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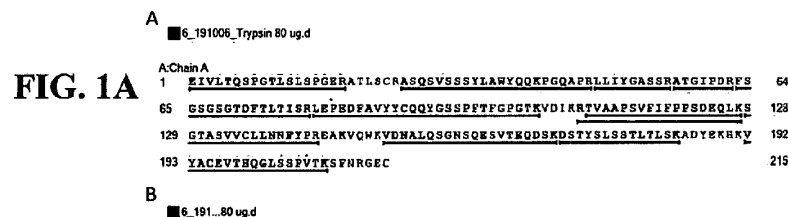
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(54) Title: NOVEL STEROID PAYLOADS, STEROID LINKERS, ADCs CONTAINING AND USE THEREOF



(57) **Abstract:** The invention provides novel glucocorticosteroids, glucocorticosteroid-linkers and antibody drug conjugates (ADC's) comprising an antibody or antibody fragment which binds to an antigen expressed on immune cells, optionally an antigen expressed on human immune cells. In some instances the ADCs comprise an anti-human VISTA (V-region Immunoglobulin-containing Suppressor of T cell Activation(1)) antibody or anti-VISTA antigen-binding antibody fragment which binds to VISTA expressing cells at physiologic pH having a short serum half-life (≈ 24 -72 or 24-48 or 12-24 hours or less in a human VISTA knock-in rodent or (≈ 1 -3.5 days or less in a human or non-human primate). In some instances these ADCs have a rapid onset of action and are potent for prolonged duration as they are very effectively internalized by immune cells in large amounts where they are cleaved releasing large amounts of active steroid payload. The invention also relates to the use of such ADCs and novel steroids for the treatment of autoimmune, allergic and inflammatory conditions. The invention further relates to methods for reducing the adverse side effects and/or enhancing the efficacy of glucocorticoid receptor agonists by using such ADCs to selectively deliver these anti-inflammatory agents to target immune cells, such as monocytes, neutrophils, B cells, T cells, Tregs, eosinophils, NK cells, macrophages, myeloid cells, et al., and particularly myeloid cells, thereby reducing potential toxicity to non-target cells.

[Continued on next page]

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