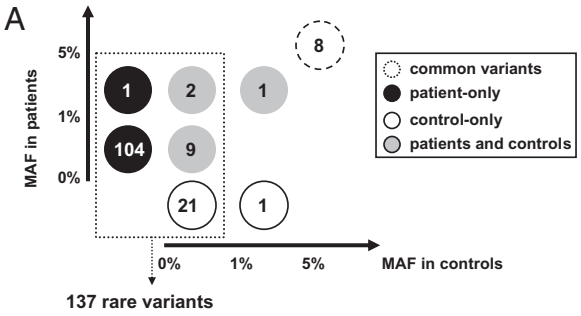
Supporting Information

Sykiotis et al. 10.1073/pnas.1009622107

A



B

Rare variants		*FGFR1*	*KAL1*	*PROKR2*	*GNRHR*	*FGF8*	*KISS1R*	*NELF*	*PROK2*
all	137	43	23	19	14	12	5	17	4
syn	38	9	4	5	2	6	1	10	1
non	10	3	6					1	
fra	6	1	4						1
spl	4	2					1	1	
mis	79	28	9	14	12	6	3	5	2
99 rare protein-altering variants									

C

Rare variants	IHH patients (n=397)	controls (n=179)
none	69% (n=274)	80% (n=145)
≥1 syn only	9% (n=35)	10% (n=17)
≥1 protein-altering (±syn)	22% (n=88)	10% (n=17)

Fig. S1. (*A*) Classification of identified sequence variants by minor allele frequency (MAF) in controls and patients. (*B*) Categorization of rare variants by gene and predicted effect on protein sequence. syn, synonymous; non, nonsense; fra, frameshift; spl, splice site; mis, missense. (*C*) Percentages of patients and controls with no rare variants, synonymous-only variants, or protein-altering variants.

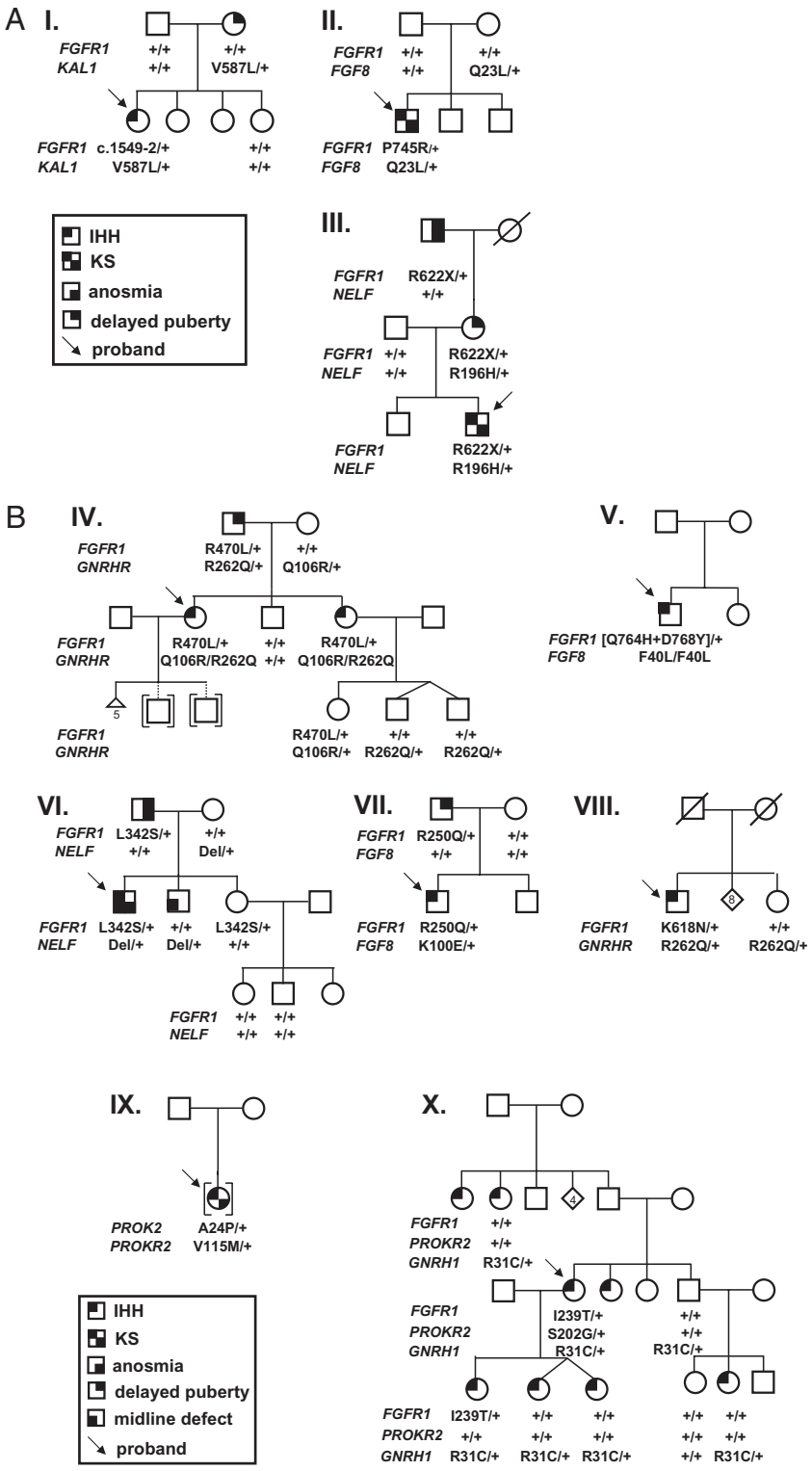


Fig. S2. (*A*) New pedigrees showing oligogenicity in isolated GnRH deficiency. (*B*) Pedigrees of probands with isolated GnRH deficiency included in the present study that were previously identified as oligogenic: IV (32), V (16), VI (32), VII (16), VIII (36), XI (33), and X (35). Del, c.1165-14_22del. +, wild-type allele.

Other Supporting Information Files

Table S1. Identified sequence variants (listed in order of decreasing MAF in unaffected control subjects)

Table S1 (XLS)

Table S2. Patients with rare protein-altering variants

Table S2 (XLS)

Table S3. Unaffected control subjects with rare protein-altering variants

Table S3 (XLS)