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(71) Applicant *(for all designated States except US)*: BASF AKTIENGESELLSCHAFT [DE/DE]; D-67056 Ludwigshafen (DE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: SEKUT, Les [US/US]; 4 Roy Street, Westborough, MA 01581 (US). CARTER, Adam [US/US]; 5 Pond Street, Newburyport, MA 01950 (US). GHAYUR, Tariq [PK/US]; 6 Oak Street, Grafton, MA 01519 (US). BANERJEE, Subhashis [IN/US]; 35 Hapgood Way, Shrewsbury, MA 01545 (US). TRACEY, Daniel, E. [US/US]; 149 Shaker Road, Harvard, MA 01451 (US).

(74) Agents: KARA, Catherine, J. et al.; Lahive & Cockfield, LLP, 28 State Street, Boston, MA 02109 (US).

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(54) Title: METHODS AND COMPOSITIONS FOR MODULATING RESPONSIVENESS TO CORTICOSTEROIDS

(57) Abstract

Method for modulating responsiveness to corticosteroids in a subjet are provided. In the method of the invention, an agent which antagonizes a target that regulates production of IFN-γ in the subject is administered to the subject in combination with a corticosteroid such that responsiveness of the subject to the corticosteroid is modulated as compared to when a corticosteroid alone is administered to the subject. In one embodiment, the agent is an IL-18 antagonist. In another embodiment, the agent is an interleukin-12 (IL-12) antagonist. In yet another embodiment, the agent is an NK cell antagonist. In a preferred embodiment, the agent is an inhibitor of a caspase family protease, preferably an ICE inhibitor. In another preferred embodiment, the agent is an anti-IL-12 monoclonal antibody. In yet another preferred embodiment, the agent is an anti-asialo-GM1 antibody or an NK1.1 antibody. Other preferred agents include phosphodiesterase IV inhibitors and beta-2 agonists. The methods of the invention can be used in the treatment of a variety of inflammatory and immunological diseases and disorders. Pharmaceutical compositions comprising an agent which antagonizes a target that regulates production of IFN-γ in a subject, a corticosteroid and a pharmaceutically acceptable carrier are also provided. A preferred composition comprises an ICE inhibitor, a corticosteroid and a pharmaceutically acceptable carrier.