Protein Drugs

Cpg-oligodeoxynucleotide, immunogenic composition including the same, and use of preparing medical for inducing immune response by the same

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CpG-oligodeoxynucleotides (CpG-ODNs) are known as potent immune modulators which induce the production of inflammatory cytokines and a T helper 1 (Th1) polarized immune response, resulting in the expression of costimulatory molecules in antigen-presenting cells and increased activation of B cells, T cells, NK cells and other immunocytes.

CpG-ODNs have species-specific activities based on the compositions and lengths thereof. Various kinds of CpG-ODN have been designed and artificially synthesized for inducing the immune responses of a specific receptor in a specific species. Using Toll-like receptors (TLRs) as a target induced by the CpG-ODNs in a host may be a better choice because of its key role in the innate immune system.

The present invention discloses a CpG-oligodeoxynucleotide (CpG-ODN) for inducing a TLR9 activated immune response, a TLR21 activated immune response or a combination thereof in a host. The CpG-ODN includes one or more copies of the sequences of GTCGTT, one or more copies of the sequences of GTT and one or more copies of the sequences of TTTT, wherein at least one copy of the sequence of GTCGTT is encoded between the sequence of GTT and the sequence of TTTT. Further, an immunogenic composition including the CpG-ODN and a method of inducing immune response by the same are also provided.

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Methods to upregulate and suppress an expression of immunomodulatory cells

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One population of T lymphocytes (Thl7 cells) which has moved into greater prominence are interleukin (IL)-17A secreting T cells. This T helper cell subpopulation is important in mediating host responses towards microbial infections, as well as participating in the pathogenesis of many autoimmune and chronic inflammatory diseases that had been long believed to be caused by Thl cells. The mechanisms involved in hMSC-Thl7 lymphocyte interactions, which have important implications in the clinical use of hMSCs given the role of Thl7 cells in human diseases.

The research team found that hMSCs suppress Thl7 responses through both paracrine and cell-cell contact mechanisms, involving IL-25 (known as IL17E) as well as PD-L1, a ligand of the PD-1 family. The present invention demonstrate that hMSCs constitutively secrete IL-25 to upregulate the cell surface expression of PD-L1 through JNK and STAT3, with STAT3 involved in the transcriptional control of PD-L1.

The present application provides a method of upregulating an expression of immumodulatory cells in vitro comprising treating the immumodulatory cells with IL-25 to increase an expression of PD-L1. The present application also provides a method for treatment of immune disorders by the aforementioned methods. The present application also provides a method to suppress an expression of immumodulatory cells comprising suppressing an expression of PD-L1. The immumodulatory cells can be human monocytes or hMSCs. The present application further provides a method for treatment of immune-evasive diseases by using the aforementioned method to suppress an expression of immumodulatory cells.

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