

Identification of a Cell-Surface Co-Receptor that Mediates the Uptake and Immunostimulatory Activity of "D" Type CpG Oligonucleotides

Technology Summary

Unmethylated CpG motifs are present at high frequency in bacterial DNA. They provide a danger signal to the mammalian immune system that triggers a protective immune response characterized by the production of Th1 and proinflammatory cytokines and chemokines. Although the recognition of CpG DNA by B cells and plasmacytoid dendritic cells is mediated by TLR 9, these cell types differ in their ability to bind and respond to structurally distinct classes of CpG oligonucleotides. The inventors' work established that CXCL16, a membrane-bound scavenger receptor, influences the uptake, subcellular localization, and cytokine profile induced by D oligonucleotides.

Knowing that CXCL16 can be used to selectively internalize ODN could be useful for (1) improving the activity of D type ODN, (2) improving recognition (and side effects) of other types of ODNs by deleting regions that interact with CXCL16, (3) potentially improving the targeting of any drug or biologic to CXCL16 expressing cells, (4) targeting antisense ODNs to immune cells or preventing side effects from antisense therapy, and also applications to (5) DNA vaccines and other agents that require targeting to CXCL16 expressing cells such as dendritic cells and monocytes.

This application claims methods of inducing an immune response that include administering agents that increase the activity and/or expression of CXCL16 and a D ODN. The application also claims methods of decreasing an immune response to a CpG ODN, including administering agents that decrease the activity and/or expression of CXCL16. Compositions including one or more D type ODNs and an agent that modulates the activity and/or expression of CXCL16 are also claimed.

Potential Commercial Applications

- Vaccine production, vaccine adjuvants
- Immunotherapeutics

Competitive Advantages

- Improves drug and biological targeting to CXCL 16 expressing cells
- Improves activity of D type ODN

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Publications: M Gursel et al. CXCL16 influences the nature and specificity of CpG-induced immune activation. J Immunol. 2006 Aug 1;177(3):1575-1580.PMID: [16849465](#)

Intellectual Property:

U.S. Pat: [7,892,569](#) issued 2011-02-22

U.S. Pat: [8,470,342](#) issued 2013-06-25

PCT Application [No. PCT/US2006/033774](#)

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