

Supplementary Materials for

Fetal genome profiling at 5 weeks of gestation after noninvasive isolation of trophoblast cells from the endocervical canal

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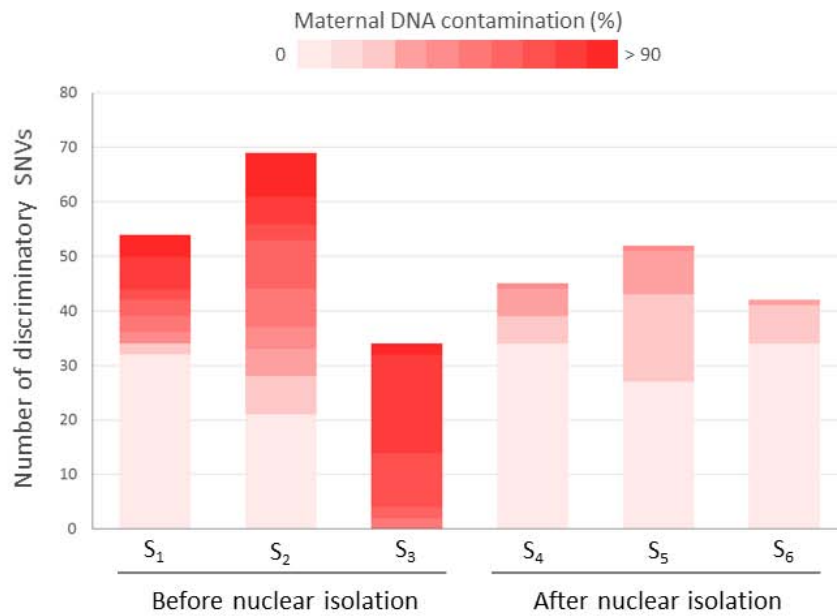


Figure S1. Comparison of fetal fractions obtained with and without nuclear isolation.

The stacked bar graph shows the distribution of co-purifying maternal DNA (calculated as percentages and represented by deeper red color) in DNA from TRIC-isolated fetal trophoblast cells among discriminatory SNVs (y-axis). Samples S1-3, sequenced without fetal cell nuclear isolation, show high proportions of maternal SNVs. Samples S4-6 were subjected to nuclear isolation before sequencing and show that detection reduced the number of maternal SNVs.

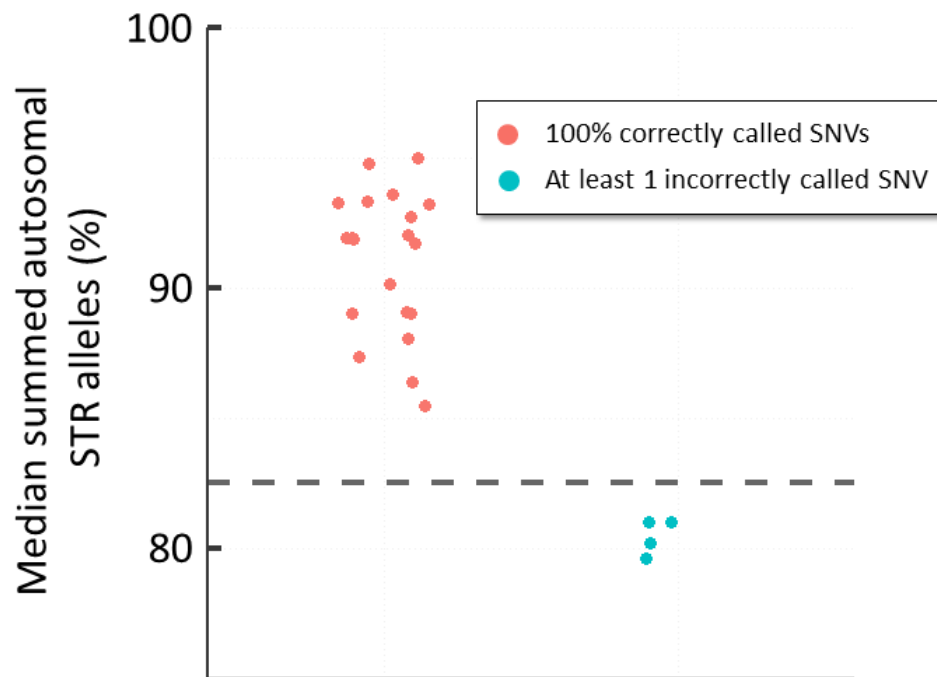


Figure S2. Cutoff determination for STR allele percentages. The scatter plot visualizes the median percentage of summed autosomal STR alleles in TRIC isolated fetal trophoblast cells (n=24). Percentage above 82.5% resulted in 100% correct fetal haplotyping and was therefore used as a threshold to ensure sample quality in the presented study.

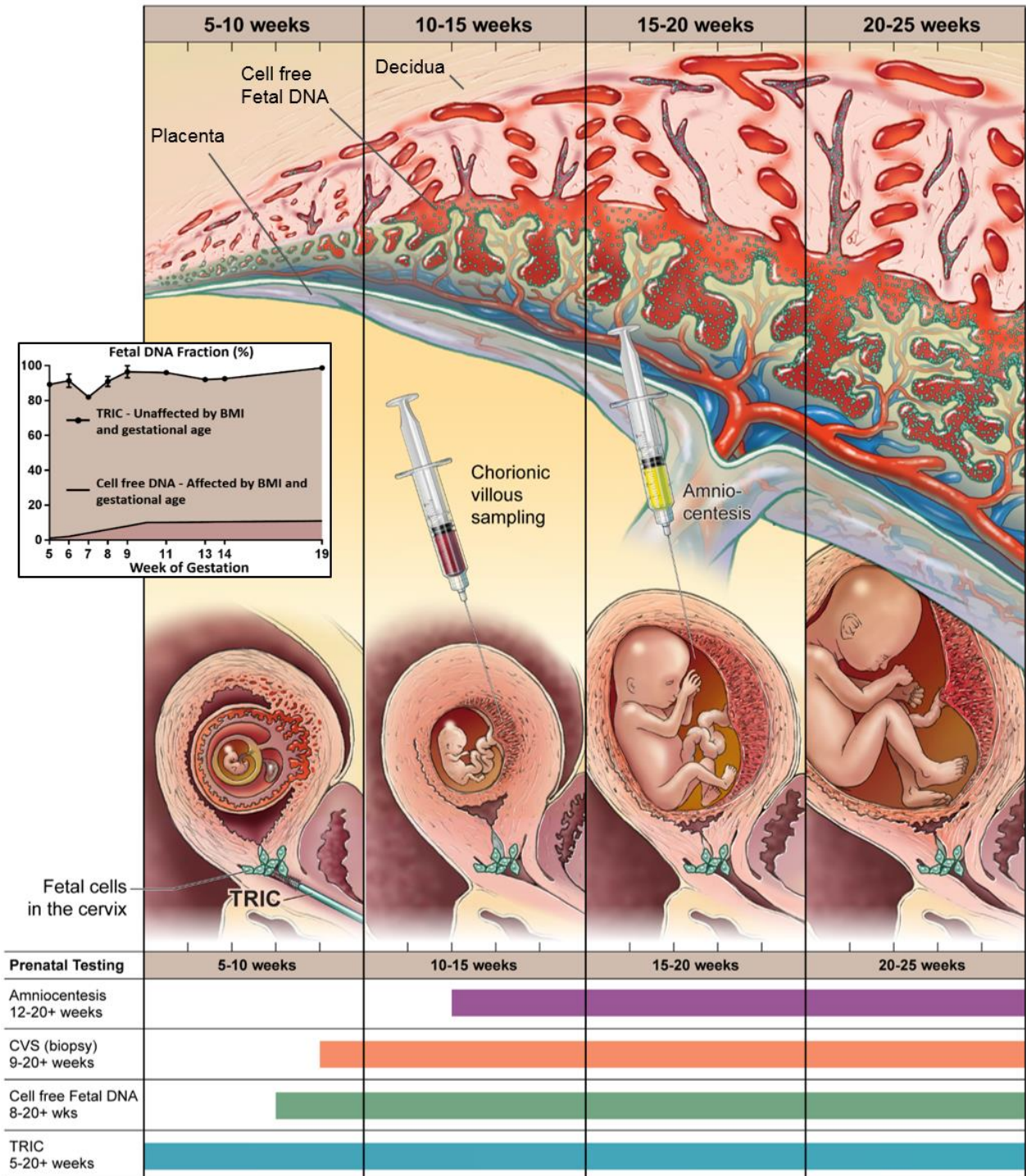


Figure S3. Comparison of approaches to obtain fetal DNA in ongoing pregnancies. Sources of fetal DNA throughout early pregnancy are illustrated according to their accessibility during gestation. Amniocentesis is available beginning at 12 weeks of gestational age (GA) and is invasive, but provides intact fetal cells from amniotic fluid that are adequate for genetic diagnosis. Chorionic villous sampling (CVS), first available at 9 weeks of GA, provides fetal DNA from intact cells of a placental biopsy obtained invasively. Fetal trophoblast cells are extremely rare in maternal blood; however, the plasma concentration of fetal DNA fragments, released as syncytiotrophoblast cells turn over, rises with increasing GA. This cell-free fetal DNA can be obtained non-invasively from maternal blood, as early as 8 weeks of GA, and can be analyzed using multiple parallel sequencing combined with extensive computational analysis to distinguish it from cell-free maternal DNA. Hundreds of intact trophoblast cells that enter the reproductive tract can be safely retrieved from noninvasive Pap smears using a cytobrush. TRIC captures these trophoblast cells beginning at 5 weeks of GA. The inset graphically compares the fetal fraction of DNA that is available between 5 and 19 weeks of GA using cell-free DNA in maternal serum and genomic DNA that we have isolated after TRIC.

Sr.No	SNP name	Sr.No	SNP name	Sr.No	STR name	Sr.No	STR name
01	rs1490413	48	rs1498553	01	D1S1656	48	DYS438
02	rs560681	49	rs901398	02	TPOX	49	DYS612
03	rs1294331	50	rs10488710	03	D2S441	50	DYS390
04	rs10495407	51	rs2076848	04	D2S1338	51	DYS643
05	rs891700	52	rs2107612	05	D3S1358	52	DYS533
06	rs1413212	53	rs2269355	06	D4S2408	53	Y- GATA- H4
07	rs876724	54	rs2920816	07	FGA	54	DYS385a-b
08	rs1109037	55	rs2111980	08	D5S818	55	DYS460
09	rs993934	56	rs10773760	09	CSF1PO	56	DYS549
10	rs12997453	57	rs1335873	10	D6S1043	57	DYS392
11	rs907100	58	rs1886510	11	D7S820	58	DYS448
12	rs1357617	59	rs1058083	12	D8S1179	59	DYF387S1
13	rs4364205	60	rs354439	13	D9S1122		
14	rs2399332	61	rs1454361	14	D10S1248		
15	rs1355366	62	rs722290	15	TH01		
16	rs6444724	63	rs873196	16	vWA		
17	rs2046361	64	rs4530059	17	D12S391		
18	rs279844	65	rs1821380	18	D13S317		
19	rs6811238	66	rs8037429	19	PentaE		
20	rs1979255	67	rs1528460	20	D16S539		
21	rs717302	68	rs729172	21	D17S1301		
22	rs159606	69	rs2342747	22	D18S51		
23	rs13182883	70	rs430046	23	D19S433		
24	rs251934	71	rs1382387	24	D20S482		
25	rs338882	72	rs9905977	25	D21S11		
26	rs13218440	73	rs740910	26	PentaD		
27	rs1336071	74	rs938283	27	D22S1045		
28	rs214955	75	rs8078417	28	DXS10135		
29	rs727811	76	rs1493232	29	DXS8378		
30	rs6955448	77	rs9951171	30	AMELX		
31	rs917118	78	rs1736442	31	DXS7132		
32	rs321198	79	rs1024116	32	DXS10074		
33	rs737681	80	rs719366	33	DXS10103		
34	rs763869	81	rs576261	34	HPRTB		
35	rs10092491	82	rs1031825	35	DXS7423		
36	rs2056277	83	rs445251	36	DYS505		
37	rs4606077	84	rs1005533	37	DYS570		
38	rs1015250	85	rs1523537	38	DYS576		
39	rs7041158	86	rs722098	39	DYS522		
40	rs1463729	87	rs2830795	40	DYS481		
41	rs1360288	88	rs2831700	41	DYS19		
42	rs10776839	89	rs914165	42	DYS391		
43	rs826472	90	rs221956	43	DYS635		
44	rs735155	91	rs733164	44	DYS437		
45	rs3780962	92	rs987640	45	DYS439		
46	rs740598	93	rs2040411	46	DYS389I		
47	rs964681	94	rs1028528	47	DYS389II		

Table S1. List of SNVs and STRs targeted by ForenSeq.