Table 1. Web list of syndromes with which spontaneous 46,XX primary ovarian insufficiency has been associated

Syndrome	Gene	OMIM Number	Prominent associated findings
Fragile X associated disorders[1, 2]	FMR1	*309550	Family history of intellectual disability due to fragile X syndrome or tremor ataxia disorder
Autoimmune polyendocrine syndrome, type 1[3]	AIRE	#240300	Adrenal insufficiency, hypoparathyroidism, chronic mucocutaneous candidiasis
Autoimmune polyendocrine syndrome, type 2[4]	Unknown	%269200	Adrenal insufficiency, type 1 diabetes mellitus, autoimmune thyroid disease
Congenital adrenal hyperplasia due to 17-alpha hydroxylase deficiency[5]	CYP17A1	#202110	Hypertension, hypokalemic alkalosis

Lipoid congenital adrenal hyperplasia[6, 7]	STAR	*600617	Congenital adrenal insufficiency, testis function is more severely affected than ovarian function
Aromatase deficiency[8-10]	CYP19A1	+107910	Maternal virilization during pregnancy due to absence of placental aromatase
Blepharophimosis, ptosis, epicanthus inversus syndrome[11, 12]	FOXL2	#110100	Dysmorphic eyelids
Progressive external ophthalmoplegia with mitochondrial DNA deletions[13]	POLG	#157640	Adult onset weakness of external eye muscles and exercise intolerance
Galactosemia[14]	GALT	#230400	Hepatomegaly, cataracts, and intellectual disability
Congenital disorder of glycosylation, type 1A[15, 16]	PMM2	#212065	Neonatal encephalopathy, hypotonia, psychomotor

			retardation, cerebellar hypoplasia, retinitis pigmentosa
Fanconi anemia[17]	FANCA, FACA, FA1, FA, FAA	#227650	Anemia, leucopenia, thrombocytopenia; cardiac, renal and limb malformations; dermal pigment changes
Ataxia telangiectasia[18-20]	ATM	#208900	Cerebellar ataxia, telangiectases, immune defects, a predisposition to malignancy, premature aging, genome instability
Bloom syndrome[21]	BLM	#210900	Premature aging, a predisposition to malignancy, genome instability
Werner syndrome[21]	WRN	#277700	Premature aging, a predisposition to

			malignancy, genome instability
Rapp-Hodgkin syndrome[22]	TP73L	#129400	Ectodermal dysplasia, cleft lip, cleft palate
Demirhan syndrome[23]	BMPR1B	#609441	Severe limb malformation, genital anomolies
Marinesco-Sjogren syndrome[24]	SIL1	#248800	Cerebellar ataxia, congenital cataracts, retarded somatic and mental maturation
Leukoencephalopathy with vanishing white matter[25, 26]	EIF2B2, EIF2B4, EIF2B5	#603896	Encephalopathy with leukodystrophy
Mental retardation, X linked[27]	FRAXE	+309548	Intellectual disability
Perrault syndrome[28]	Unknown	%233400	Deafness
Malouf syndrome[29, 30]	Unknown	212112	Cardiomyopathy
Woodhouse-Sakati syndrome[31, 32]	Unknown	%241080	Alopecia, diabetes mellitus, intellectual disability, extrapyramidal

			syndrome
Bassoe syndrome[33, 34]	Unknown	254000	Muscular dystrophy and infantile cataract
Cerebellar ataxia with hypergonadotropic hypogonadism[35]	Unknown	605672	Ataxia, sensorineural deafness with vestibular hypofunction, peripheral sensory impairment
Fryns syndrome[36]	Unknown	249599	Intellectual disability, craniofacial dysmorphism

Web Table 1 Reference List

1. Hagerman RJ, Hagerman PJ. The fragile X premutation: into the phenotypic fold. Curr Opin Genet Dev 2002; 12(3):278-283.

2. Wittenberger MD, Hagerman RJ, Sherman SL et al. The FMR1 premutation and reproduction. Fertil Steril 2007; 87(3):456-465.

3. Mathis D, Benoist C. A decade of AIRE. Nat Rev Immunol 2007; 7(8):645-650.

4. Betterle C, Dal PC, Mantero F, Zanchetta R. Autoimmune adrenal insufficiency and autoimmune polyendocrine syndromes: autoantibodies, autoantigens, and their applicability in diagnosis and disease prediction. Endocr Rev 2002; 23(3):327-364.

5. New MI. Inborn errors of adrenal steroidogenesis. Mol Cell Endocrinol 2003; 211(1-2):75-83.

6. Bose HS, Sugawara T, Strauss JF, III, Miller WL. The pathophysiology and genetics of congenital lipoid adrenal hyperplasia. International Congenital

Lipoid Adrenal Hyperplasia Consortium. N Engl J Med 1996; 335(25):1870-1878.

7. Nakae J, Tajima T, Sugawara T et al. Analysis of the steroidogenic acute regulatory protein (StAR) gene in Japanese patients with congenital lipoid adrenal hyperplasia. Hum Mol Genet 1997; 6(4):571-576.

8. Conte FA, Grumbach MM, Ito Y, Fisher CR, Simpson ER. A syndrome of female pseudohermaphrodism, hypergonadotropic hypogonadism, and multicystic ovaries associated with missense mutations in the gene encoding aromatase (P450arom). J Clin Endocrinol Metab 1994; 78(6):1287-1292.

9. Ito Y, Fisher CR, Conte FA, Grumbach MM, Simpson ER. Molecular basis of aromatase deficiency in an adult female with sexual infantilism and polycystic ovaries. Proc Natl Acad Sci U S A 1993; 90(24):11673-11677.

10. Bulun SE. Clinical review 78: Aromatase deficiency in women and men: would you have predicted the phenotypes? J Clin Endocrinol Metab 1996; 81(3):867-871.

11. Crisponi L, Deiana M, Loi A et al. The putative forkhead transcription factor FOXL2 is mutated in blepharophimosis/ptosis/epicanthus inversus syndrome. Nat Genet 2001; 27(2):159-166.

12. Uda M, Ottolenghi C, Crisponi L et al. Foxl2 disruption causes mouse ovarian failure by pervasive blockage of follicle development. Hum Mol Genet 2004; 13(11):1171-1181.

13. Pagnamenta AT, Taanman JW, Wilson CJ et al. Dominant inheritance of premature ovarian failure associated with mutant mitochondrial DNA polymerase gamma. Hum Reprod 2006; 21(10):2467-2473.

14. Guerrero NV, Singh RH, Manatunga A, Berry GT, Steiner RD, Elsas LJ. Risk factors for premature ovarian failure in females with galactosemia. J Pediatr 2000; 137(6):833-841.

15. Matthijs G, Schollen E, Pardon E et al. Mutations in PMM2, a phosphomannomutase gene on chromosome 16p13, in carbohydrate-deficient glycoprotein type I syndrome (Jaeken syndrome). Nat Genet 1997; 16(1):88-92.

16. Coman D, McGill J, MacDonald R et al. Congenital disorder of glycosylation type 1a: three siblings with a mild neurological phenotype. J Clin Neurosci 2007; 14(7):668-672.

17. Giri N, Batista DL, Alter BP, Stratakis CA. Endocrine abnormalities in patients with Fanconi anemia. J Clin Endocrinol Metab 2007; 92(7):2624-2631.

18. Healy DL, Bacher J, Hodgen GD. Thymic regulation of primate fetal ovarian-adrenal differentiation. Biol Reprod 1985; 32:1127-1133.

19. Paller AS. Ataxia-telangiectasia. Neurol Clin 1987; 5:447-449.

20. Barlow C, Liyanage M, Moens PB et al. Atm deficiency results in severe meiotic disruption as early as leptonema of prophase I. Development 1998; 125(20):4007-4017.

21. Du X, Shen J, Kugan N et al. Telomere shortening exposes functions for the mouse Werner and Bloom syndrome genes. Mol Cell Biol 2004; 24(19):8437-8446.

22. Holder-Espinasse M, Martin-Coignard D, Escande F, Manouvrier-Hanu S. A new mutation in TP63 is associated with age-related pathology. Eur J Hum Genet 2007; 15(11):1115-1120.

23. Demirhan O, Turkmen S, Schwabe GC et al. A homozygous BMPR1B mutation causes a new subtype of acromesomelic chondrodysplasia with genital anomalies. J Med Genet 2005; 42(4):314-317.

24. Anttonen AK, Mahjneh I, Hamalainen RH et al. The gene disrupted in Marinesco-Sjogren syndrome encodes SIL1, an HSPA5 cochaperone. Nat Genet 2005; 37(12):1309-1311.

25. Schiffmann R, Tedeschi G, Kinkel RP et al. Leukodystrophy in patients with ovarian dysgenesis. Ann Neurol 1997; 41(5):654-661.

26. Fogli A, Rodriguez D, Eymard-Pierre E et al. Ovarian failure related to eukaryotic initiation factor 2B mutations. Am J Hum Genet 2003; 72(6):1544-1550.

27. Murray A, Webb J, Dennis N, Conway G, Morton N. Microdeletions in FMR2 may be a significant cause of premature ovarian failure. J Med Genet 1999; 36(10):767-770.

28. Marlin S, Lacombe D, Jonard L et al. Perrault syndrome: report of four new cases, review and exclusion of candidate genes. Am J Med Genet A 2008; 146A(5):661-664.

29. Malouf J, Alam S, Kanj H, Mufarrij A, Der K, V. Hypergonadotropic hypogonadism with congestive cardiomyopathy: an autosomal-recessive disorder? Am J Med Genet 1985; 20(3):483-489.

30. Narahara K, Kamada M, Takahashi Y et al. Case of ovarian dysgenesis and dilated cardiomyopathy supports existence of Malouf syndrome. Am J Med Genet 1992; 44(3):369-373.

31. Woodhouse NJ, Sakati NA. A syndrome of hypogonadism, alopecia, diabetes mellitus, mental retardation, deafness, and ECG abnormalities. J Med Genet 1983; 20(3):216-219.

32. Al-Semari A, Bohlega S. Autosomal-recessive syndrome with alopecia, hypogonadism, progressive extra-pyramidal disorder, white matter disease, sensory neural deafness, diabetes mellitus, and low IGF1. Am J Med Genet A 2007; 143(2):149-160.

33. Bassoe HH. Familial congenital muscular dystrophy with gonadal dysgenesis. J Clin Endocrinol Metab 1956; 16:1614-1621.

34. Skre H, Bassoe HH, Berg K, Frovig AG. Cerebellar ataxia and hypergonadotropic hypogonadism in two kindreds. Chance concurrence, pleiotropism or linkage? Clin Genet 1976; 9(2):234-244.

35. Amor DJ, Delatycki MB, Gardner RJ, Storey E. New variant of familial cerebellar ataxia with hypergonadotropic hypogonadism and sensorineural deafness. Am J Med Genet 2001; 99(1):29-33.

36. Fryns JP, Vogels A, van den BH. Mental retardation, craniofacial dysmorphism, hypogonadism, diabetes mellitus and epilepsy in four siblings. A "new" mental retardation syndrome. Clin Genet 1990; 37(2):111-116.