into host cells. More specifically, this multimeric CD4 inhibits the interaction between HIV–1 gp120 and CD4 present on the surface of CD4 T-cells, the major HIV–1 target cell. There is strong evidence that binding between gp120, as part of a virion spike, and CD4 on cell surface is the first step for HIV entry into host cells. This multimeric CD4 provides a number of advantages over inhibitory CD4 molecules previously developed. First, this CD4 multimer is capable of binding at least 10 gp120 simultaneously with high avidity. Second, it does not enhance HIV infection at suboptimal concentrations, a phenomenon observed with previously developed recombinant CD4 molecules. Third, it has been demonstrated that this CD4 fusion protein hyper-crosslinks CD16 on natural killer (NK) cells and as a consequence delivers an exceptionally strong signal to NK cells, promoting potent Antibody-Dependent Cellular Cytotoxicity (ADCC) and lysis of HIV-infected cells. The inventors have shown that this recombinant CD4 multimer efficiently neutralizes primary isolates from different HIV subgroups.

The invention comprises an immunoglobulin construct having up to 12 amino terminal domains of CD4 (D1D2), the epitope responsible for HIV–1 gp120 binding activity. It also comprises domains of a human IgG1 heavy chain, as well as the IgA tailpiece that drives its polymerization. The two amino terminal domains of CD4 are fused to the CH2CH3 domains (which bears the FC receptor recognition epitopes) of a human IgG1 heavy chain.

Applications: HIV therapeutics and HIV vaccine development.

Advantages: Efficient inhibition of HIV–1 viral entry without enhancement of infection at suboptimal concentrations. Potent activation of Antibody-Dependent Cellular Cytotoxicity (ADCC) and lysis of HIV-infected cells.

Development Status: The anti-HIV activity of this multimeric CD4 protein has been well characterized in vitro.

Inventors: James Arthos, Claudia Cicala, Anthony S. Fauci (NIAID).

Publications:

• U.S. Patent No. 7,368,114 issued 06 May 2008
• European Application No. 02799169.4 (recently allowed)

Licensing Status: Available for licensing.

Licensing Contact: RC Tang, JD, LLM; 301–435–5031; tangle@mail.nih.gov.

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases, Laboratory of Immunoregulation, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this invention. Please contact William Ronnenberg at 301–451–3522 or wronnenberg@niaid.nih.gov for more information.


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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the meeting of the National Cancer Advisory Board.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

A portion of the meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.