

Supplementary Data

Figure S 1. TSAb specific for the human-TSHR and the mouse-TSHR in parental strains of BXH mice (C3H and B6). Sera were tested one month week after three immunizations (3x) with A sub-Ad.

A) Human-TSHR -TSAb; * $p=0.026$, (Rank Sum test).

B) Mouse -TSHR TSAb; ** $p=0.006$ (Rank sum test);

C) Ratio of mouse to human-TSHR TSAb

TSAb data (mean + SEM) are the responses expressed as a percentage for sera from mice immunized with control adenovirus (indicated by dashed lines in A to D). Number of mice studied: C3H and B6, $n=10$.

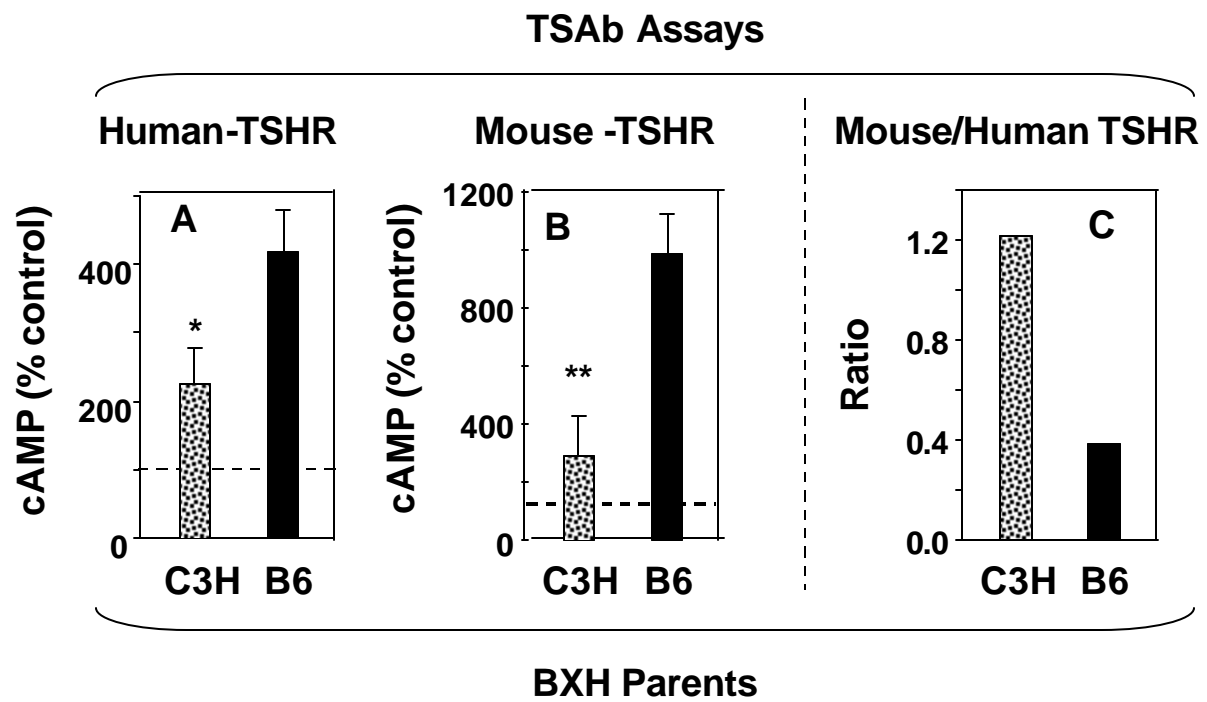


Figure S1

Supplementary Table S1. Chr linkage for TSAb in **CXB** and **BXH** mice immunized three times with TSHR A-subunit adenovirus. TSAb activity was measured with mouse (m)-TSHR cells and human (h)-TSHR cells; from these data, the TSAb ratio (human: mouse, h:m or mouse: human, m:h) was calculated. Loci and chromosomal locations (megabases, Mb) are presented for LRS scores suggestive of linkage. Possible candidate genes are included with the corresponding (or likely) human chromosome in parentheses. Genenetwork identifiers (GN) are included.

Strain	LRS	Chr	Locus	Mb	Candidate	Hu
human-TSAb						
BXH (3x)^a	19.884	9	rs13480317 rs6224819	85.581 96.718		(6) (3)
	18.642	12	rs13459138 rs3705923 rs3692361 rs3679276	113.270 117.869 118.161 120.329	Igh V region genes	14
CXB (3x)^b	14.323	17	gnf17.035.152 rs6395893 D17Mit66 rs3690039	34.663 38.786 47.186 48.900	MHC region genes	6
	14.323	X	rs13483834 rs13483877	72.576 83.201	Il1rapl1	X
mouse-TSAb						
BXH (3x)^c	14.388	9	gnf09.094.244 rs13480367	97.499 98.732		(3)
	14.388	13	rs13481870 rs13481871 rs3669221	71.470 71.761 84.210		(5)
CXB (3x)^d	13.832	10	rs13480631 D10Mit223	67.396 67.608		
TSAb Ratio						
BXH m:h (3x)^e	18.323	12	rs13459138 rs3705923 rs3692361 rs3679276	113.271 117.869 118.161 120.329	Igh V region genes	14
	16.343					14
CXB h:m (3x)	17.927	4	rs13477645 rs13477662	35.751 39.980		(9)

^a From McLachlan SM *et al. Endocrinol.* 2008;**149**: 2001-2009

^b below LRS 14.5 cut-off for association

^c excluding BXH9 (outlier)

^d; without SEM

^e similar observations for h:m TSAb (GN10160) but lower LRS values.

LRS = LOD X 4.6.












Candidates:MHC region: C2 (34.470663), Hspa1 (34.577246);Tnf (34.807461; Ltb (34.802573);
Il1rapl1, interleukin 1 receptor; Igh V region genes, immunoglobulin heavy chain variable region genes.

GN identifiers (after 3 immunizations):- Human TSAb: BXH GN10148; CXB GN10684; Mouse TSAb
BXH GN10156, CXB GN10688; TSAb Ratio: BXH m:h GN10158, CXB h:m GN 10689.

Supplementary Table S2. List of genes within the mouse Chr 12 locus linked to the preferential recognition by thyroid stimulating antibodies for the mouse- versus human-TSHR. Within this locus (113.595 - 118.161 Mb), 32 of 66 genes encode immunoglobulin H chain variable regions genes. The latter genes are highlighted in yellow to provide a visual impression; the amount of information on individual genes requires a type too small to be legible. Of the 34 non-highlighted genes, only 7 are identified (*Crip 1*, *Crip 2*, *Tmem 121*, *Adam6*, *Vipr*, *ptprn2* and *Rapgef5*).

	Marker/Gene	Mb start	Gene Length	SNP	SNP/Kb	Mb start	
897	Crip2	113.588354	4.958	1	0.201694	105.0122	cysteine rich protein 2
898	9230109C02Rik	113.598197	0.969	5	5.159959		RIKEN cDNA 9230109C02 gene
899	Crip1	113.599819	1.868	5	2.67666	105.0237	cysteine-rich protein 1 (i...
900	4930427A07Rik	113.604228	9.038	69	7.634432		RIKEN cDNA 4930427A07 gene
901	Tmem121	113.63371	3.62	4	1.104972		transmembrane protein 121
902	Igh-2	113.702706	1596.779	2047	1.281956		immunoglobulin heavy chain...
903	LOC677563	113.706524	1388.292	1724	1.241814		similar to Ig heavy chain ...
904	Igh-VJ558	113.707998	4.927	0	0		immunoglobulin heavy chain...
905	Gm900	113.719922	0.32	0	0		gene model 900, (NCBI)
906	Igh-VX24	113.720994	315.352	370	1.173292		immunoglobulin heavy chain...
907	Igh-1a	113.73546	0.05	0	0		immunoglobulin heavy chain...
908	Ighg	113.754412	0.05	0	0		Immunoglobulin heavy chain...
909	Igh-V3609N	113.777676	1028.171	1120	1.089313		immunoglobulin heavy chain...
910	AI324046	113.807417	0.05	1	20		expressed sequence AI32404...
911	Ighv14-2	113.854416	23.855	4	0.16768		immunoglobulin heavy varia...
912	LOC630279	113.876323	431.092	408	0.946434		similar to Ig heavy chain ...
913	EG633457	113.876323	0.053	0	0		predicted gene, EG633457
914	Ighv5-9	113.876892	233.209	75	0.3216		immunoglobulin heavy varia...
915	Igh-V3660	113.876894	605.008	494	0.816518		immunoglobulin heavy chain...
916	LOC380804	113.877277	196.308	66	0.336206		Ig heavy chain V region
917	Ighv7-3	113.877277	724.175	689	0.951427		immunoglobulin heavy varia...
918	4930523C11Rik	113.937318	2.162	3	1.387604		RIKEN cDNA 4930523C11 gene
919	Adam6	113.991715	2.507	0	0		a disintegrin and metallo...
920	Igh-V7183	114.183919	0.281	2	7.117438		immunoglobulin heavy chain...
921	Igh-V10	114.18419	0.157	2	12.73885		immunoglobulin heavy chain...
922	LOC382653	114.274454	0.295	1	3.389831		immunoglobulin heavy chain...
923	Igh-V11	114.496047	0.465	6	12.90323		immunoglobulin heavy chain...
924	Ighv14-3	114.507652	0.294	1	3.401361		immunoglobulin heavy varia...
925	LOC544905	114.588499	0.294	4	13.60544		Ig heavy chain V region
926	Igh-VS107	114.600988	0.303	2	6.60066		immunoglobulin heavy chain...

927	Ighv7-4	114.670605	0.53	2	3.773585		immunoglobulin heavy varia...
928	LOC432699	114.735961	0.294	0	0		VH gene product
929	EG636260	114.747769	0.428	2	4.672897		predicted gene, EG636260
930	EG633674	114.770182	0.292	0	0		predicted gene, EG633674
931	Ighv6-6	114.839518	64.374	86	1.335943		immunoglobulin heavy varia...
932	EG380809	114.97125	0.445	3	6.741573		predicted gene, EG380809
933	Igh-V15	115.012385	0.311	0	0		immunoglobulin heavy chain...
934	EG629860	115.063657	0.469	1	2.132196		predicted gene, EG629860
935	Igh	115.094379	0.267	0	0		immunoglobulin heavy chain...
936	Ighv1-26	115.236181	0.292	0	0		immunoglobulin heavy varia...
937	Ighv1-47	115.438915	0.473	2	4.22833		immunoglobulin heavy varia...
938	LOC382693	115.567556	0.293	0	0		similar to immunoglobulin ...
939	AB069917	115.606209	0.295	1	3.389831		cDNA sequence AB069917
940	EG211331	115.641482	0.434	0	0		predicted gene, EG211331
941	V165-D-J-C mu	115.655906	0.29	1	3.448276		IgM variable region
942	Ighv1-61	115.806946	0.295	0	0		immunoglobulin heavy varia...
943	Ighv1-72	116.20579	0.434	1	2.304147		immunoglobulin heavy varia...
944	Igh-6	116.205791	0.294	0	0		immunoglobulin heavy chain...
945	Ighv1-77	116.309674	0.434	0	0		immunoglobulin heavy varia...
946	EG434609	116.428509	0.433	0	0		predicted gene, EG434609
947	Zfp386	116.495531	12.869	5	0.388531		zinc finger protein 386 (K...
948	Vipr2	116.519808	67.576	203	3.004025	158.3203	vasoactive intestinal pept...
949	Wdr60	116.649065	55.969	192	3.43047	158.1487	WD repeat domain 60
950	LOC100042963	116.722406	0.591	0	0		hypothetical protein LOC10...
951	D12Ertd551e	116.72323	91.875	272	2.960544		DNA segment, Chr 12, ERATO...
952	2310058N22Rik	116.82261	0.05	0	0		RIKEN cDNA 2310058N22 gene
953	D430020J02Rik	116.843955	3.189	0	0		RIKEN cDNA D430020J02 gene
954	Ncapg2	116.84741	58.129	215	3.69867		non-SMC condensin II compl...
955	Ptprn2	116.927841	790.961	873	1.103721	156.8312	protein tyrosine phosphata...
956	5730406E14Rik	117.473439	1.557	0	0		RIKEN cDNA 5730406E14 gene
957	ENSMUSG00000072	117.586538	6.686	1	0.149566		predicted gene, ENSMUSG000...
958	LOC432713	117.724601	54.43	50	0.918611		hypothetical gene supporte...
959	Rapgef5	117.958487	240.167	148	0.616238	21.93116	Rap guanine nucleotide exc...
960	2900082C11Rik	117.973837	0.465	0	0		RIKEN cDNA 2900082C11 gene

961	 A930023M06Rik	118.044047	1.723	0	0		RIKEN cDNA A930023M06 gene
962	 D830016K09Rik	118.072022	3.767	0	0		RIKEN cDNA D830016K09 gene
963	 Cdca7l	118.285869	36.942	16	0.433111		cell division cycle associ...
964	 Dnahc11	118.322087	321.058	341	1.062113		dynein, axonemal, heavy ch...
965	 Sp4	118.679034	66.437	0	0	21.24093	trans-acting transcription...
966	 Sp8	119.291657	5.021	0	0	20.59514	trans-acting transcription...
967	 Abcb5	119.380328	30.195	1	0.033118	20.46028	ATP-binding cassette, sub-...
968	 Itgb8	119.606904	75.474	57	0.755227	20.14399	integrin beta 8
969	 8030462D06Rik	119.609983	0.873	0	0		RIKEN cDNA 8030462D06 gene
970	 4732474O15Rik	119.910833	0.05	0	0		RIKEN cDNA 4732474O15 gene
971	 Tmem196	120.389923	1.607	0	0		transmembrane