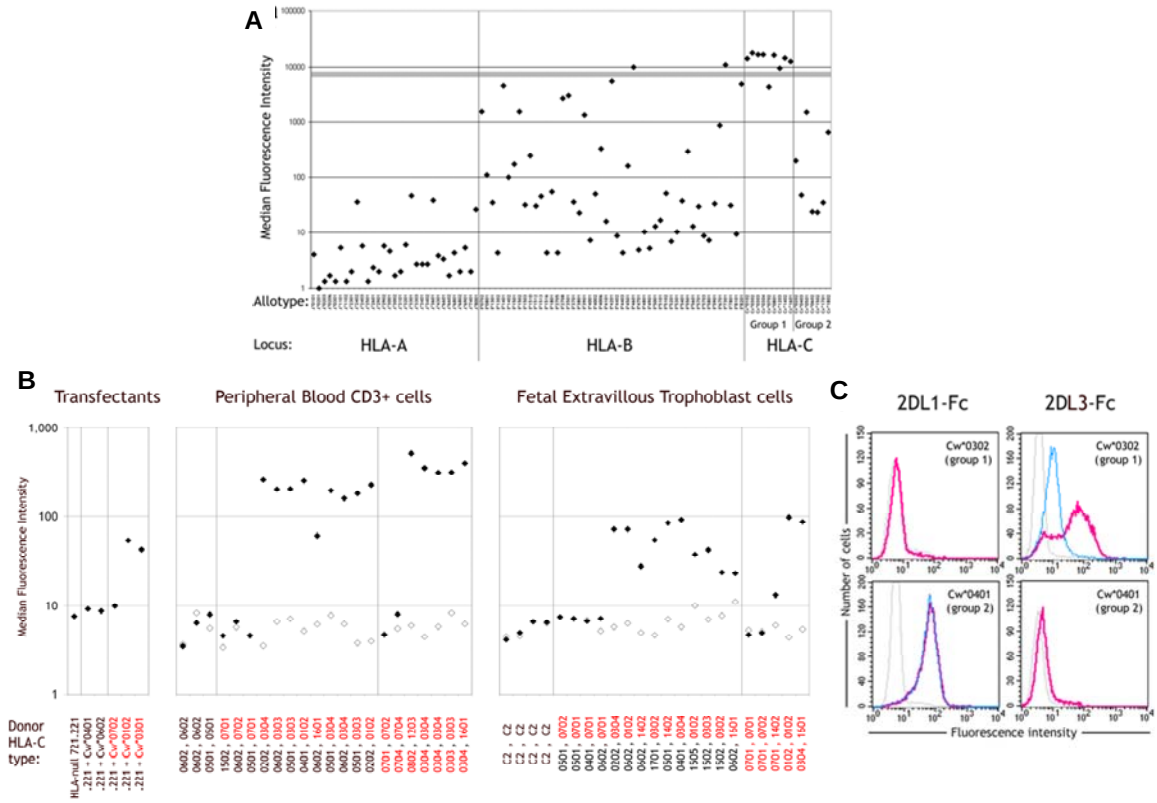
Supplementary Table I. Characterisation of the specificity of mAb WK4C11 by binding to HLA class I conjugated beads (LAB screen Single Antigen Beads from ONE Lamda).

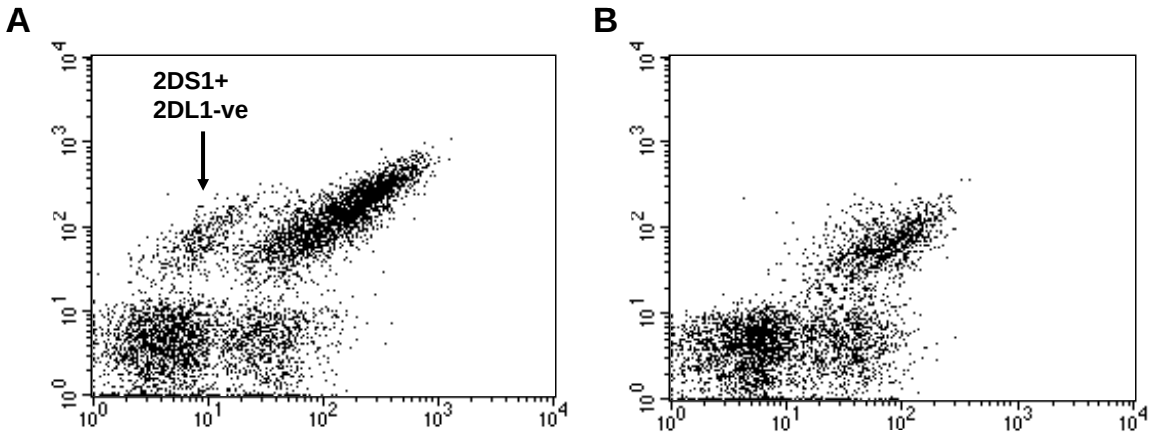
HLA-C allotype	Control IgG	W6/32	BBM.1	4C11	HLA-B allotype	Control IgG	W6/32	BBM.1	4C11	HLA-A allotype	Control IgG	W6/32	BBM.1	4C11
Group 1:					**B*0702**	14	10,616	11,470	**1,540**	**A*0101**	6	9,667	11,013	**4**
Cw*0102	89	10,649	5,369	**14,200**	**B*0801**	28	13,516	14,190	**110**	**A*0201**	4	12,964	14,036	**1**
Cw*0302	36	12,435	6,235	**17,871**	**B*1301**	18	9,112	9,854	**35**	**A*0203**	13	12,655	13,878	**1**
Cw*0303	112	11,378	5,745	**16,826**	**B*1302**	27	9,837	10,772	**4**	**A*0206**	17	12,351	13,598	**2**
Cw*0304	58	11,530	5,794	**16,731**	**B*1401**	120	12,744	13,969	**4,432**	**A*0301**	45	11,874	13,399	**1**
Cw*0702	88	9,698	4,893	**4,218**	**B*1402**	6	7,943	8,665	**99**	**A*1101**	9	12,354	13,773	**5**
Cw*0801	55	12,134	6,095	**16,360**	**B*1501**	18	13,400	14,238	**170**	**A*1102**	15	13,847	14,890	**1**
Cw*1203	26	6,830	3,428	**9,361**	**B*1502**	11	12,766	13,703	**1,548**	**A*2301**	13	12,598	13,745	**2**
Cw*1402	73	10,746	5,410	**14,423**	**B*1503**	10	12,004	12,772	**32**	**A*2402**	28	11,249	12,471	**37**
Cw*1601	97	9,055	4,576	**12,586**	**B*1510**	68	12,826	13,745	**243**	**A*2403**	25	12,008	13,357	**6**
					B*1512	7	12,156	13,033	**31**	**A*2501**	128	12,875	13,764	**1**
Group 2:					**B*1513**	11	11,335	12,454	**46**	**A*2601**	14	13,045	14,157	**2**
Cw*0202	86	8,530	4,308	**199**	**B*1516**	30	9,004	9,892	**4**	**A*2901**	12	11,942	13,087	**2**
Cw*0403	79	6,003	3,041	**48**	**B*1801**	7	12,096	12,907	**55**	**A*2902**	30	12,740	13,854	**6**
Cw*0501	80	10,999	5,540	**1,492**	**B*2705**	16	12,712	13,480	**4**	**A*3001**	34	12,497	13,898	**5**
Cw*0602	16	7,090	3,553	**24**	**B*2708**	17	13,677	14,457	**2,639**	**A*3002**	11	8,613	9,918	**2**
Cw*1502	32	6,028	3,030	**24**	**B*3501**	72	12,528	13,636	**2,968**	**A*3101**	7	11,635	13,011	**2**
Cw*1701	21	6,417	3,219	**35**	**B*3701**	13	12,742	13,864	**36**	**A*3201**	63	12,337	13,680	**6**
Cw*1802	106	11,302	5,704	**651**	**B*3801**	22	12,536	13,346	**23**	**A*3301**	25	10,936	12,141	**46**
					B*3901	21	12,053	13,057	**1,320**	**A*3303**	53	11,966	13,048	**3**
					B*4001	11	6,560	6,636	**7**	**A*3401**	29	11,493	12,534	**3**
					B*4002	23	9,644	10,460	**51**	**A*3402**	12	12,271	13,417	**3**
					B*4006	59	9,787	10,745	**333**	**A*3601**	155	9,726	10,857	**39**
					B*4101	10	6,477	7,244	**16**	**A*4301**	54	10,631	12,225	**4**
					B*4201	12	13,938	14,554	**5,344**	**A*6601**	23	13,141	14,342	**3**
					B*4402	15	9,520	10,213	**9**	**A*6602**	10	11,663	12,739	**2**
					B*4403	9	7,522	8,576	**4**	**A*6801**	68	12,423	13,757	**4**
					B*4501	79	13,346	14,198	**160**	**A*6802**	23	12,079	13,340	**2**
					B*4601	21	8,459	9,170	**10,008**	**A*6901**	73	11,000	12,394	**5**
					B*4701	18	8,172	8,712	**5**	**A*7401**	19	13,276	14,397	**2**
					B*4801	21	9,862	10,485	**10**	**A*8001**	30	12,223	13,466	**26**
					B*4901	20	10,100	11,299	**5**					
					B*5001	26	12,999	13,988	**13**					
					B*5101	27	12,500	13,470	**17**					
					B*5102	11	12,609	13,670	**52**					
					B*5201	6	9,748	10,734	**7**					
					B*5301	72	11,148	12,370	**10**					
					B*5401	32	11,999	12,736	**38**					
					B*5501	25	14,411	14,976	**298**					
					B*5601	9	10,307	11,284	**13**					
					B*5701	32	9,895	10,947	**30**					
					B*5703	13	9,467	10,002	**9**					
					B*5801	12	8,782	9,834	**7**					
					B*5901	25	9,711	10,647	**33**					
					B*6701	9	10,666	11,417	**868**					
					B*7301	39	10,345	11,711	**10,845**					
					B*7801	49	11,645	12,561	**31**					
					B*8101	23	11,524	12,251	**9**					
					B*8201	74	13,481	14,357	**4,816**					

Median fluorescence intensities are shown for the mAb, WK4C11, compared to W6/32 (binds all fully conformed class I molecules), BBM.1 (binds to ß2-microglobulin) and control IgG. Staining with W6/32 and BBM.1 showed similar levels of HLA class I were present for each allotype. WK4C11 preferentially bound to most HLA-C group 1 molecules and also to two HLA-B allotypes, *4601 and *7301, that share the same C1 epitope (Moesta et al., 2008. ref 54). HLA-Cw*07, all HLA-C2, all other HLA-B and all HLA-A allotypes did not bind WK4C11.



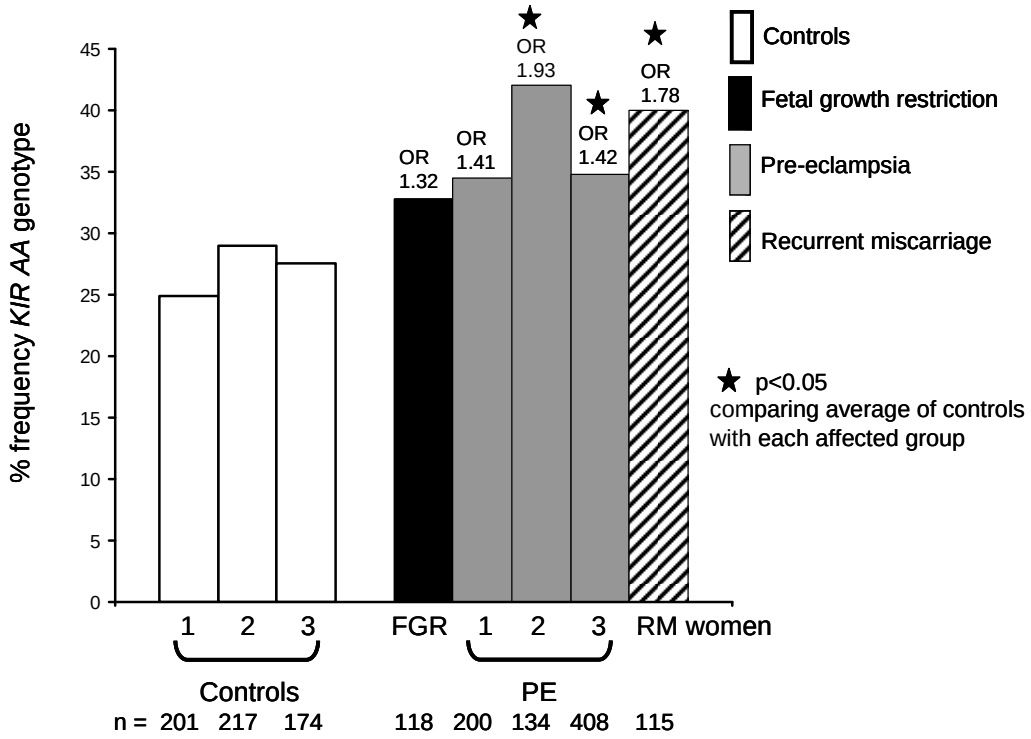
Supplementary Figure 1. Further characterisation of mAb WK4C11 reactivity using HLA-conjugated beads, transfectants and primary cells.

(A) Reactivity of the mAb WK4C11 was characterised against common HLA class I allotypes using beads coated with individual HLA class I molecules (see Table S1 for raw data). The median fluorescence intensity of WK4C11 binding to each allele is plotted. The grey bar indicates the threshold of binding to these beads which results in binding to live cells and was determined by testing binding of the mAb to donors with selected HLA class I type. The mAb WK4C11 recognises all C1 alleles except Cw*07. (B) HLA-C transfectants, peripheral blood CD3+ cells, or HLA-G+ first trimester extravillous trophoblast cells are shown according to HLA-C type, with C1 alleles highlighted in red. Median fluorescence intensity of WK4C11 binding (filled) or secondary alone (open points) is plotted. WK4C11 binds all samples where a group 1 HLA-C allele is present, except where this allele is Cw*07. (C) As expected for a mAb preferentially reactive with C1 alleles, WK4C11 blocks binding of KIR2DL3-Fc fusion protein to HLA-Cw*0302 (C1) transfectants, but had no effect on KIR2DL1-Fc binding HLA-Cw*0401 (C2). Binding of KIR-Fc is shown in red, compared to secondary reagent alone (grey) or cells pre-incubated with the mAb, WK4C11 (blue).



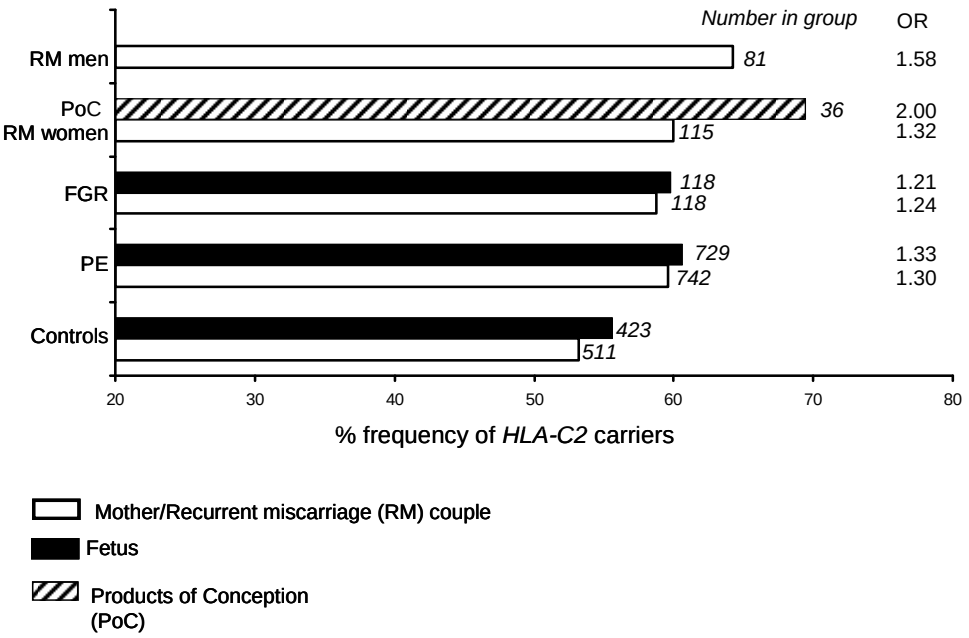
Supplementary Figure 2. **Identification of uterine NK cells (uNK) expressing KIR2DS1 but not KIR2DL1**.

CD56+ve, CD14-ve uNK cells were stained with mAbs, EB6 and 8C11. EB6 recognises KIR2DL1 and KIR2DS1. 8C11 recognizes most KIR2DL1 alleles but not KIR2DS1, allowing uNK cells expressing 2DS1 but not 2DL1 to be identified (i.e. EB6+, 8C11-). (A) uNK cell sample from a KIR2DS1 positive woman. (B) uNK cell sample from a KIR2DS1 negative woman. The maternal KIR2DL1 alleles were confirmed by sequencing to be those recognised by the 8C11 antibody.



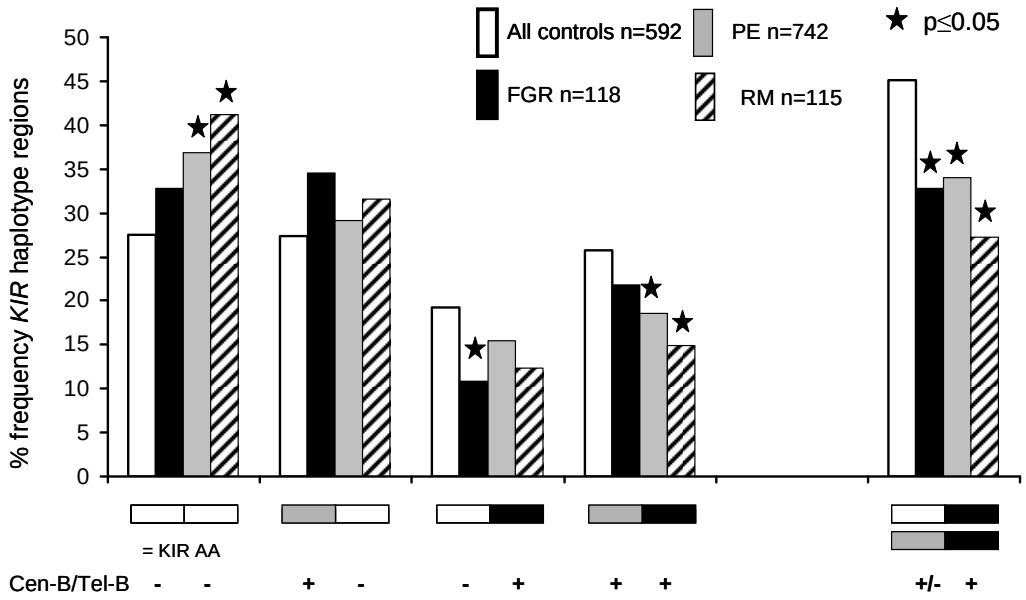
Supplementary Figure 3. Maternal *KIR AA* frequency in each cohort of control and affected pregnancies.

Maternal *KIR AA* frequency was similar in all 3 cohorts of normal control pregnancies (Controls 1, 2 and 3) and is higher in all affected pregnancies: fetal growth restriction (FGR), three cohorts with pre-eclampsia (PE1, 2 and 3) and recurrent miscarriage women (RM). Two of the PE study groups and the RM women had significantly higher *KIR AA* frequencies. Initial results for Controls1 and PE1 have been reported (Hiby et al., 2004, ref.2) and the RM data is updated and re-analysed from our previous publication with additional samples from the same hospital clinic (Hiby et al., 2008, ref 3).



Supplementary Figure 4. Frequency of *HLA-C2* carriers in controls and affected cohorts.

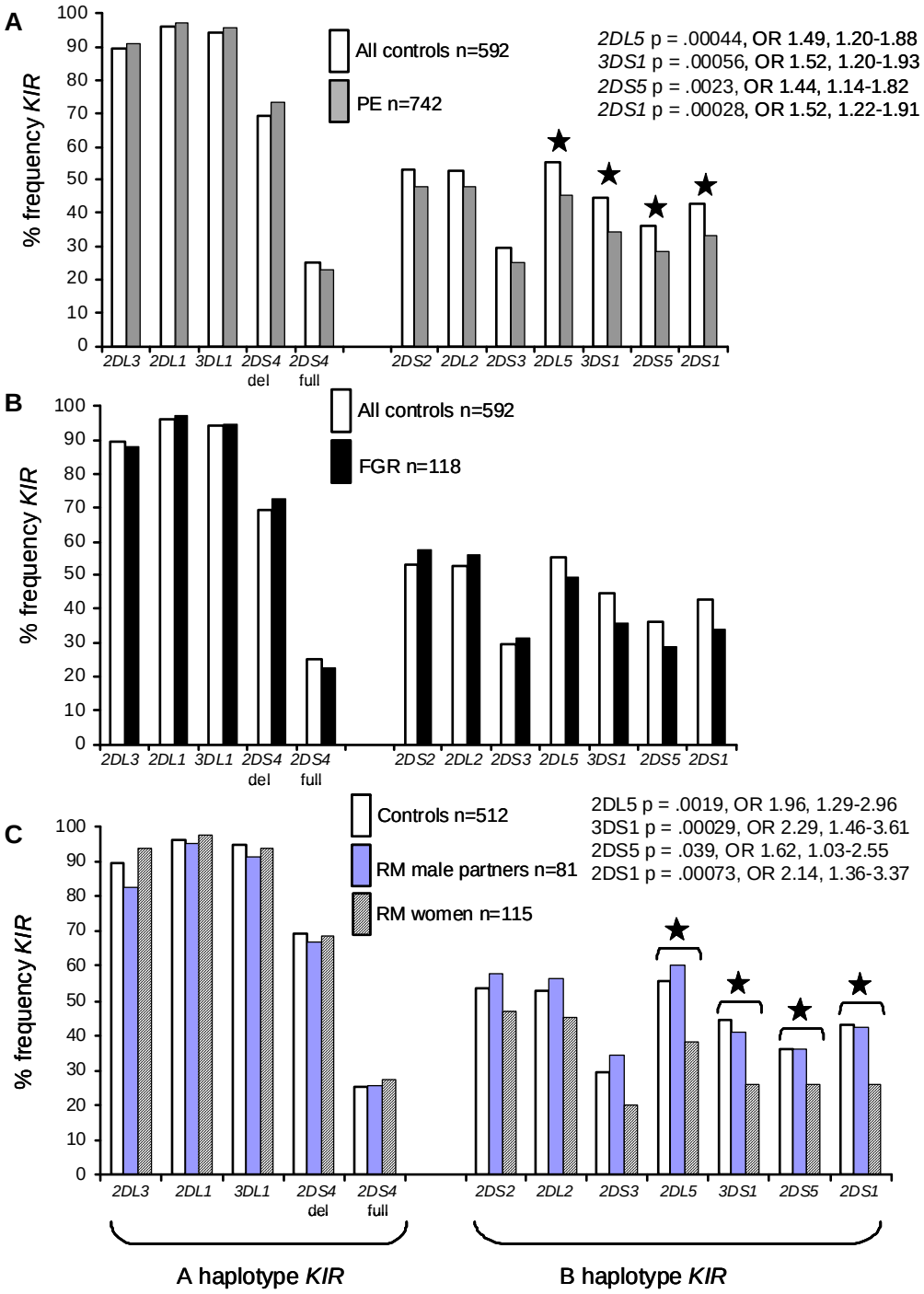
HLA-C2 carriers tend to be more frequent in the fetuses and mothers of affected pregnancies compared to controls (odds ratios shown). The male partners of the women with RM also had an increased *HLA-C2* frequency. The products of conception (PoC) from the miscarrying pregnancies had the highest frequency of *C2*.



Supplementary Figure 5. Frequency of maternal *KIR Cen-B* and *Tel-B* regions, comparing controls with affected pregnancies complicated by pre-eclampsia (PE), fetal growth restriction (FGR) and recurrent miscarriage (RM).

All affected pregnancies show the same increase in maternal *KIR AA* (*Cen-B-*/*Tel-B-*) genotype and significant lack of the *Tel-B* region.

p for trend for PE is $8x10^{-6}$, for RM $3x10^{-4}$ and for FGR 0.06. KIR haplotype regions were defined by presence of particular *KIR* genes: *Cen-A* /*2DL3*; *Tel-A* /*3DL1* and *2DS4*; *Cen-B* /*2DL2* and *2DS2*; *Tel-B* /*2DS1*and *3DS1*.



Supplementary Figure 6. Individual maternal *KIR* gene frequencies in control and affected pregnancies. The *KIR* genes are depicted as usually located on the *A* and *B haplotypes* from centromeric to telomeric end.(**A**) Pre-eclampsia (PE) mothers compared to controls. (**B**) fetal growth restriction (FGR) mothers compared to controls and (**C**) Recurrent miscarriage (RM) women and their male partners compared to the controls.The RM men have the same *KIR* gene frequencies as normal controls but are shown separately in (**C**) to contrast with their RM women partners. There was a highly significant lack of the *KIR* genes usually located telomeric to *KIR2DL4* on the *B haplotype* in the pre-eclamptic and recurrent miscarriage women. The FGR mothers showed the same trend but this did not reach significance.