



Supplementary Figure 2. Phenotypes of the *Alms1* S701X mouse model.

- A. Weight of male mice recorded from 3 to 24 weeks after birth ($n=5$, $*p < 0.05$ at 14-16 weeks, $**p < 0.01$ at 17-24 weeks). B. Comparison of the results of glucose tolerance experiments in male homozygous (HO, $n=3$) and wild-type (WT, $n=4$) mice ($*p < 0.05$ in intraperitoneal injection of glucose for 120 min; $**p < 0.01$ in intraperitoneal injection of glucose for 0 min, i.e. fasting state). C. Representative micrographs of H&E-stained fat and liver sections of 24-week-old male mice. Scale Bar = 100 μm .

FSH Reference Ranges:				
From 2006 – 2016 Method: DPC Immulite 2000 Reference range source: Adult range from Regional Endocrinology lab Queen Elizabeth Hospital Birmingham. Paediatric data – extracted from Immulite and Immulite 2000 Reference Range (18).	Age		Range (IU/L)	
			Male	Female
	Children	0 – 15d	<1	<1
		15d – 6y	0.2 – 3.0	0.2 – 3.0
		7y – 10y	0.2 – 4.0	0.2 – 6.0
		10y – 14y	0.5 – 7.0	-
		15y – 60y	1.0 – 11.0	-
	Adult female	follicular	0.6 – 11	
		mid-cycle	2 – 24	
		luteal	0.6 - 9	
Post menopausal		39 - 112		
Adult males	<60 years	2 - 11		
From 2017 to date: change from existing FSH Immulite 2000 reference ranges with introduction of the Roche assay Method: Roche Cobas Paediatric ranges from Immulite 2000 Compendium (1 st Ed) (central 90%) (18)	Biological Reference interval/ Clinical decision values			
	Age		Range (IU/L)	
			Male	Female
	Children	0 – 15d	<1	<1
		15d – 6y	0.2 – 3.0	0.2 – 3.0
		7y – 10y	0.2 – 4.0	0.2 – 6.0
11y – 14y		0.5 – 7.0	-	

		15y – 60y	1.0 – 11.0	-
	Adult female	Follicular	0.6 – 11	
		Mid-cycle	2 – 24	
		Luteal	0.6 – 9	
		Post menopausal	39 - 112	
	Adult male	<60 years	2 - 11	

FSH Interassay variation

From 2009 – 2016 for Immulite 2000

Precision

Level	6.03 IU/L	14.1 IU/L	35.8 IU/L
Within-batch SD	0.15	0.33	1.2
Within-batch CV	5.89%	4.49%	5.93%
Between-batch SD	0.36	0.64	2.12
Between-batch CV	5.89%	4.49%	5.93%

From 2017 to date for Roche Cobas *

Sample	Mean (U/L)	Measurement of uncertainty range (U/L)
Premium 1	6.69	6.31 – 7.07
Premium 2	22.87	21.57 – 24.17

Premium 3	45.3	42.4 – 48.2
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LH Reference Ranges:

From 2007 – 2016** Method: DPC Immulite 2000 Reference range source: Adult ranges from Regional Endocrinology lab Queen Elizabeth Hospital Birmingham. Paediatric data – extracted from Immulite and Immulite 2000 Reference Range. Compendium (1 st English Ed) (central 90%) (18)	Age		Range (IU/L)	
			Male	Female
	Children	0 – 15d	<1	<1
		15d – 10y	0.7 – 2.2	0.7 – 2.2
		10y – 12y	0.3 – 5.0	-
		13y – 60y	0.5 – 8.0	-
	Adult female	follicular	1 – 11	
		mid-cycle	15 – 96	
luteal		1 - 11		
Post menopausal		15 - 61		

From 2017 to date *** Method: Roche Cobas Reference range source: Mathematical transformation of data originally from Immulite 2000 compendium following comparison between Immulite 2000 and Roche Cobas. Paediatric ranges from Immulite 2000 Compendium (1 st Ed) (central 90%) (18)	Biological Reference interval/ Clinical decision values		
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	Age	Range (IU/L)	
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				Male	Female
	Children	0 – 15d		<1.3	<1.3
		15d – 10y		<2.6	<2.6
		10y – 12y		0.5 – 5.7	-
		13y – 60y		0.7 – 9.1	-
	Adult female	Follicular		1.3 – 12.4	
		Mid-cycle		16.8 – 106.7	
		Luteal		1.3 – 12.4	
		Post menopausal		16.8 – 67.9	
LH Interassay variation					
From 2009 - 2016 for Immulite 2000					
Precision					
Level	10.0 IU/L	21.7 IU/L	47.1 IU/L		
Within-batch SD	0.29	0.55	1.01		
Within-batch CV	3.0%	2.59%	2.3%		
Between-batch SD	0.51	0.74	1.41		
Between-batch CV	5.1%	3.4%	2.98%		
From 2017 to date for Roche Cobas *					

Sample	Mean (mU/L)	Measurement of uncertainty range (mU/L)
Premium 1 QC	4.77	4.58 – 4.96
Premium 2 QC	39.33	38.14 – 40.52
Premium 3 QC	63.44	61 – 65

Testosterone Reference Ranges:

From 2006 – 2007

Samples for prepubertal children and adult females analysed in Clinical Chemistry, Edinburgh Royal Infirmary, United Kingdom,
 Adult male samples analysed in Clinical Chemistry University Hospitals Birmingham.
 Adult male reference range performed on Roche E170 analyser

Pre-pubertal/pubertal/post-pubertal – Edinburgh’s own data developed on the Immuno and adjusted for the Centaur based on regression.

Age	Range (nmol/l)		
	Male	Female	
Children	1 – 6d	2 – 7	<2
	1 – 9 weeks	3.0 - 24	-
	9 – 12 weeks	2 - 8	-
	12 – 16 weeks	<2	-
Females	Pre pubertal >6 d	<1	
	Late puberty/adult	0.4 – 2.8	
Males	Pre-pubertal >16 weeks	<1	
	Pubertal stage G2	<8	

		Pubertal stage G3	1 - 18
		Pubertal stage G4/G5	4.5 - 25
		Adult males	10 - 30
From 2008 to date:			
Method: LC - Tandem Mass Spectrometry at University Hospital Birmingham			
Age range	Male	Female	
1 - <10y	<0.7 (Tanner stage 1)	<0.6 (Tanner stage 1)	
10 – 18y	both Tanner stage 1 and adult range reported (without ‘falls with age’ comment)	both Tanner stage 1 and adult range reported (without ‘falls with age’ comment)	
>18y	7.0 – 27.0 (falls with age)	<1.9 (falls with age)	

Supplementary table 1 showing references ranges for FSH, LH, testosterone and the methodology adopted with inter-assay variation used over a period of study duration between 2006 and 2023 for UK paediatric cohort; *measurement uncertainty is calculated using imprecision data from between batch analysis of quality control materials and expressed as mean and range representing +/-2 standard deviations (95% confidence level). This data is collected during routine operation, hence takes into account routine changes such as those of reagent, calibrator, operator and maintenance; **Additional comments for reports female >10y and <18y LH pre pubertal range 0.7 – 2.2, female >10y LH adult female follicular 1 – 11, mid cycle 15 – 96, luteal 1 – 11; * Female>10y and <18y LH pre pubertal range 0.7 – 2.2, Female >10y LH adult female follicular 1 – 11, mid-cycle 15 – 96, luteal 1 – 11.**

Patient	Right Testis (mL)	Left Testis (mL)
1	0.5304	0.5824
2	2.8392	Not visualized
3	1.0275	0.8044
4	2.1965	3.8631
5	2.9203	3.0420
6	1.3832	1.3385
7	2.3400	2.9250
8	1.4602	1.6744
9	0.6989	0.7779
10	2.1091	1.7160
11	Not visualized	Not visualized
12	Not visualized	Not visualized
13	Atrophic, hypoechoic	Atrophic, hypoechoic
14	Atrophic, hypoechoic	Atrophic, hypoechoic

Supplementary Table 2. Testicular volumes in patients with Alstrom syndrome with hypogonadism assessed by testicular ultrasound; values are presented in milliliters (mL); ‘not visualized’ indicates the testes couldn’t be seen on ultrasound; atrophic, hypoechoic’ refers to qualitative ultrasound findings with no measure of volume provided in ml.