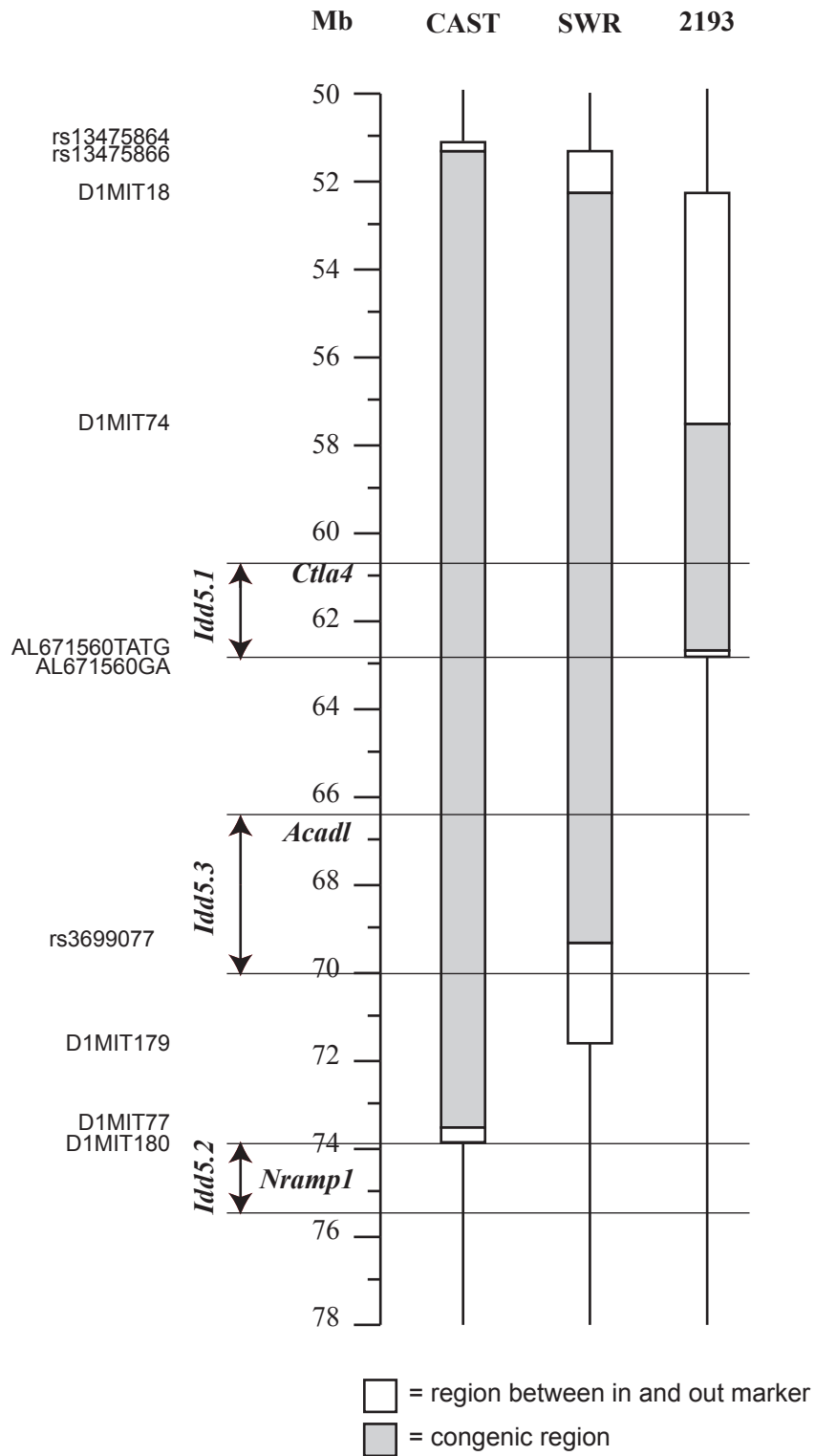


Type of file: table

Label: Supp Info

Filename: Supplemental materal.pdf



**Supplementary Figure 1: Genetic map of the NOD *Idd5.1* congenic strains used in this study.** The grey shaded areas represent CAST, SWR or B10-derived DNA introgressed onto the NOD background. Open boxes represent the region between the in and out markers. Mouse Ensembl build 54 was used to map the markers used in this study.

a.

```
SWR      GCTGTTGACACGGGACTGTA
NOD      GCTGTTGACACGGGACTGTA
B6       GCTGTTGACACGGGACTGTA
CAST     GCTGTTGACACGGGACTGTA
Human    GCCATGGACACGGGACTCTA
**      ***** **
```

b.

```
SWR      CAACGGGACGCAGATTTA
NOD      CAACGGGACGCAGATTTA
B6       CAACGGGACGCAGATTTA
CAST     CAACGGGACGCAGATTTA
Human    CAACGGAACCCAGATTTA
*** ** ** *****
```

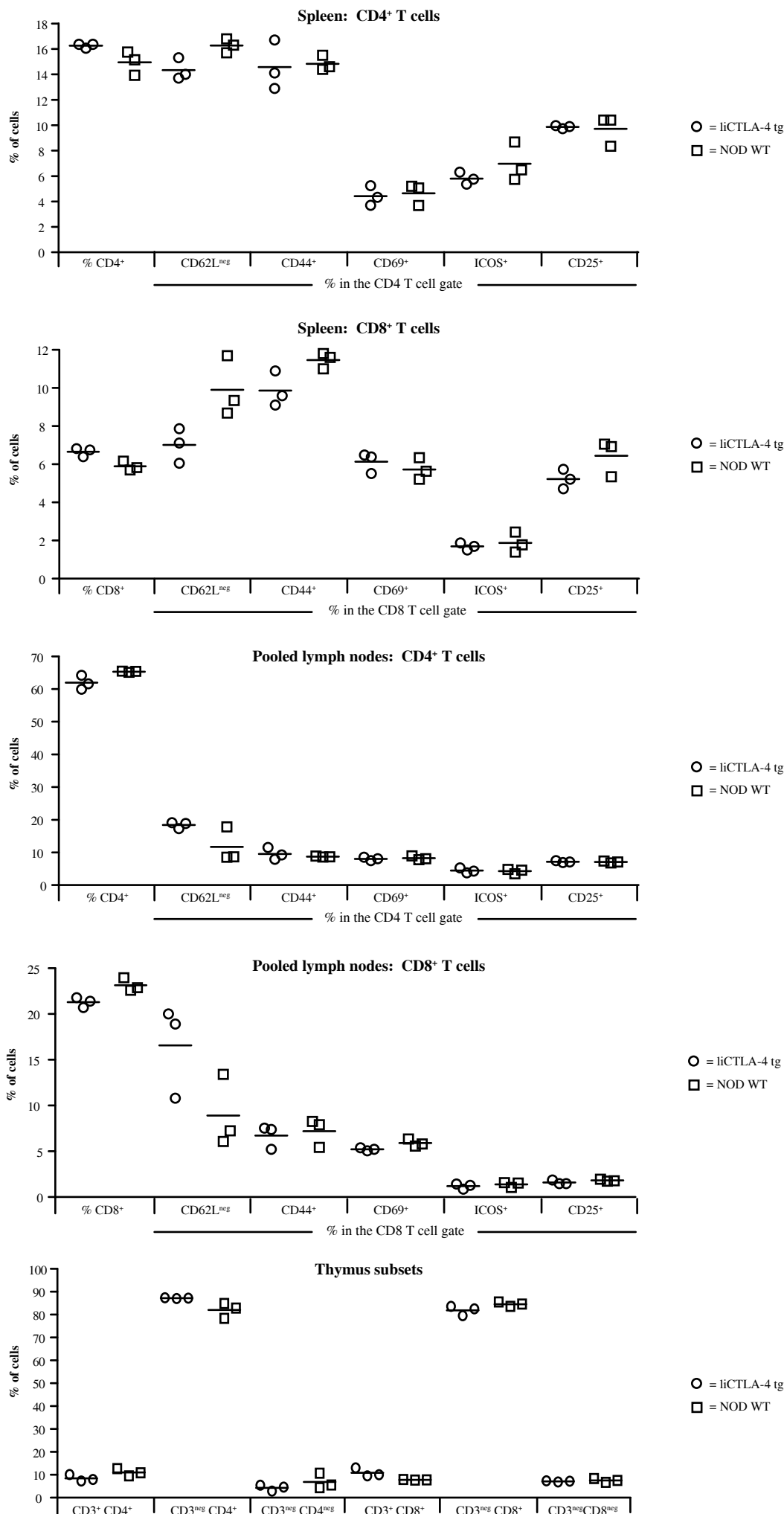
**Supplementary Figure 2: CAST-specific SNPs at (a) 263 and (b) 332 bp in exon 2 of *Ctla4* alter exon splicing enhancer motifs in regions that are conserved in exon 2 of human *CTLA4*.**

Exon 2 sequences from human *CTLA4*, as well as from SWR, NOD, B6 and CAST mouse *Ctla4* were aligned using Clustal ([www.ebi.ac.uk/clustalw](http://www.ebi.ac.uk/clustalw)). An asterisk indicates bases that are conserved in all five sequences. SNPs at (a) 263 and (b) 332 bp are shown in bold.

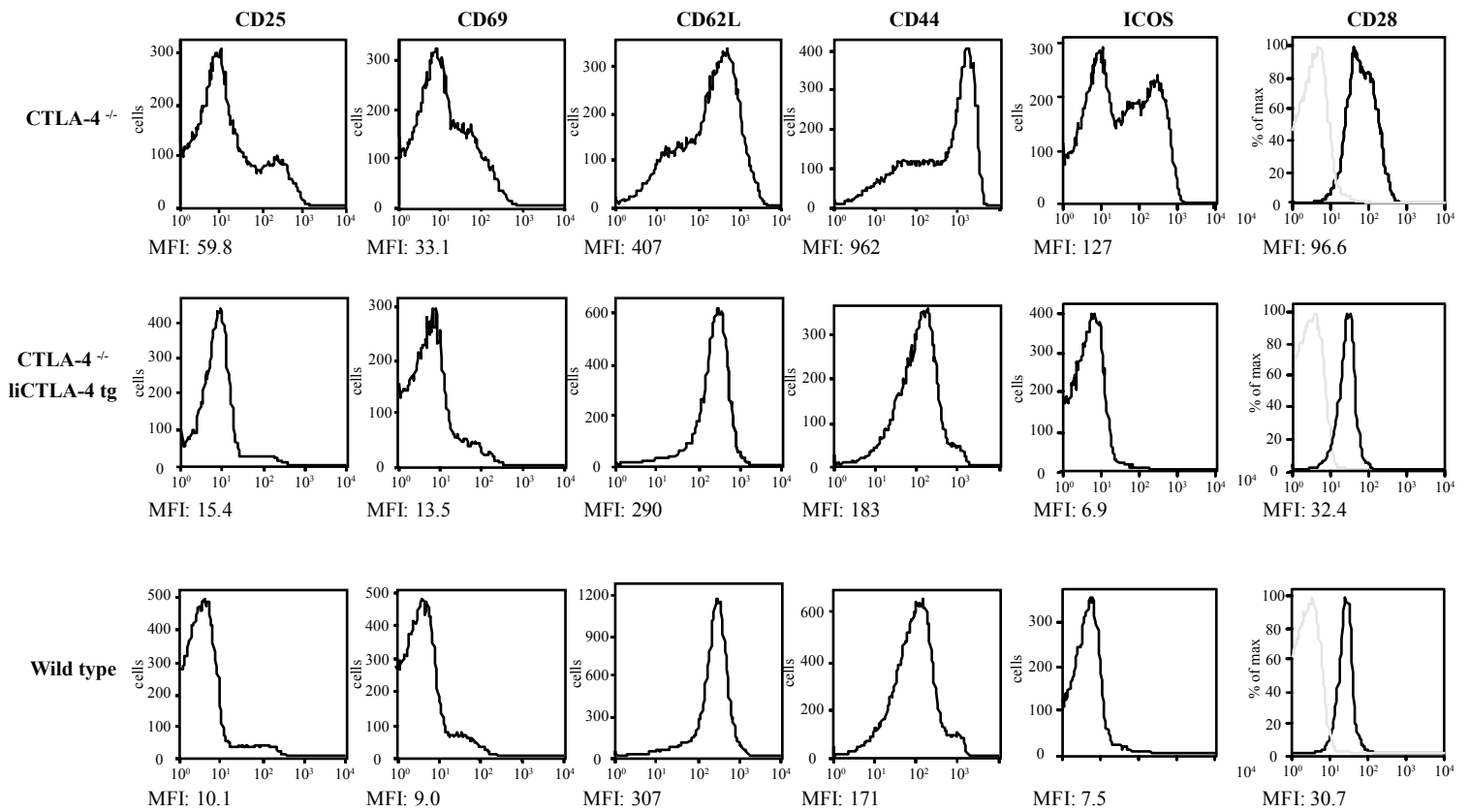
Exon splicing enhancer (ESE) motifs were predicted using ESEfinder (1,2), and the strength of the predictions are depicted. ESE motifs with a prediction score of 1 to 2 above threshold are noted in purple, those with a score greater than 2 but less than 3 are green, and those with a score greater than 3 are red.

1. Smith, P. J., Zhang, C., Wang, J. Chew, S. L., Zhang, M. Q. and Krainer, A. R. 2006. An increased specificity score matrix for the prediction of SF2/ASF-specific exonic splicing enhancers. *Hum. Mol. Genet.* 15: 2490-2508.

2. Cartegni L., Wang J., Zhu Z., Zhang M. Q. and Krainer A. R.; 2003. ESEfinder: a web resource to identify exonic splicing enhancers. *Nucleic Acid Research* 31: 3568-3571.



**Supplemental Figure 3:** NOD and liCTLA-4 tg NOD mice (females, 3 weeks of age) were compared for the percentages of CD4 and CD8 T cells in cells prepared from thymus, pooled lymph nodes and spleen. The percentages of the indicated activation markers were determined in spleen and lymph node cells for CD4 and CD8 T cells. None of the parameters were significant ( $P > 0.05$ ) as assessed using the Mann-Whitney test. This experiment is representative of 4 experiments performed in total (total of 10 mice evaluated from each strain).



**Supplemental Figure 4:** Representative FACS profiles of the activation markers CD25, CD69, CD62L, CD44, ICOS and CD28 on CD4<sup>+</sup> T cells from CTLA-4<sup>-/-</sup>, CTLA-4<sup>-/-</sup> liCTLA-4 tg and wild type mice as described in Figure 5 are shown above. The MFI for each activation marker was calculated from T cells within the CD4<sup>+</sup> gate.

**Supplementary Table I:** Primer sequences used to detect NOD/B6 SNPs in multiple mouse strains.

Marker Number	Marker Name	RFLP or +/-	Position (Mb)	Gene	Forward primer	Reverse Primer
1	L1 repetitive element	+	60.827	Intragenic	ctgaaagttggagatgctttt	ctgctgctgtgcttaggtc
		-	60.827	Intragenic	ctgaaagttggagatgctttt	ataggaaggaacccgcaaga
2	retroviral sequence element	+	60.834	Intragenic	gcacatttaggcagcatcag	taaggatctccaagcctcca
		-	60.834	Intragenic	gcacatttaggcagcatcag	aggcaagcaagctcaaaaag
3	Prox_Ctla4_SNP1	Hae III	60.844	Intragenic	ggaaagctgctaatacaatca	ctccacagtctgaccaca
4	Prox_Ctla4_SNP4	Msp I	60.849	Intragenic	caagtactatggggaagtactgta	tggagccatataccacctg
5	CTLA4_Intron1_SNP	Mae III	60.855	Ctla4	tggaccctgagcatctctct	caggtgtctgctagccttc
6	CTLA4_Exon2_SNP	Mae III	60.857	Ctla4	gcctcaggtgtggcctaata	ggactccaaccaaggaaca
7	CTLA4_3utr_SNP1	Aci I	60.86	Intragenic	gccatgtaccagccgttate	ctctacgtctgtaaaatgcca
8	L1 repetitive element	+	60.865	Intragenic	gcctcaggtgggaaaaaca	ggatatggggacttttgggt
		-	60.865	Intragenic	gcctcaggtgggaaaaaca	aaaccaattgttgctttgc
9	Distal_Ctla4_Snp1	Bcl I	60.871	Intragenic	acgataagcatgccaaaac	aacctatgccacactcttc
10	Proximal_Icos_SNP1	Hinc II	60.888	Intragenic	gtgcggctgaaagtctgttt	ccttgatgactccaacgatca
11	Proximal_Icos_SNP4	BsaJI	60.903	Intragenic	tcttgtagaggtgtctcaa	catcgtaggggatgtctatgaa
12	Icos_Exon1_SNP	Nla III	60.922	Icos	caacctccacaaccactt	gaactcaataagagctatggatgg
13	Icos_Intron1_SNP	Mlu I	60.937	Icos	tcattgctgtggttcaggtt	gagaaatgggctttcatctgtg
14	Icos_Intron4_SNP	Sca I	60.941	Icos	ggctgggaaggagatttag	gctctgtttctttcctgtcc
15	Distal_Icos_SNP1	Taq I	60.946	Intragenic	gccaaccatgaggactct	tgggtttgccatctctacc
16	Distal_Icos_SNP3	Hae III	60.952	Intragenic	gacatcaatagttacaacagtcca	ttgctagatcatagggtaaaagga
17	Distal_Icos_SNP4	Hpy188 III	60.954	Intragenic	tgtacggcatattgaacagca	cccaatgaagtgaactgt