

AMENDMENTS TO THE SPECIFICATION

Please replace the title on p. 1 of the specification with the following amended title:

HUMAN DNAX TOLL-LIKE RECEPTOR 4 PROTEINS,[[;]] RELATED REAGENTS AND METHODS

- Please replace the paragraph from p. 4, line 21 to p. 5, line 10 of the specification with the following amended paragraph:

Figures 2A-2C show conserved structural patterns in the signaling domains of Toll- and IL-1-like cytokine receptors, and two divergent modular proteins.

Figures 2A-2B show a sequence alignment of the common TH domain. TLRs are labeled as in Figure 1; the human (Hu) or mouse (Mo) IL-1 family receptors (IL-1R1-6) are sequentially numbered as earlier proposed (Hardiman, et al., Oncogene 13, 2467 (1996)); Myd88 and the sequences from tobacco (To) and flax, *L. usitatissimum* (Lu), represent C- and N-terminal domains, respectively, of larger, multidomain molecules. The amino acid sequences spanning Figures 2A-2B are as follows (from left to right):

HuIL-1R5: SEQ ID NOS: 76-84;

MoIL-1R3: SEQ ID NOS: 85-92;

MoIL-1R4: SEQ ID NOS: 93-97;

HuIL-1R6: SEQ ID NOS: 98-104;

HuIL-1R1: SEQ ID NOS: 105-111;

ChIL-1R1: SEQ ID NOS: 112-118;

HuMyD88: SEQ ID NOS: 119-126;

MoMyD88: SEQ ID NOS: 127-134;

HuTLR1: SEQ ID NOS: 135-143;

HuTLR2: SEQ ID NOS: 144-152;

HuTLR3: SEQ ID NOS: 153-160;

HuTLR4: SEQ ID NOS: 161-167;

HuTLR5: SEQ ID NOS: 168-175;

Dm18wh: SEQ ID NOS: 176-185;

DmMst: SEQ ID NOS: 186-194;

DmToll: SEQ ID NOS: 195-203;

ToDRgN: SEQ ID NOS: 204-212; and

LuL6: SEQ ID NOS: 213-221.

Ungapped blocks of sequence (numbered 1-10) are boxed. Triangles indicate deleterious mutations, while truncations N-terminal of the arrow eliminate bioactivity in human IL-1R1 (Heguy, et al., J. Biol. Chem. 267, 2605 (1992)). PHD (Rost and Sander, Proteins 19, 55 (1994)) and DSC (King and Sternberg, Protein Sci. 5, 2298 (1996)) secondary structure predictions of α -helix (H), β -strand (E), or coil (L) are marked. The amino acid shading scheme depicts chemically similar residues: hydrophobic, acidic, basic, Cys, aromatic, structure-breaking, and tiny. Diagnostic sequence patterns for IL-1Rs, TLRs, and full alignment (ALL) were derived by Consensus at a stringency of 75%. Symbols for amino acid subsets are (see internet site for detail): o, alcohol; l, aliphatic; ., any amino acid; a, aromatic; c, charged; h, hydrophobic; -, negative; p, polar; +,

positive; s, small; u, tiny; t, turnlike. Figure 2C shows a topology diagram of the proposed TH β/α domain fold. The parallel β -sheet (with β -strands A-E as yellow triangles) is seen at its C-terminal end, α -helices (circles labeled 1-5) link the β -strands; chain connections are to the front (visible) or back (hidden). Conserved, charged residues at the C-end of the β -sheet are noted in gray (Asp) or as a lone black (Arg) residue (see text).

- Please replace Table 1 from p. 49, line 30 to p. 51, line 8 of the specification with the following amended Table:

Table 1. Sequences of PCR primers.

Reverse transcriptase PCR primers.

Forward primers/Reverse primers

TLR#

| | | |
|---|---------------------------|------------------------|
| 1 | CGTAAAACTGGAAGCTTTGCAAGA | <u>(SEQ ID NO: 46)</u> |
| | CCTTGGGCCATTCCAAATAAGTCC | <u>(SEQ ID NO: 47)</u> |
| 2 | GGCCAGCAAATTACCTGTGTG | <u>(SEQ ID NO: 48)</u> |
| | CCAGGTAGGTCTTGGTGTTCA | <u>(SEQ ID NO: 49)</u> |
| 3 | ATTGGGTCTGGGAACATTTCTCTTC | <u>(SEQ ID NO: 50)</u> |
| | GTGAGATTTAACATTCCTCTTCGC | <u>(SEQ ID NO: 51)</u> |
| 4 | CTGCAATGGATCAAGGACCA | <u>(SEQ ID NO: 52)</u> |
| | TCCCACTCCAGGTAAGTGTT | <u>(SEQ ID NO: 53)</u> |
| 5 | CATTGTATGCACTGTCCTC | <u>(SEQ ID NO: 54)</u> |

| | | |
|----|--------------------------|-----------------|
| | CCACCACCATGATGAGAGCA | (SEQ ID NO: 55) |
| 6 | TAGGTCTCATGACGAAGGAT | (SEQ ID NO: 56) |
| | GGCCACTGCAAATAAGTCCG | (SEQ ID NO: 57) |
| 7 | AGTGTCTAAAGAACCTGG | (SEQ ID NO: 58) |
| | CTTGGCCTTACAGAAATG | (SEQ ID NO: 59) |
| 8 | CAGAATAGCAGGCGTAACACATCA | (SEQ ID NO: 60) |
| | AATGTCACAGGTGCATTCAAAGGG | (SEQ ID NO: 61) |
| 9 | TTATGGACTTCCTGCTGGAGGTGC | (SEQ ID NO: 62) |
| | CTGCGTTTTGTCGAAGACCA | (SEQ ID NO: 63) |
| 10 | CAATCTAGAGAAGGAAGATGGTCC | (SEQ ID NO: 64) |
| | GCCCTTATAAACTTGTGAAGGTGT | (SEQ ID NO: 65) |

β-actin

| | | |
|--|----------------------------------|-----------------|
| | ATCTGGCACCACACCTTCTACAATGAGCTGCG | (SEQ ID NO: 66) |
| | CGTCATACTCCTGCTTGCTGATCCACATCTGC | (SEQ ID NO: 67) |

Real time PCR primers.

Forward primers/Reverse primers

Toll like
receptor

| | | |
|---|--------------------------|-----------------|
| 2 | GGCCAGCAAATTACCTGTGTG | (SEQ ID NO: 68) |
| | AGGCGGACATCCTGAACCT | (SEQ ID NO: 69) |
| 4 | CTGCAATGGATCAAGGACCA | (SEQ ID NO: 70) |
| | TTATCTGAAGGTGTTGCACATTCC | (SEQ ID NO: 71) |
| 7 | TTACCTGGATGGAAACCAGCTACT | (SEQ ID NO: 72) |

TCAAGGCTGAGAAGCTGTAAGCTA

(SEQ ID NO: 73)

9 TGAAGACTTCAGGCCCAACTG

(SEQ ID NO: 74)

TGCACGGTCACCAGGTTGT

(SEQ ID NO: 75)

- Please replace the Sequence Listing submitted on April 9, 2008 with the enclosed Substitute Sequence Listing, and insert a copy of the Substitute Sequence Listing submitted herewith (pp. 1-193) at the end of the specification, after the Abstract.