

Supplementary table 1. Number of screened control chromosomes from different ethnic groups for the various mutations and variants

New mutation	Ethnic origin of the patient	Women of European descent with 5 to 16 children	Lebanese (general population)	Chinese (general population)	Pakistani (general population)	African American (general population)	Total number of controls
c.750C>A, p.Phe250Leu	African/Indian	208	42		76		326
c.930_931delGC, p.Q310HfsX38	Caucasian	208		98	-	-	306
c.1018_1020delGAGinsCAAAA, p.Glu340GlnfsX11	Caucasian	208		98	-	-	306
c.1018G>A, p.Glu340Lys	Pakistani	208		98	76	-	382
c.2444G>A, p.Arg815His	Algerian	220		-	-	-	220
c.2791_2792delTG, p.Cys931X	Caucasian	208		94	76	-	378
c.1169G>A, p.Arg390His	Guadeloupean	208		98	76		174
c.1237C>T, p.Arg413Trp	Haitian	208		98	76		174

Supplementary table 2. New mutations/variants and reproductive outcomes of the patients

Family ID	Patient ID	<i>NLRP7</i>	Reproductive Outcomes of the patients
MoUs167	712	p.[P716A];[Cys931X]	SA, PHM, PHM
MoNz170	725	p. [Q310HfsX38;A481T];[R693W]	CHM, SA, CHM, HM
MoCa179	744	p.[Glu340GlnfsX11];[R693W]	HM, BO, 3 SA, 2 HM
MoCa186	758	p.[V319I;G487E];[V319I;G487E];[F250L(;)A481T]	LB, CHM, LB
MoPa214	814	p.[V319I(;)E340K]	SA, SA, PHM (uterus retroverted, small leiomyoma)
MoGu248	897	p.[A481T];[A481T];[V319I(;)R390H(;)G487E]	ET, ET, SA, CHM, SA, SA, SA-CC, NP
MoHa259	919	p.[V319I(;)R413W(;)G487E]	NP, PHM-GTN (I-5)
MoAl17	M36	p.[G487E(;)R815H]	HM no other data

LB, stands for live birth; HM, for hydatidiform mole; PHM, partial HM; CHM, complete HM; SA, spontaneous abortion; BO, blighted ovum; ET, elective termination; CC, choriocarcinoma; GTN, gestational trophoblastic neoplasia grade I-5 according to HUPO nomenclature. New mutations are in red.

Supplementary table 3. Protein-truncating mutations in familial versus singleton case:

References	Familial cases		Singletons	
	N. of Families	≥1 Protein-truncating	N. of singleton	≥1 Protein-truncating
Murdoch et al. 2006	4	2	1	0
Qian et al., 2007	1	1		
Kou et al., 2008	3	2	5	3
Puechberty et al., 2008			1	0
Deveault et al., 2009	3	1	8	0
Hayward et al., 2009	5	3	8	2
Wang et al., 2009	7	3	13	5
Current study			5	3
Total	23	12	41	13
Protein-truncating		52.17%		31.71%

N, stands for number.

Supplementary table 4. Non synonymous variants and reproductive histories of patients of European descent			
Family ID	Patient ID	Reproductive history by chronological order	Non synonymous changes
MoPa25	M4	HM no other data	p.[V319I]+[=]
MoPa26	M6	HM no other data	p.[=]+[=]
MoPa27	M20	HM no other data	p.[=]+[=]
MoCr51	399	2 HM-Lung adenocarcinome-died	p.[A481T]+[=]
MoCa58	433	HM, NP	p.[V319I]+[V319I]
MoCa63	700	NP, HM, NP	p.[=]+[=]
MoSw67	466	PHM, NP, 5 HM, HM	p.[=]+[=]
MoUs79	539	1 CHM, 4 IUI, 1 IVF, 1 NP	p.[V319I]+[=]
MoCa80	540	1 CHM and multiple failed IVF	p.[V319I]+[=]
MoAu81	541	4 HM, 10 SA	p.[V319I]+[=]
MoCa115	701	PHM-GTN	p.[V319I]+[=]
MoFr119	M264	2 PHM/SA	p.[V319I(+)+A481T]
MoFr121	M116	1 NP, 1 HM	p.[=]+[=]
MoCa168	747	infertility, clomiphene-HM-GTN (RP 2 D&C)	p.[G487E]+[=]
MoSw177	741	HM, EP, now pregnant	p.[Q310R;L311I;A481T]+[=]
MoCa178	742	HM	p.[=]+[=]
MoGe181	753	HM	p.[=]+[=]
MoCa182	754	NP, twin (HM+dead fetus), EA (RP 2 D&C)	p.[A481T]+[=]
MoCa189	764	SA, SA, SA-GTN	p.[A481T]+[=]
MoCa205	799	SA (RP requiring 3 D &C), BO	p.[A481T]+[=]
MoCa207	802	NP, SA, CHM-GTN(L-3) (2 D&C)	p.[G487E]+[=]
MoCa210	806	SA, SA, NP, NP, SA, NP, SA, SA	p.[V319I(+)+A481T]
MoCa215	815	SA, SA, SA, SA, Pregnant	p.[=]+[=]
MoCa216	817	SA, SA, CHM (2 D&C), NP-CC	p.[=]+[=]
MoCa217	818	BO, NP [#] , EP, BO, BO	p.[=]+[=]
MoIt218	819	BO, BO, NP, SA, SA	p.[A481T]+[=]
MoCa220	821	SA, SA (RP 2 D&C), SA	p.[Q310R(+)+L311I(+)+A481T]
MoCa223	830	SA, SA, SA, SA, EP, EP	p.[A481T]+[=]
MoCa224	831	NP, SA, SA, SA, SA, SA, SA (RP 2 D&C)	p.[V319I]+[=]
MoCa228	840	CHM-GTN (L4), pregnant	p.[G487E]+[=]
MoFr229	842	HM, HM	p.[=]+[=]
MoIt230	846	SA, CP, CP, CP, NP, SA, Pregnant	p.[V319I]+[=]
MoCa231	847	SA, SA, SA, Pregnant	p.[=]+[=]
MoCa232	856	TA, SA, SA, SA, Pregnant	p.[=]+[=]
2353	3	NP, SA, PHM, CHM	p.[K511R]+[=]
2364	3	2 NP, PHM, CHM	p.[V319I]+[=]
2546	3	PHM, NP, EA, PHM	p.[G487E]+[=]
2576	3	3 SA, 2 PHM (order unknown)	p.[G487E]+[=]
2805	3	3 SA, NP, 4 SA	p.[V319I(+)+A481T]
2806	3	PHM, CHM	p.[=]+[=]
2926	3	4 SA, SB with pseudo molar placenta	p.[V319I]+[=]
2992	3	CHM, SB *(22w), IUFD (24 w, IUGR and malformations [#]), LB (33 w)	p.[A481T]+[=]
3914	3	HM, 3NP	p.[A481T]+[=]
3915	3	HM, 2NP	p.[=]+[=]
MoCa88	565	2 NP, 7 SA	p.[K511R]+[=]
MoCa234	864	1st pregnancy CHM	p.[=]+[=]
MoGr 235	871	SA, SA, SA, NP, SA, PR	p.[V319I(+)+A481T]
MoNz238	875	PHM, SA, SA	V319I, M427T, F430L
MoCa239	880	SA, SA, SA, SA, HM-GTN	p.[=]+[=]
MoCa240	881	TA, SA, NP, PHM, SA, NP	p.[V319I]+[=]
MoIt241	882	NP, TA, NP, NP, HM-GTN	p.[K511R];[=]
MoIg243	885	SA, SA, SA, SA, SA	p.[G487E]+[=]
MoCa244	887	SA, SA, SA, SA, SA, SA, SA, Pregnant	p.[=];[=]

*The chronological order of the different pregnancies is unknown. CHM, indicates complete HM; PHM, partial HM; SA, spontaneous abortion; BO, blighted ovum; EP, ectopic pregnancy; EA, elective abortion; END, early neonatal death; CP, chemical pregnancy documented by a hormonal test; NP, normal pregnancy; IVF, in-vitro fertilization; IUI, intrauterine insemination; CC, choriocarcinoma; IUFD, intra uterine fetal demise; RP, retained placenta; D&C, dilatation and curettage * maternal hypertension; # the reported malformations are hypoplastic left forearm, agenesis of the left hand, and micropenis.

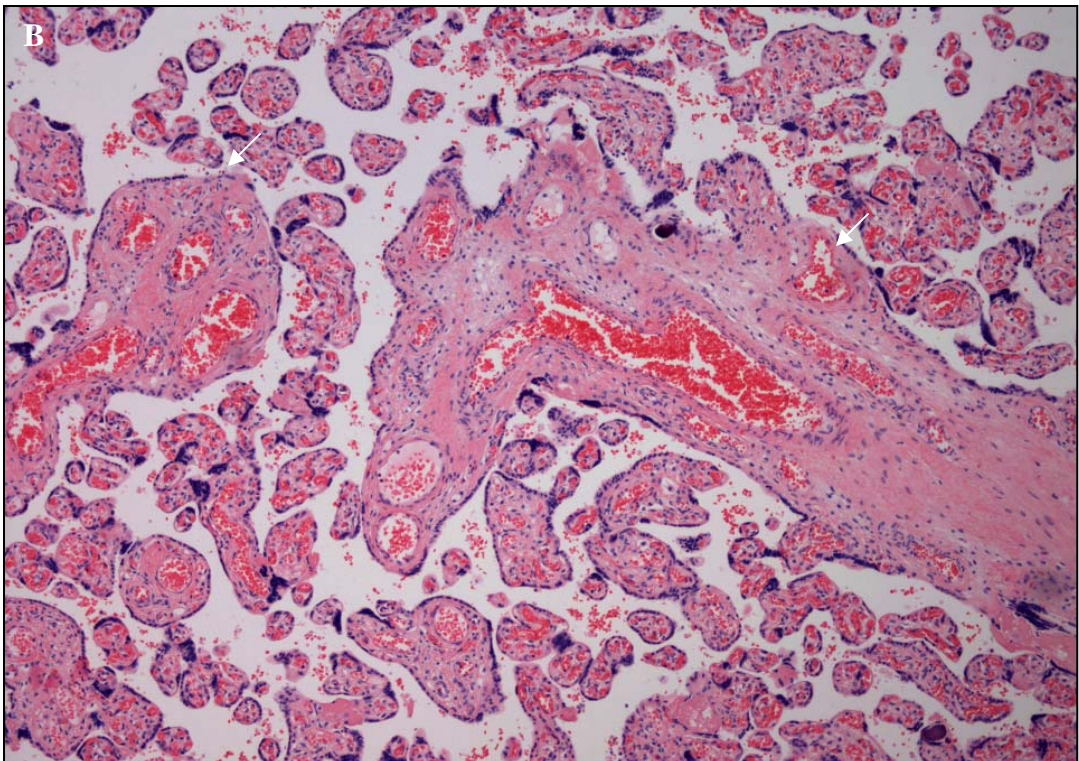
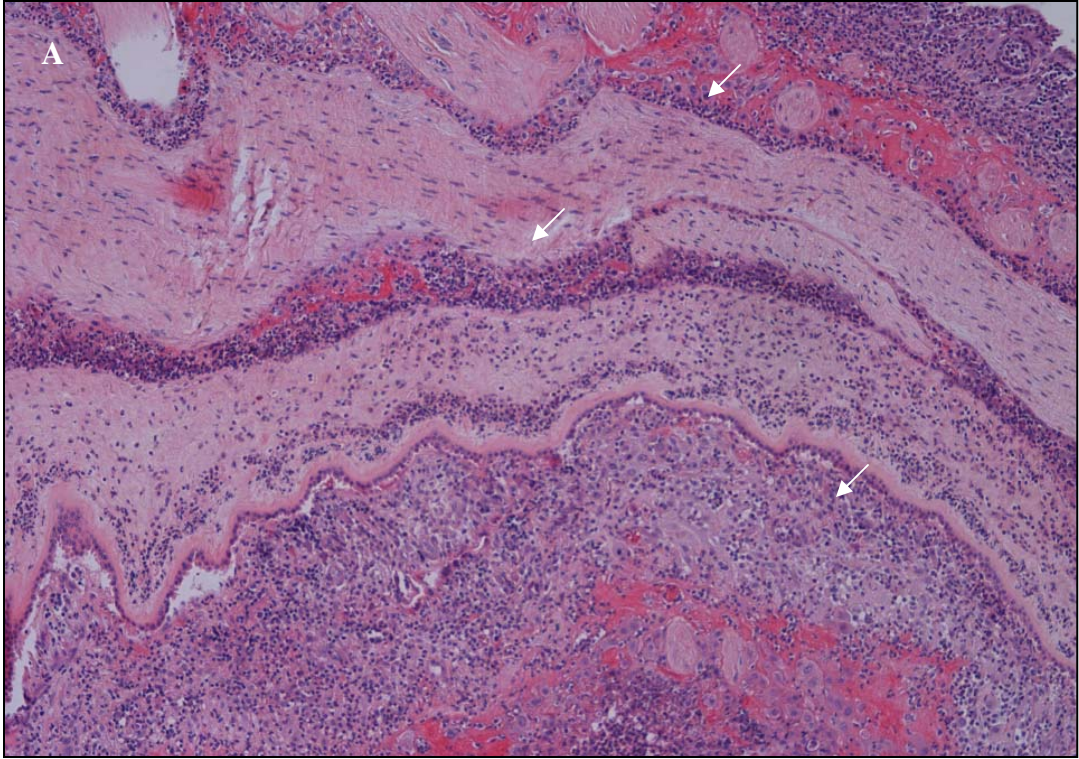
Supplementary table 5. Description provided by the gynecologists about 4 stillbirths from patients with *NLRP7* mutations

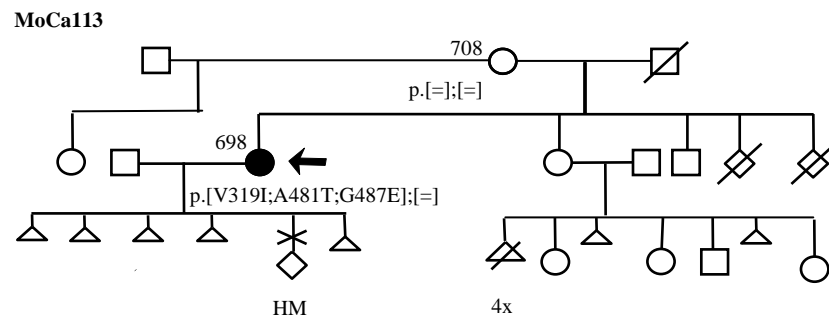
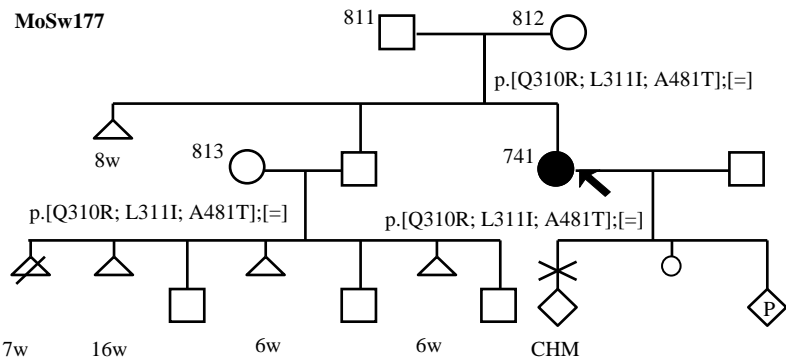
Family ID	Patient ID	Mutations	Description by the patient and available medical record
MoLb1	4	p.[G118X];[G118X]	According to the patient: GA 28 w, no preeclampsia, no bleeding.
		p.[G118X];[G118X]	According to the patient: GA full term pregnancy, home delivery of a baby 3.5 kb after uncomplicated pregnancy. The baby died one week later after suddening turning blue and being hypoxic for no apparent reason.
MoIn68	474	p.[R693P];[R693P]	According to the patient: GA full term pregnancy, vaginal delivery of a dead baby with no obvious mophological malformations. No preeclampsia during the pregnancy.
MoIn109	691	p.[N913S];[N913S]	According to the patient: GA 32 w.

GA indicates gestational age; w, indicates weeks

Supplementary table 6. Available medical information from 2 stillbirths from patients with *NLRP7* mutations

Family ID	Patient ID	Mutations	Description by the patient and available medical record
MoLb1	6	p.[G118X];[G118X]	Medical record: GA 26 w. Preterm labor and vaginal bleeding. The patient had <u>preeclampsia</u> with <u>severe placental abruption</u> . She then delivered a live male of 450 g (small for 26 w) who died later. Histopathology of the placenta revealed normal decidua and villi with <u>areas of infarction and calcification</u> .
MoBa169	723	p.[G380R];[=]	Medical record: GA 29 w. Clinical manifestation: lower abdominal pain, <u>reduced foetal movement for 7 days</u> . Ultrasonography: Intra uterine fetal demise, <u>no amniotic fluid</u> was seen. There was a <u>posterior haematoma in the placenta</u> . Vaginal delivery of a morphologically normal dead fetus.





- Ectopic pregnancy
- △ Spontaneous abortion
- △/ Elective termination
- ◇* Hydatidiform mole, complete or partial

Supplementary figure 2