Docket #: S24-355

Engineered Antibody Constant Region Polypeptides and Related Methods

Researchers at Stanford have identified amino acid modifications in the IgG Fc region which extend its therapeutic half-life and improve its in vivo receptor binding.

Biologic therapeutics, including therapeutic antibodies, that incorporate the Fc domain of antibodies are an important and growing class of drugs that have revolutionized the treatment of a broad range of diseases, ranging from infectious diseases to cancer and autoimmunity. However, across most applications, the clinical viability of biologic therapeutics is undermined by their relatively short half-life in vivo, requiring frequent administration to maintain effective levels in serum. Thus, there remains a critical unmet need for a broadly applicable solution that can extend the half-life of biologic therapeutics. Among the various classes of immunoglobulins, Immunoglobulin G (IgG) is most often developed for antibody therapies. The pharmacokinetics of the resulting therapeutic antibodies are predominantly mediated by their interaction with the neonatal Fc receptor (FcRn), which provides the antibodies in vivo with protection from catabolism.

Stage of Development
Research: in vitro

Stage of Research
The inventors have discovered new amino acid modifications in IgG in the Fc region which extend its in vivo half-life. In addition, these beneficial mutations are not strictly within the FcRn-Fc interface and thereby do not interfere with binding affinity for human FcRn, and many variants even exhibit increased binding affinity to FcRn at acidic pH.

Applications

- Treatment for various diseases or conditions including, but not limited to:
  - Autoimmune disease
  - A genetic disease or condition
  - Respiratory diseases or conditions
  - A cardiovascular disease
  - A neurological disease
  - An ophthalmological disease
  - A musculoskeletal disease

Advantages

- Increased in vivo half-life, thereby reducing the need for frequent administrations to maintain high levels of antibody in serum.
- Increased binding affinity in the FcRn-Fc interface, thereby increasing antibody effector functions such as (but not limited to) antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cell-mediated phagocytosis (ADCP), complement-dependent cytotoxicity (CDC) or opsonized phagocytosis killing (OPK).
- And in some examples:
  - increased placental transfer, thereby increasing antibody transfer from mother to fetus during pregnancy.
  - increased transcytosis in human epithelia, which may be desirable for drug delivery in transmucosal or oral delivery.
  - the molecules may have enhanced delivery across the blood-brain barrier.

Innovators

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