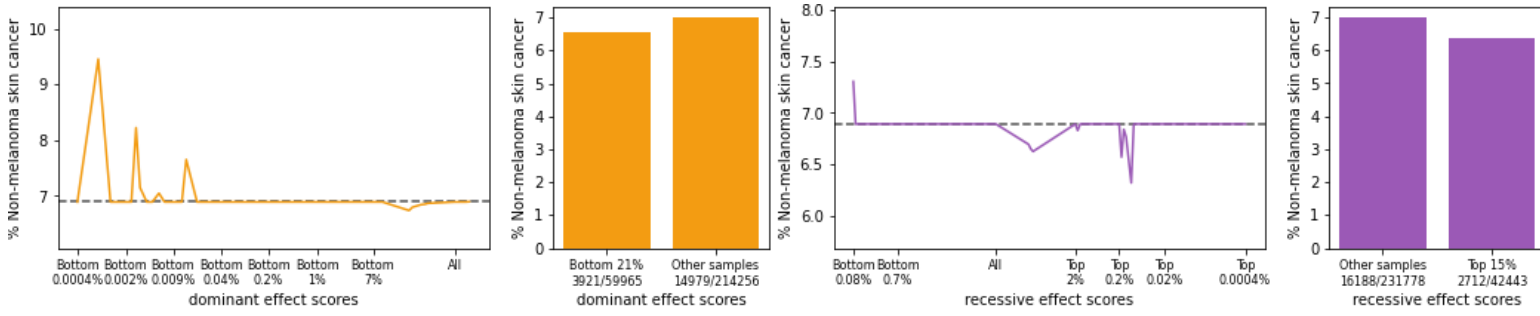
NEURL1B & Non-melanoma skin cancer: PWAS q-value = 0.03 (Dominant)



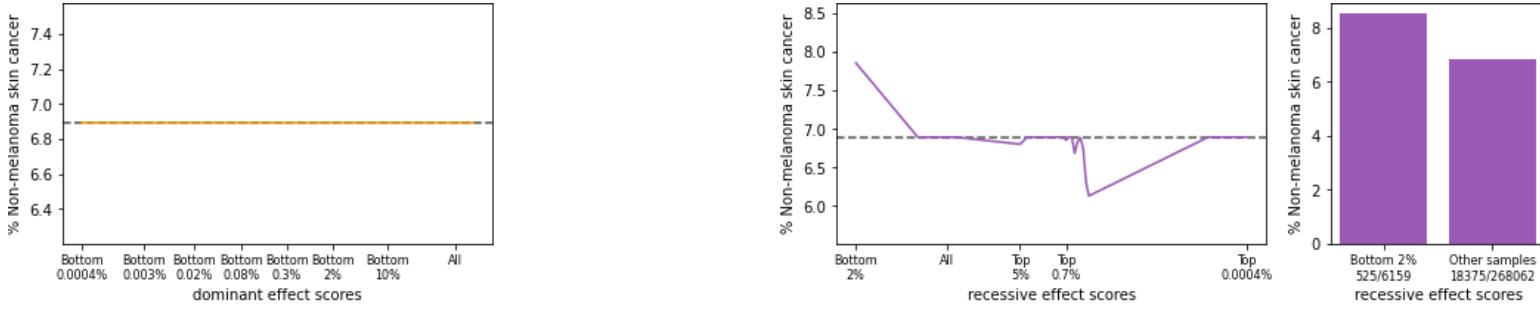
NEUROD1 & Non-melanoma skin cancer: PWAS q-value = 0.02 (None)



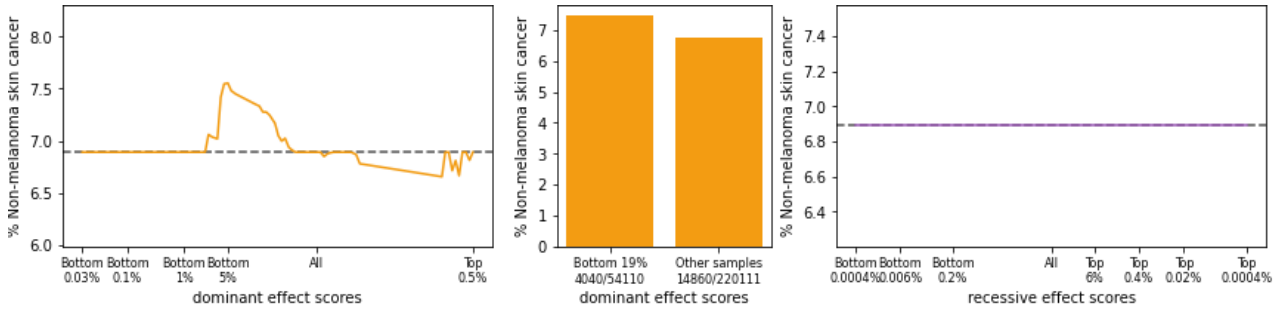
PPARGC1B & Non-melanoma skin cancer: PWAS q-value = 0.03 (None)



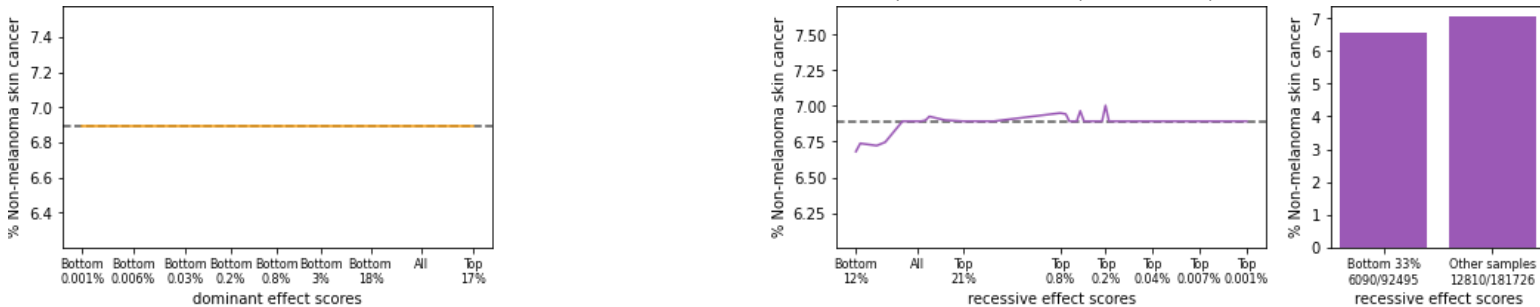
PPP1R18 & Non-melanoma skin cancer: PWAS q-value = 0.0007 (Recessive)



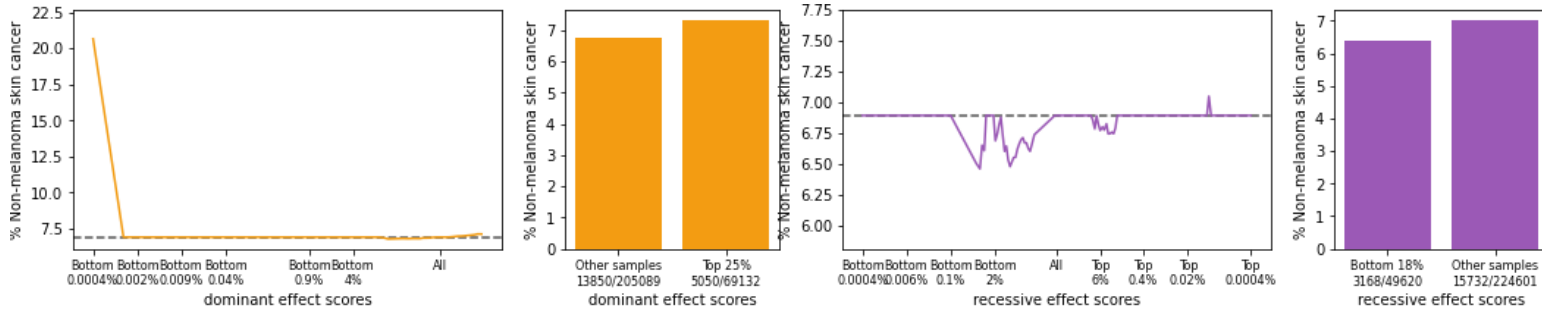
PRDM7 & Non-melanoma skin cancer: PWAS q-value = 4e-06 (Dominant)



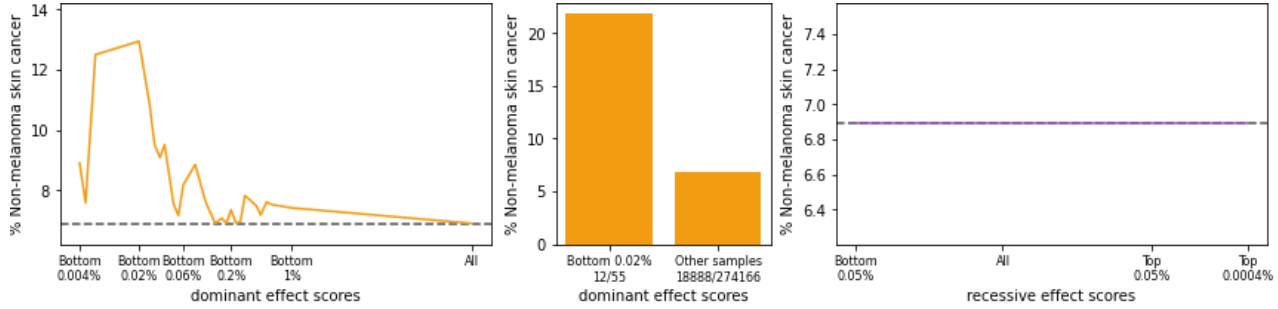
PTPN12 & Non-melanoma skin cancer: PWAS q-value = 0.02 (Recessive)



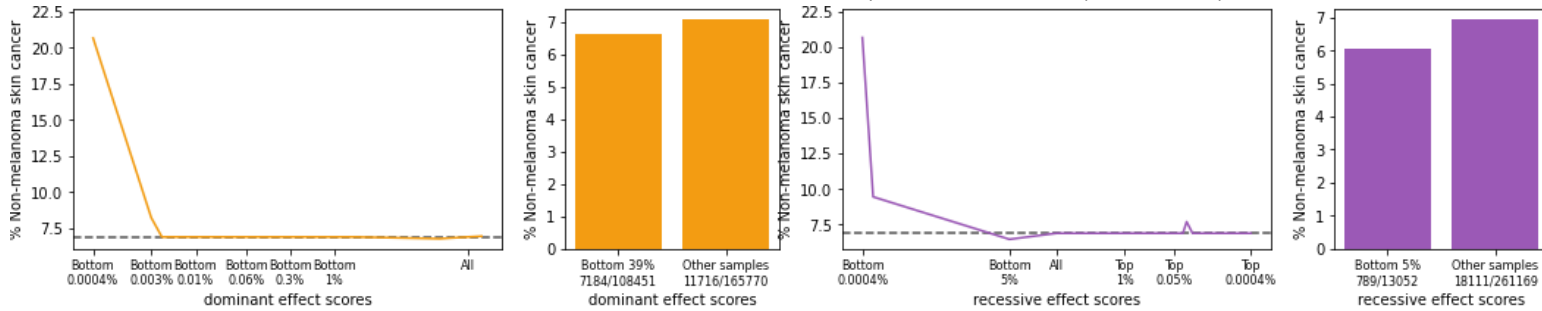
RALY & Non-melanoma skin cancer: PWAS q-value = 0.005 (Dominant)



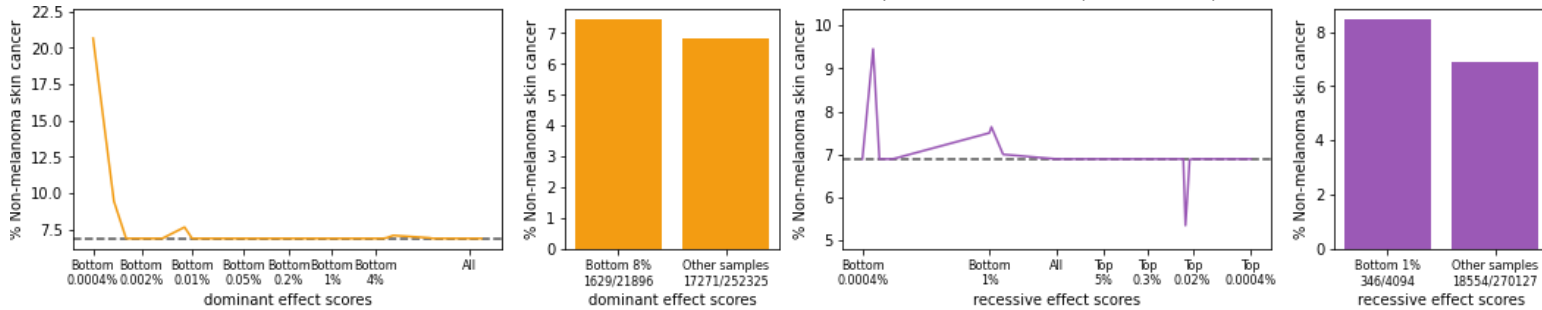
RBM17 & Non-melanoma skin cancer: PWAS q-value = 0.02 (None)



RPL13 & Non-melanoma skin cancer: PWAS q-value = 0.0004 (Dominant)

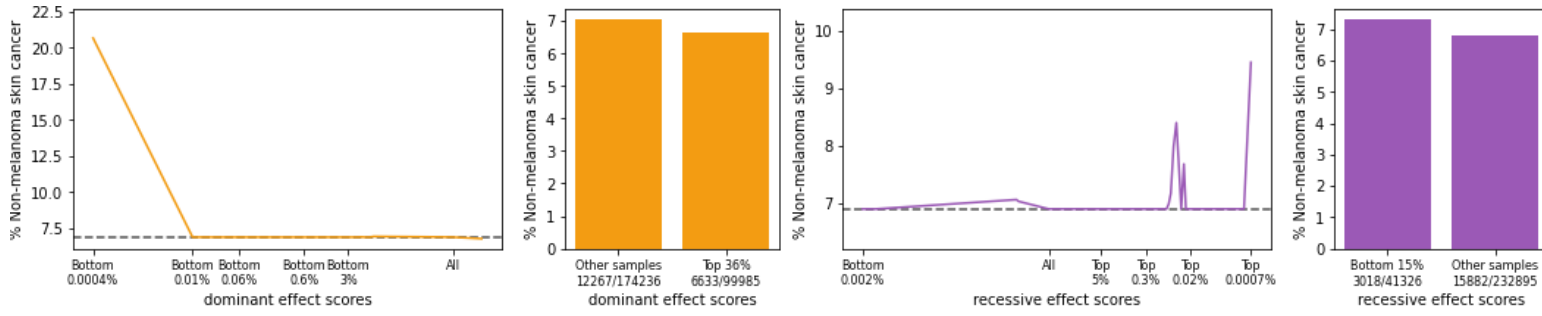


RPRD2 & Non-melanoma skin cancer: PWAS q-value = 0.008 (Recessive)

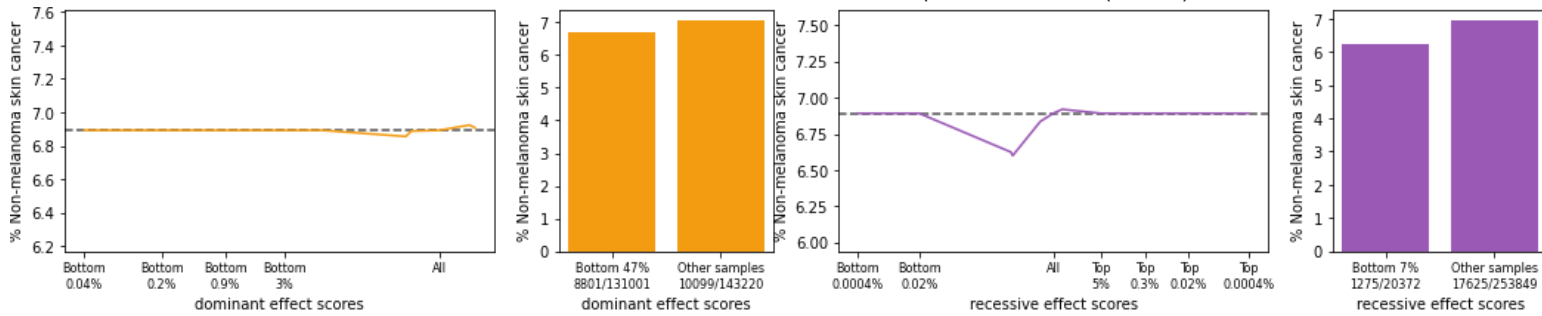




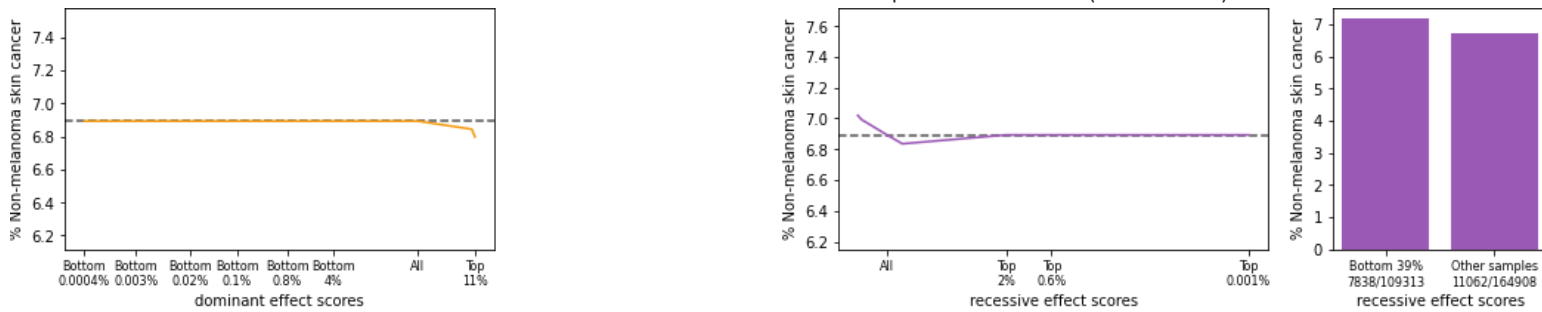
RPS6KA4 & Non-melanoma skin cancer: PWAS q-value = 0.01 (None)



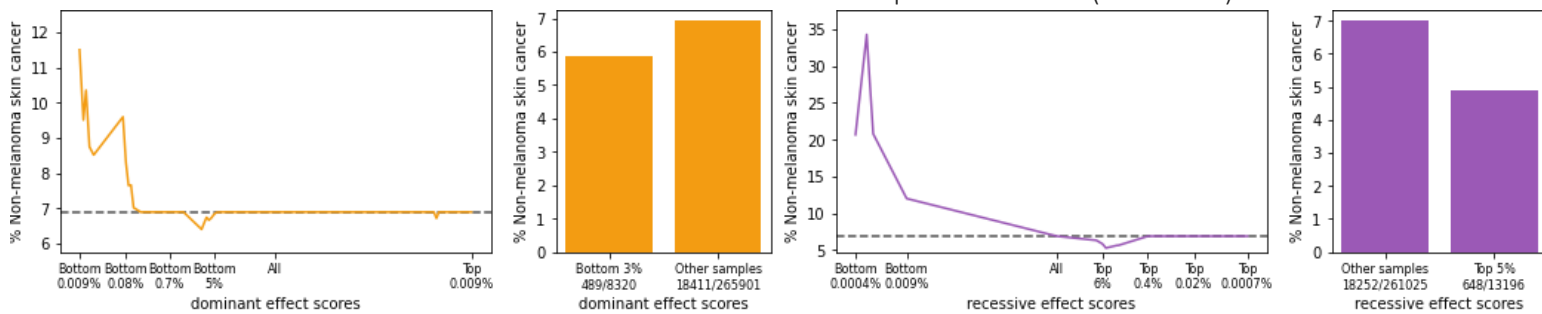
RSC1A1 & Non-melanoma skin cancer: PWAS q-value = 0.04 (None)



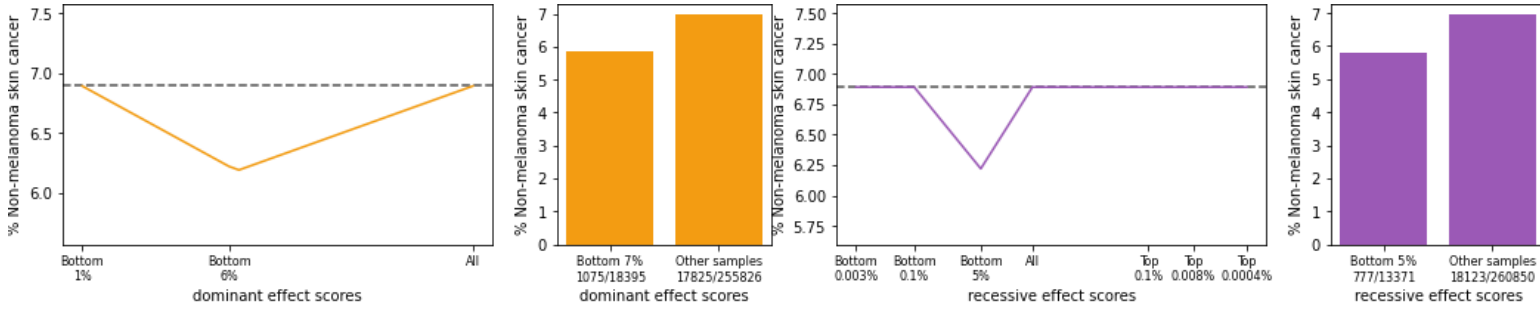
SEMA3F & Non-melanoma skin cancer: PWAS q-value = 0.008 (Recessive)



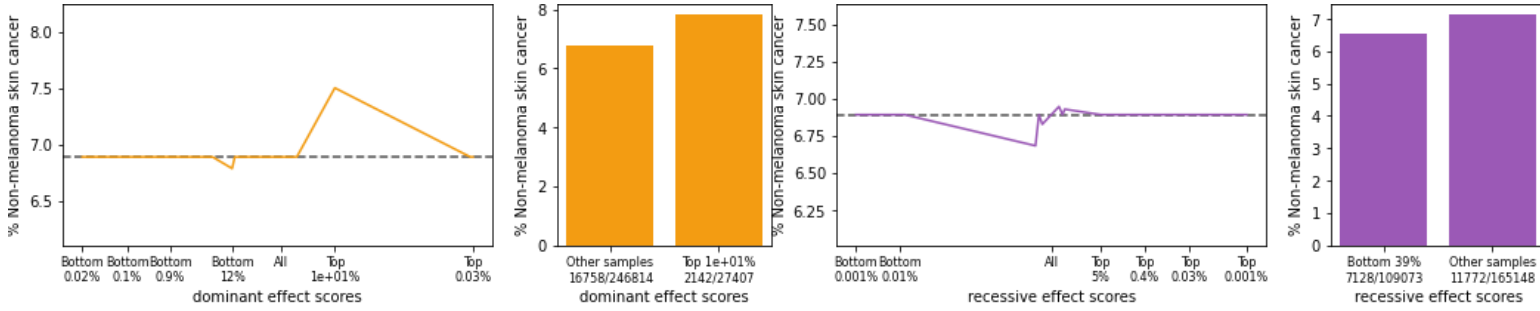
SLC45A2 & Non-melanoma skin cancer: PWAS q-value = 1e-20 (Recessive)



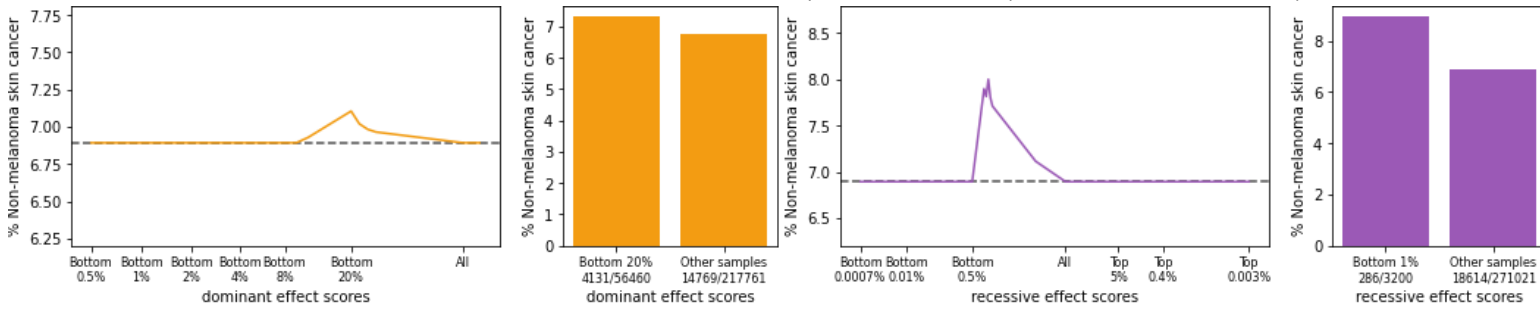
SPATA33 & Non-melanoma skin cancer: PWAS q-value = 0.003 (Dominant)



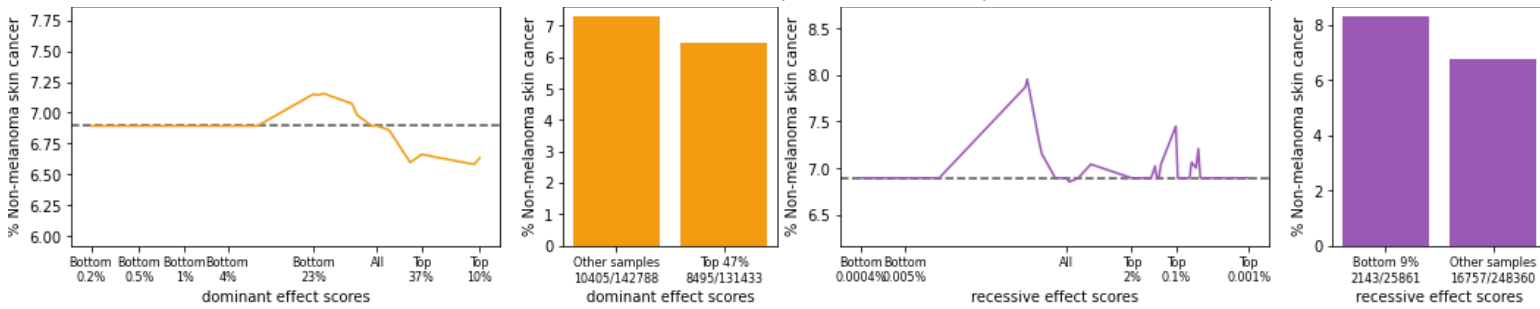
TRAK2 & Non-melanoma skin cancer: PWAS q-value = 6e-08 (Recessive)



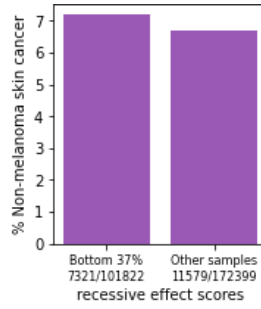
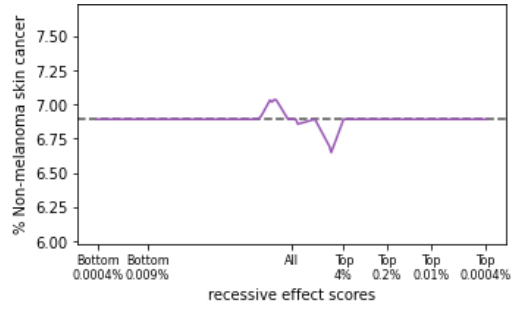
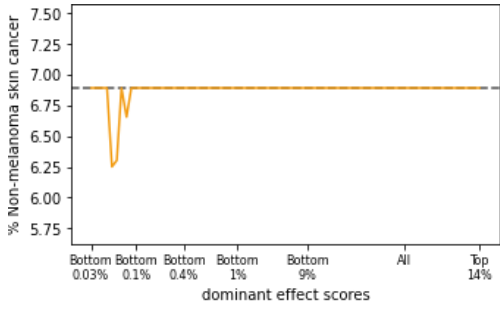
TRIM77 & Non-melanoma skin cancer: PWAS q-value = 7e-05 (Dominant & recessive)



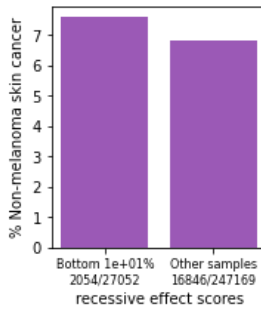
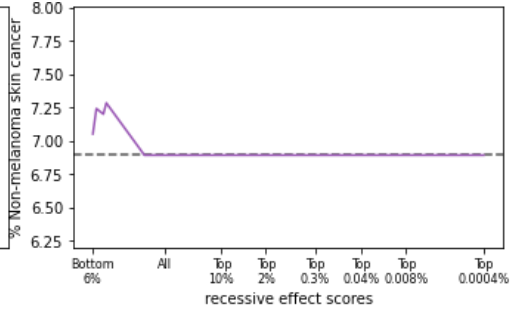
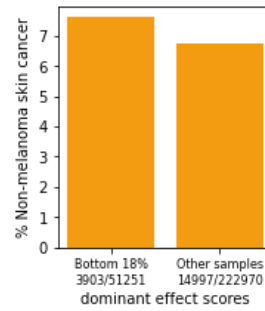
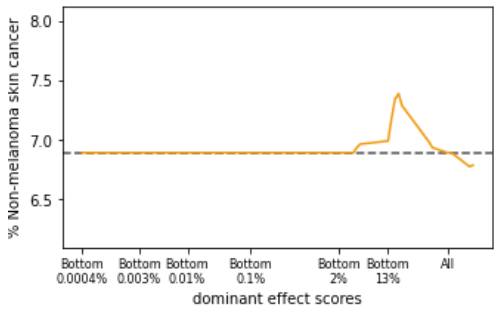
TYR & Non-melanoma skin cancer: PWAS q-value = 6e-13 (Dominant & recessive)



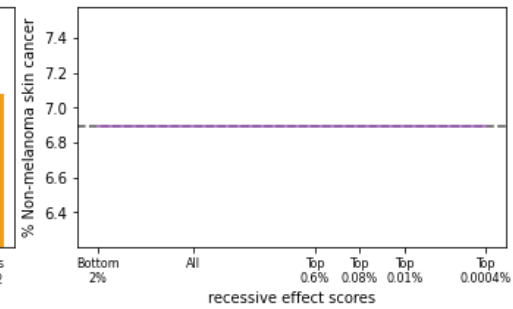
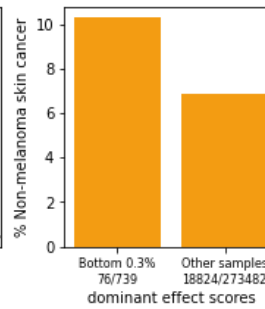
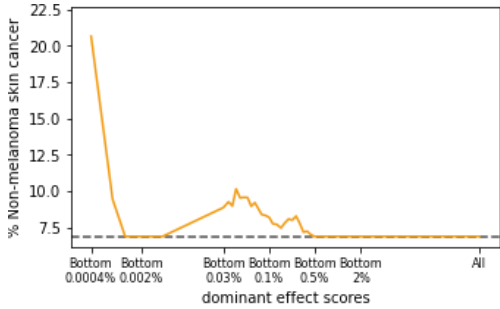
XPC & Non-melanoma skin cancer: PWAS q-value = 0.04 (Recessive)



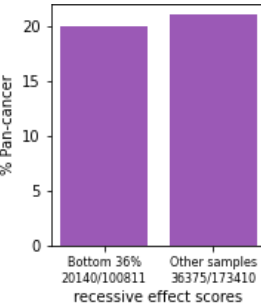
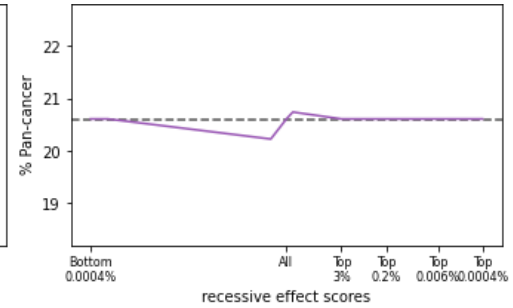
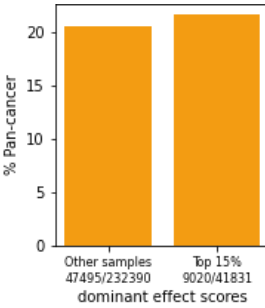
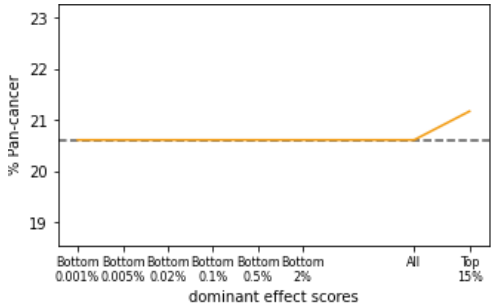
ZNF276 & Non-melanoma skin cancer: PWAS q-value = 0.0001 (Dominant & recessive)



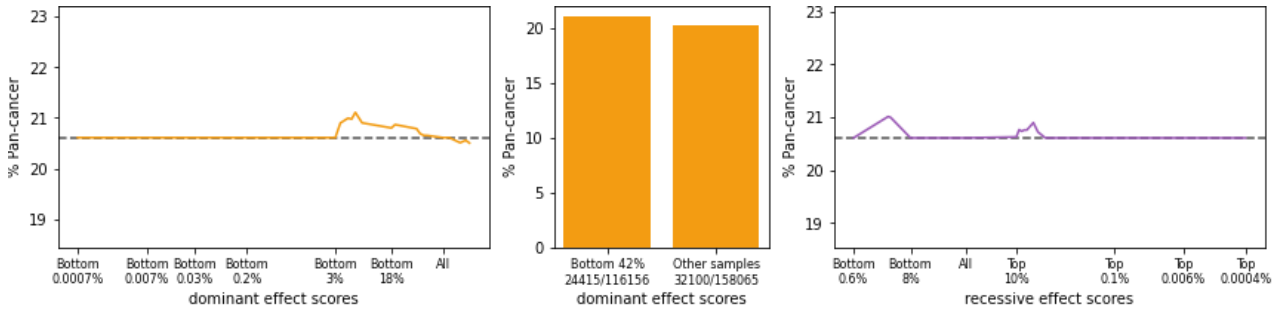
ZNF865 & Non-melanoma skin cancer: PWAS q-value = 0.04 (Dominant)



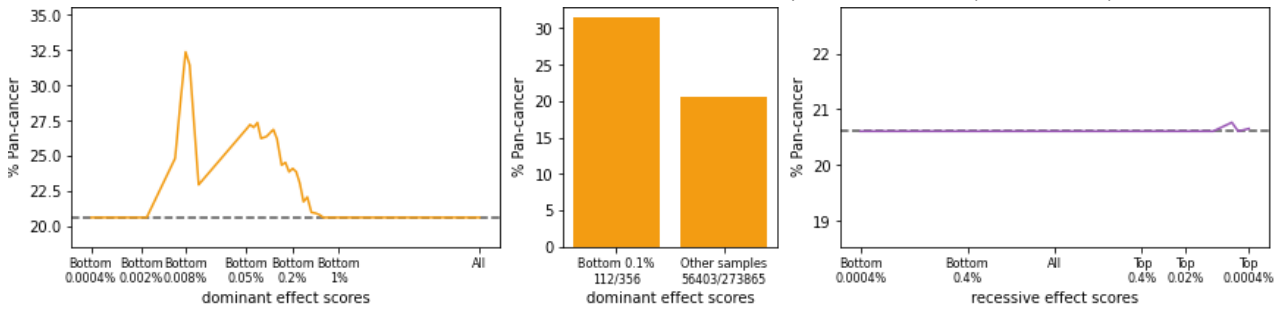
ALS2CR12 & Pan-cancer: PWAS q-value = 5e-09 (Dominant & recessive)



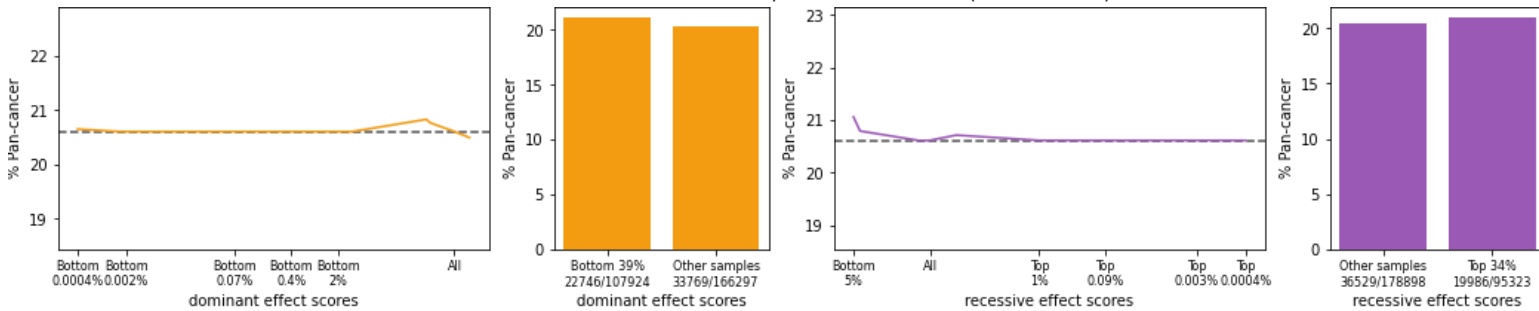
BNIPL & Pan-cancer: PWAS q-value = 0.01 (Dominant)



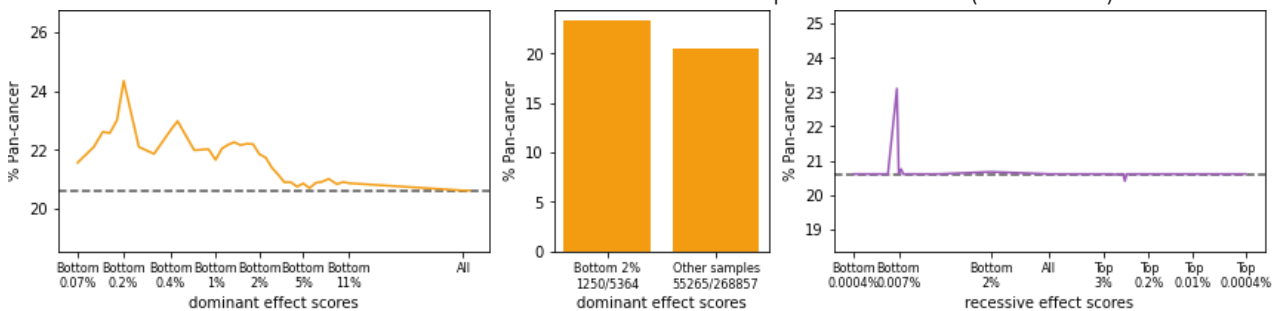
C1orf52 & Pan-cancer: PWAS q-value = 0.04 (Dominant)



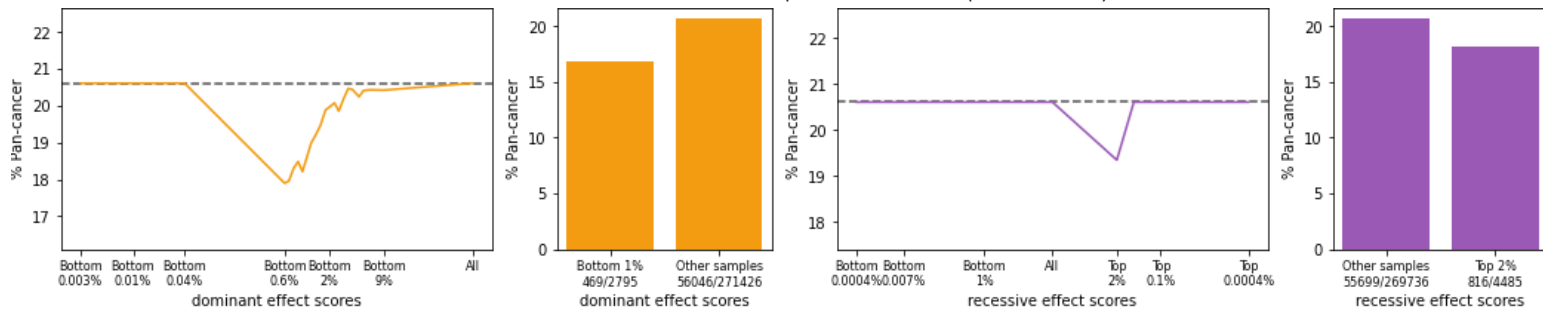
CERS2 & Pan-cancer: PWAS q-value = 0.006 (Dominant)



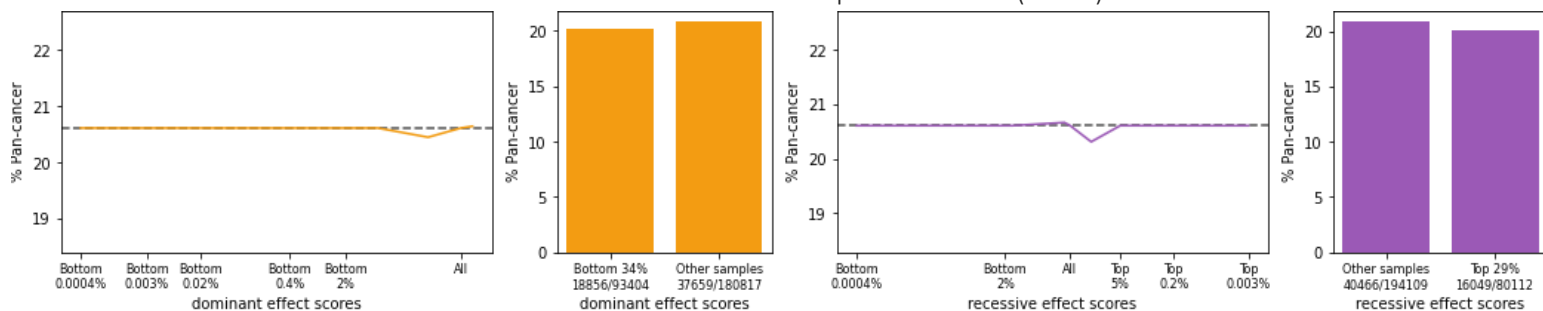
CHEK2 & Pan-cancer: PWAS q-value = 0.007 (Dominant)



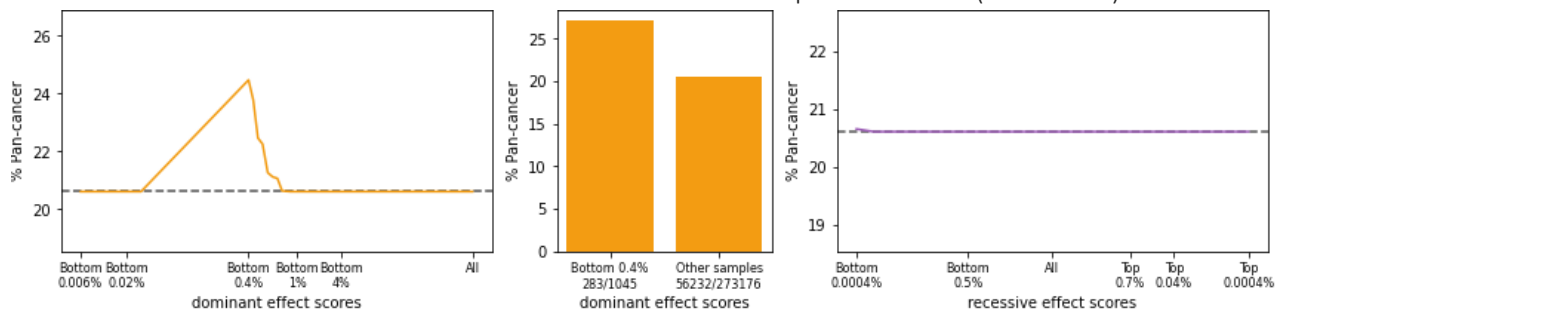
CRYAA & Pan-cancer: PWAS q-value = 0.02 (Dominant)



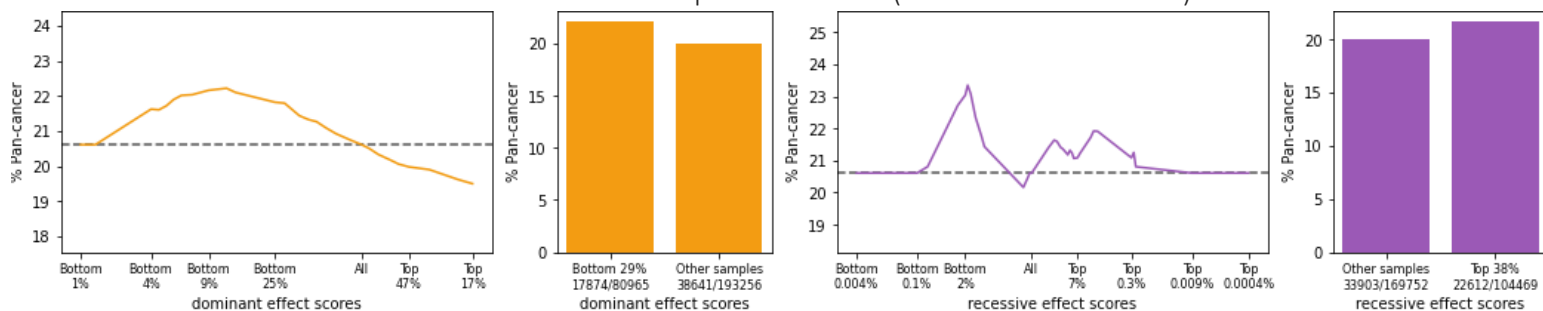
HLA-DPA1 & Pan-cancer: PWAS q-value = 0.01 (None)



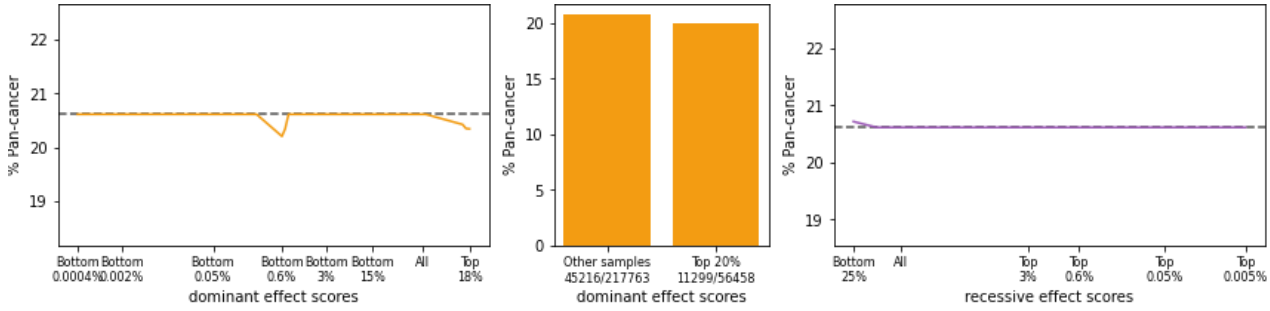
HOXB13 & Pan-cancer: PWAS q-value = 0.01 (Dominant)



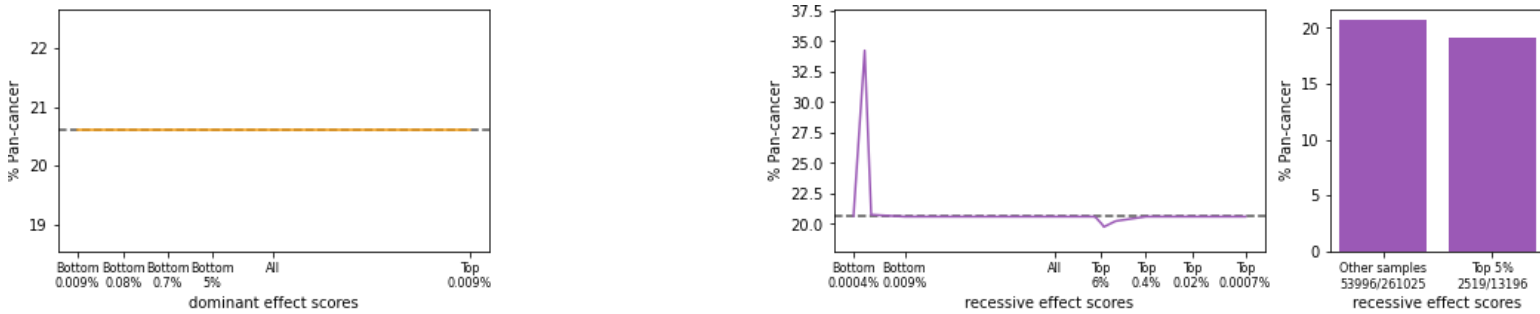
MC1R & Pan-cancer: PWAS q-value = 6e-34 (Dominant & recessive)



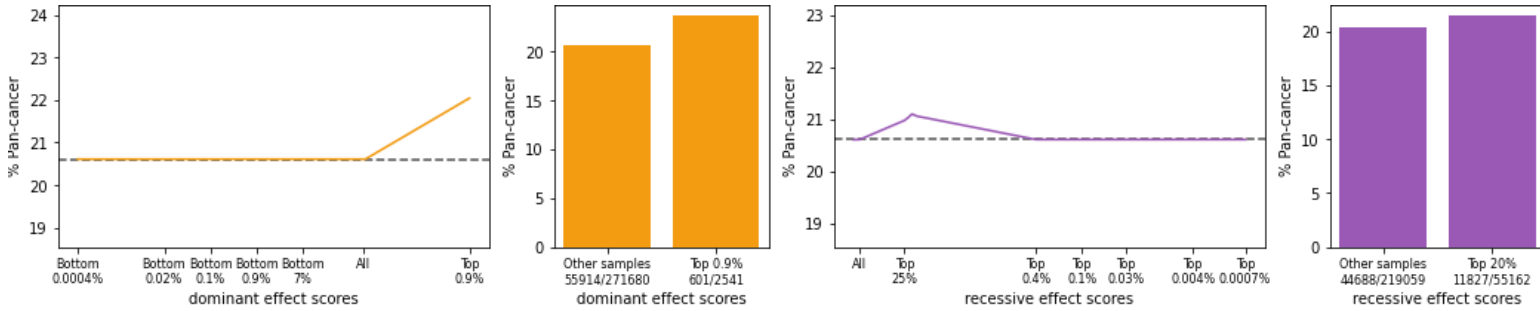
SH2B3 & Pan-cancer: PWAS q-value = 0.02 (None)



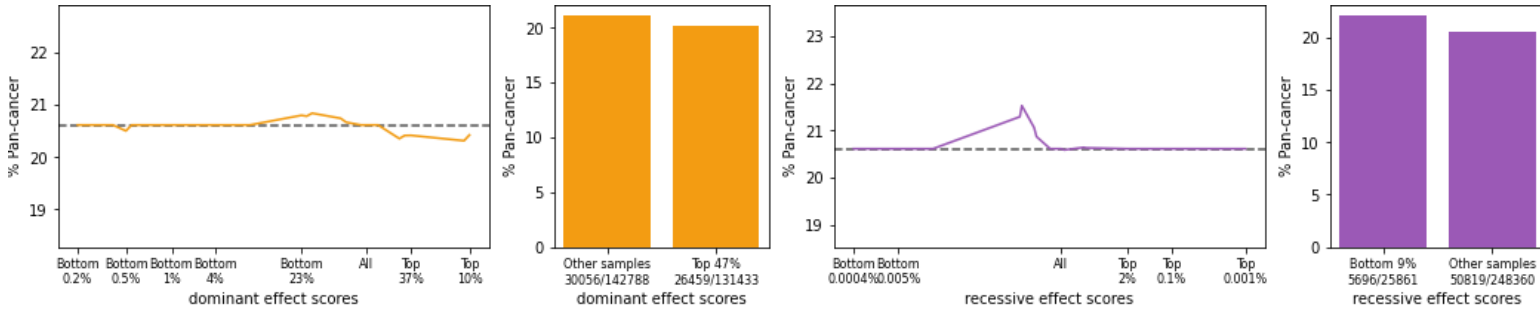
SLC45A2 & Pan-cancer: PWAS q-value = 0.02 (Recessive)



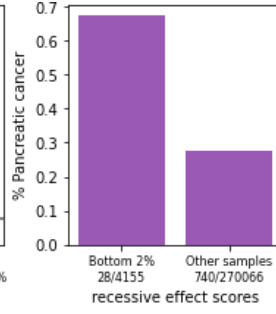
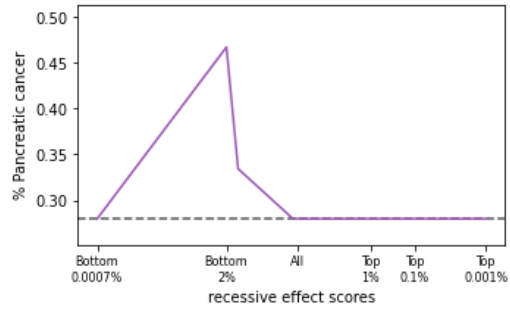
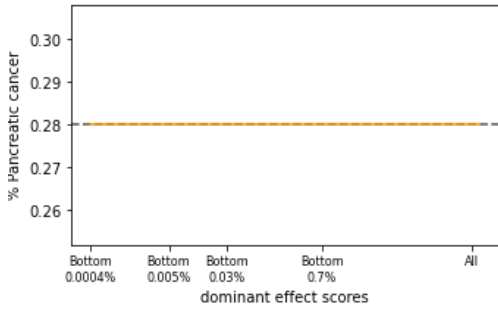
STN1 & Pan-cancer: PWAS q-value = 9e-06 (Recessive)



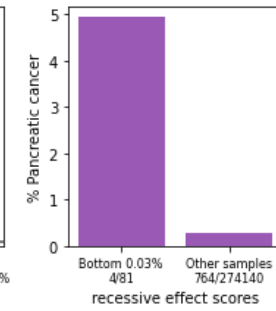
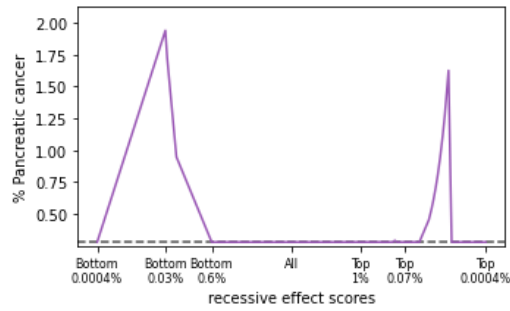
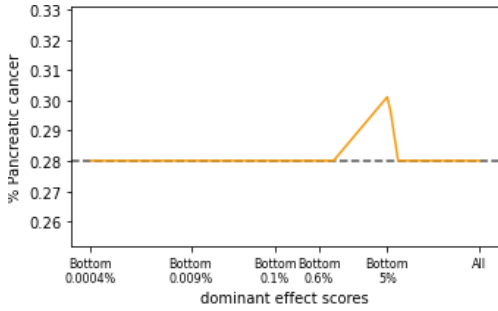
TYR & Pan-cancer: PWAS q-value = 1e-06 (Dominant & recessive)



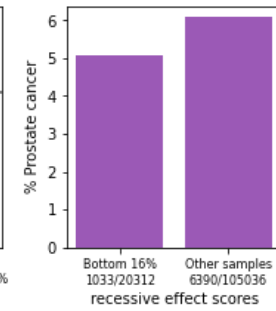
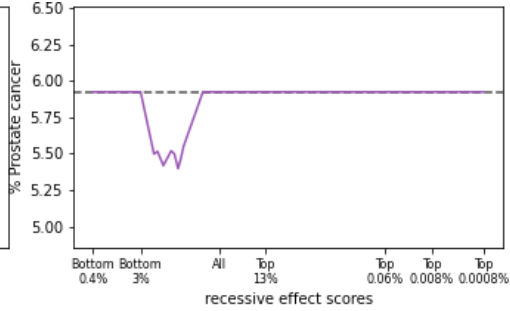
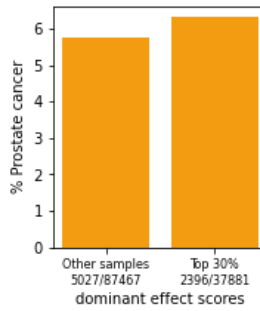
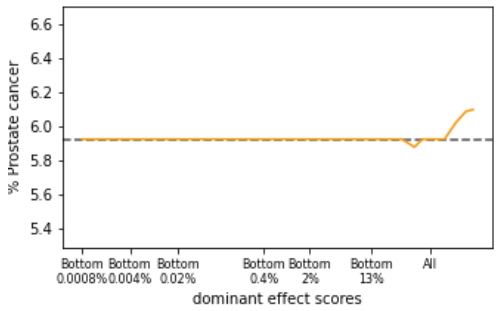
OR6K6 & Pancreatic cancer: PWAS q-value = 0.02 (Recessive)



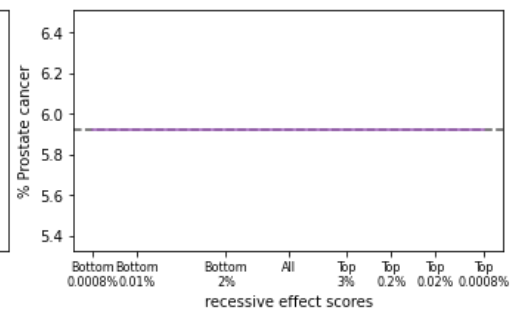
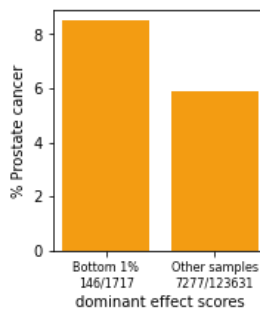
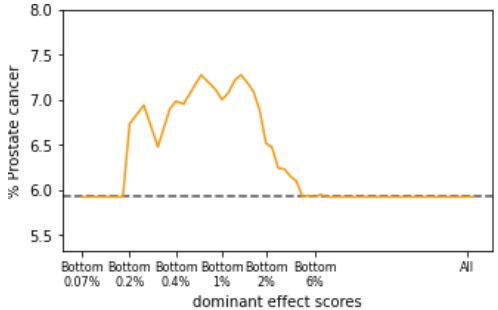
UBE3A & Pancreatic cancer: PWAS q-value = 0.0008 (Recessive)



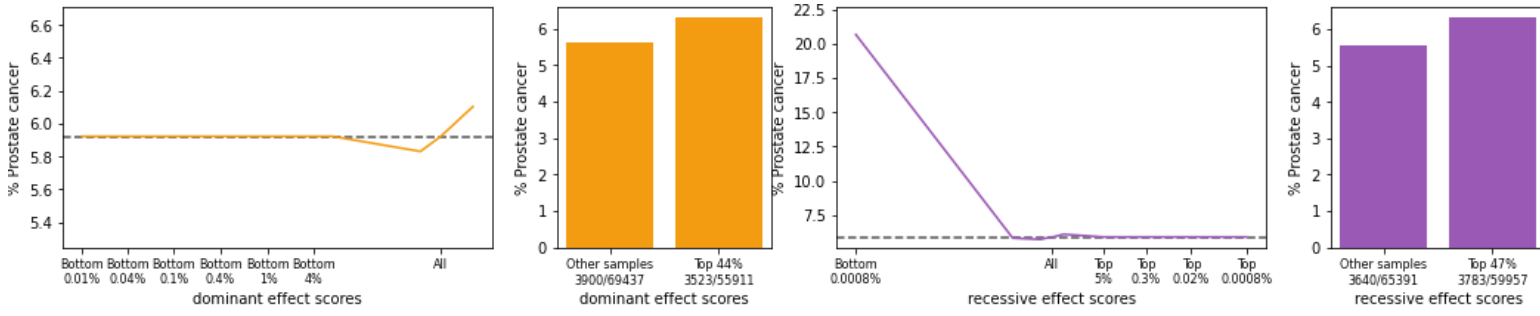
C6orf15 & Prostate cancer: PWAS q-value = 0.03 (None)



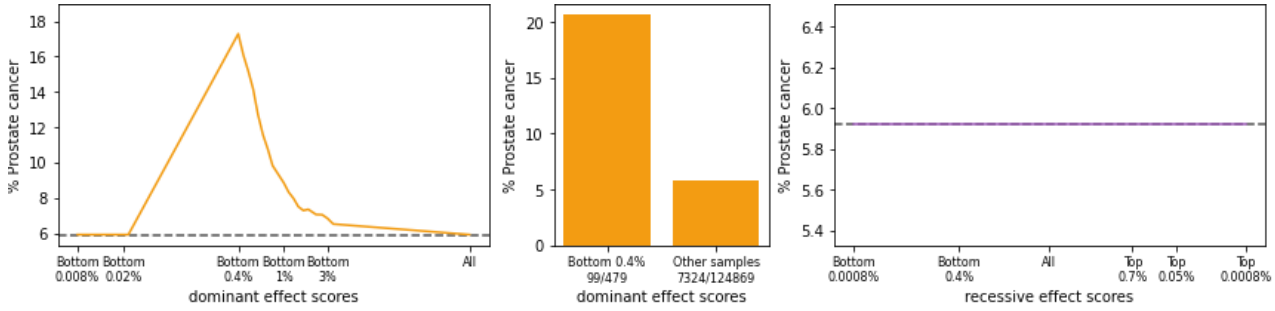
CHEK2 & Prostate cancer: PWAS q-value = 0.03 (Dominant)



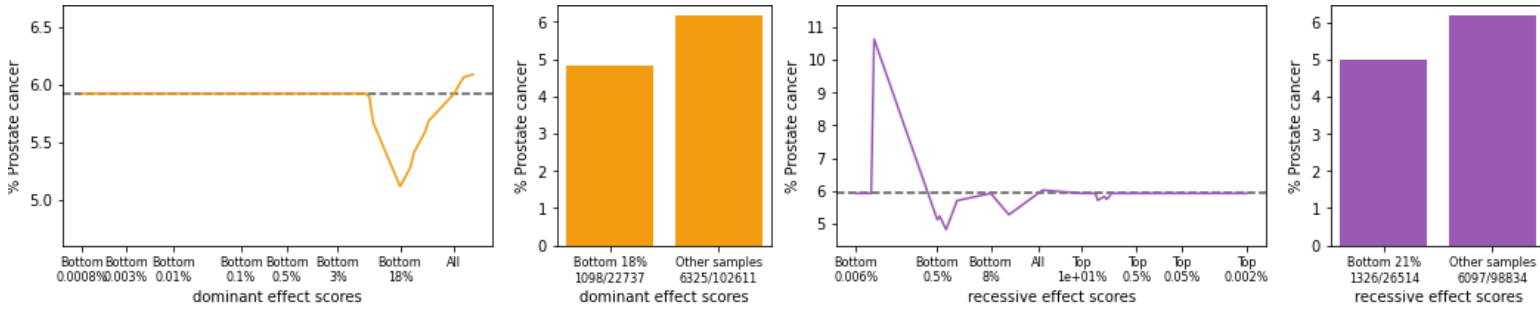
GGCX & Prostate cancer: PWAS q-value = 0.02 (Dominant)



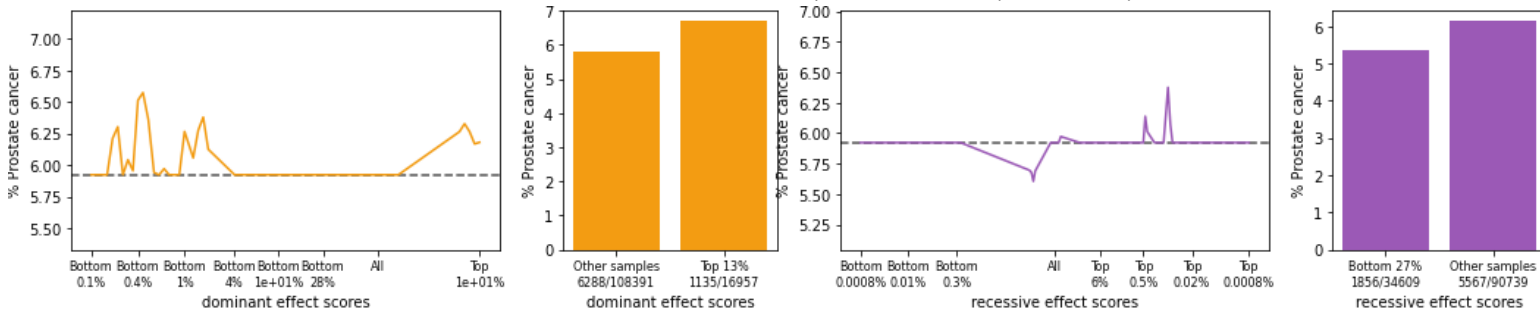
HOXB13 & Prostate cancer: PWAS q-value = 2e-31 (Dominant)



KLK3 & Prostate cancer: PWAS q-value = 4e-09 (Dominant)

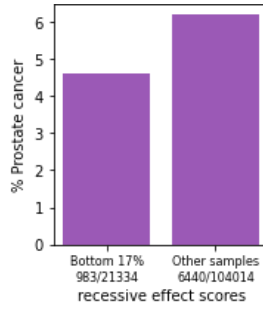
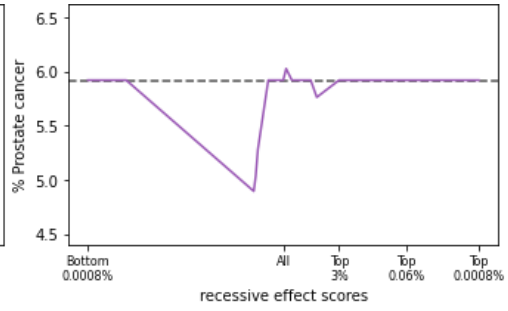
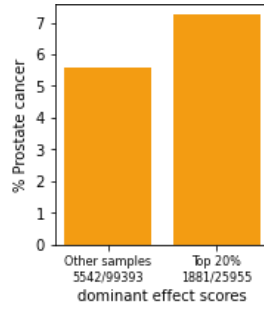
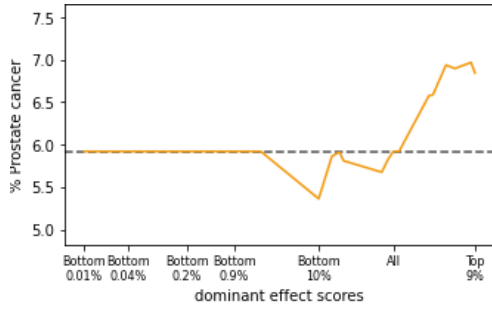


LMTK2 & Prostate cancer: PWAS q-value = 0.02 (Recessive)





POU5F1B & Prostate cancer: PWAS q-value =  $1e-22$  (Dominant & recessive)



SLC2A4RG & Prostate cancer: PWAS q-value = 0.02 (Recessive)

