The term "KIR2DL2/3" refers to either or both of the KIR2DL2 and KIR2DL3 receptors. These two receptors have a very high homology, are encoded by allelic forms of the same gene, and are considered by the art to be functionally similar.

As used herein, the terms "Programmed Death 1," "Programmed Cell Death 1," "Protein PD-1," "PD-1," PD1," "PDCD1," "hPD-1" and "hPD-I" are used interchangeably, and include variants, isoforms, species homologs of human PD-1, and analogs having at least one common epitope with PD-1. The complete PD-1 sequence can be found under GenBank Accession No. U64863 (SEQ ID NO:29).

The protein Programmed Death 1 (PD-1) is an inhibitory member of the CD28 family of receptors, that also includes CD28, CTLA-4, ICOS and BTLA. PD-1 is expressed on activated B cells, T cells, and myeloid cells (Agata *et al.*, *supra*; Okazaki *et al.* (2002) *Curr. Opin. Immunol.* 14: 391779-82; Bennett *et al.* (2003) *J Immunol* 170:711-8). The initial members of the family, CD28 and ICOS, were discovered by functional effects on augmenting T cell proliferation following the addition of monoclonal antibodies (Hutloff *et al.* (1999) *Nature* 397:263-266; Hansen *et al.* (1980) *Immunogenics* 10:247-260). PD-1 was discovered through screening for differential expression in apototic cells (Ishida *et al.* (1992) *EMBO J* 11:3887-95). The other members of the family, CTLA-4 and BTLA, were discovered through screening for differential expression in cytotoxic T lymphocytes and TH1 cells, respectively. CD28, ICOS and CTLA-4 all have an unpaired cysteine residue allowing for homodimerization. In contrast, PD-1 is suggested to exist as a monomer, lacking the unpaired cysteine residue characteristic in other CD28 family members.

The PD-1 gene is a 55 kDa type I transmembrane protein that is part of the Ig gene superfamily (Agata *et al.* (1996) *Int Immunol* 8:765-72). PD-1 contains a membrane proximal immunoreceptor tyrosine inhibitory motif (ITIM) and a membrane distal tyrosine-based switch motif (ITSM) (Thomas, M.L. (1995) *J Exp Med* 181:1953-6; Vivier, E and Daeron, M (1997) *Immunol Today* 18:286-91). Although structurally similar to CTLA-4, PD-1 lacks the MYPPPY (SEQ ID NO: 30) motif that is critical for B7-1 and B7-2 binding. Two ligands for PD-1 have been identified, PD-L1 and PD-L2, that have been shown to downregulate T cell activation upon binding to PD-1 (Freeman *et al.* (2000) *J Exp Med* 192:1027-34; Latchman *et al.* (2001) *Nat Immunol* 2:261-8; Carter *et al.* (2002) *Eur J Immunol* 32:634-43). Both PD-L1 and PD-L2 are B7 homologs that bind to PD-1, but do not bind to other CD28 family

SEQ ID NO:	SEQUENCE
	accgaagggg acaacgccac cttcacctgc agcttctcca acacatcgga gagcttcgtg ctaaactggt accgcatgag ccccagcaac cagacggaca agctggccgc cttccccgag gaccgcagcc agcccggcca ggactgccgc ttccgtgtca cacaactgcc caacgggcgt gacttccaca tgagcgtggt cagggcccgg cgcaatgaca gcggcaccta cctctgtggg gccatctccc tggcccccaa ggcgcagatc aaagagagcc tgcgggcaga gctcagggtg acagagagaa gggcagaagt gcccacagcc caccccagcc cctcacccag gccagccggc cagttccaaa ccctggtggt tggtgtcgtg ggcggcctgc tgggcagcct ggtgctgcta gtctgggtcc tggccgtcat ctgctcccgg gccgcacgag ggacaatagg agccaggcgc accggccagc ccctgaagga ggacccctca gccgtgcctg tgttctctgt ggactatggg gagctggatt tccagtggcg agagaagacc ccggagcccc ccgtgccctg tgtccctgag cagacggagt atgccaccat tgtctttcct agcggaatgg gcacctcatc ccccgcccgc aggggctcag ccgacggccc tcggagtgcc cagccactga ggcctgagga tggacactgc tcttggcccc tctgaccggc ttccttggcc accagtgttc tgcagaccct ccaccatgag cccgggtcag cgcatttcct caggagaagc aggcagggtg caggccattg caggccgtcc aggggctgag ctgcctgggg gcgaccgggg ctccagcctg cacctgcacc aggcacagcc ccaccacagg actcatgtct caatgcccac agtgagccca ggcagcaggt gtcaccgtcc cctacaggga gggccagatg cagtcactgc ttcaggtcct gccagcacag agctgcctgc gtccagctcc ctgaatctct gctgctgctg ctgctgctgc tgctgctgcc tgcggcccgg ggctgaaggc gccgtggccc tgcctgacgc cccggagcct cctgcctgaa cttgggggct ggttggagat ggccttggag cagccaaggt gcccctggca gtggcatccc gaaacgccct ggacgcaggg cccaagactg ggcacaggag tgggaggtac atggggctgg ggactcccca ggagttatct gctccctgca ggcctagaga agtttcaggg aaggtcagaa gagctcctgg ctgtggtggg cagggcagga aacccctccc acctttacac atgcccaggc agcacctcag gccctttgtg gggcagggaa gctgaggcag taagcgggca ggcagagctg gaggcctttc aggccagcca gcactctggc ctcctgccgc cgcattccac cccagcccct cacaccactc gggagaggga catcctacgg tcccaaggtc aggagggcag ggctggggtt gactcaggcc cctcccagct gtggccacct gggtgttggg agggcagaag tgcaggcacc tagggccccc catgtgccca ccctgggagc tctccttgga acccattcct gaaattattt aaaggggttg gccgggctcc caccagggcc tgggtgggaa ggtacaggcg ttcccccggg gcctagtacc cccgcgtggc ctatccactc ctcacatcca cacactgcac ccccactcct ggggcagggc caccagcatc caggcggcca gcaggcacct gagtggctgg gacaagggat ccccccttccc tgtggttcta ttatattata attataatta aatatgagag catgct
30	MYPPPY