Novel Design and Applications of Antibody Cysteine Variants
Technology #13713

Applications

This technology relates to a set of immunoglobulin (IgG 1) cysteine variants that can be used in the generation of stable immunoglobulin conjugates with reduced cross-linking.

Problem Addressed

Engineering of antibody conjugates has increased the versatility of antibody applications. In many laboratory techniques, enzymes or fluorescent probes are conjugated to antibodies to carry out an assay function, for example, quantitation of antigen abundance. In cases of targeted therapy, toxic small molecules are attached to antibodies that specifically bind biomarkers on diseased cells. Various approaches to antibody conjugation have been pursued, such as attachment to surface lysines, to Fc carbohydrates, or to partially reduced interchain disulfides.

Antibody conjugation to engineered surface cysteine remains a very attractive option because most antibodies do not have cysteines other than the ones consumed in intra- and interchain disulfide bonds. Small molecules can be attached at the specific site of cysteine substitution via a thiol reactive chemistry such as maleimides.

Although cysteine engineering of proteins - and more specifically, antibodies - has been practiced for many years, it is still difficult to predict whether an antibody cysteine variant will have the desired properties and serve the intended purposes. This technology comprises a set of human IgG 1 cysteine variants, most of which are stable, and can be conjugated efficiently and specifically without significant loss of antigen binding activity. Thus, the stable antibody variants add to the repertoire of variants for site-specific conjugation of payload molecules.

The engineered human IgG 1 surface cysteine variants provide new sites for site-specific conjugation of therapeutic antibodies, biomarkers for in vitro and in vivo laboratory research, and diverse pharmacological applications.

Technology

This technology comprises a set of improved immunoglobulin IgG cysteine variants, most of which are stable, which can be conjugated efficiently and specifically without significant loss of antigen binding activity, and can exhibit reduced crosslinking. An immunoglobulin conjugate, comprises an immunoglobulin having at least one mutation at a residue selected from the group consisting of 7(V\text{H}), 20(V\text{L}), 22(V\text{L}), 25(V\text{L}), 125(C\text{H}1), 248(C\text{H}2), 254(C\text{H}2), 286(C\text{H}2), 298(C\text{H}2), and 326(C\text{H}2), where at least one mutation is a substitution with a cysteine residue, and an atom or molecule. The atom or molecule is conjugated to the cysteine residue.

Numerous other issued and published US and Foreign applications.
**Advantages**

- Most of the improved human immunoglobulin IgG 1 cysteine variants are stable
- Immunoglobulin IgG 1 cysteine variants conjugate without significant loss of antigen binding activity
- Immunoglobulin conjugates with reduced cross-linking
- Immunoglobulin IgG 1 cysteine variants could be employed as therapeutic antibodies, biomarkers etc.

**Categories For This Invention:**

- Life Sciences
- Biotechnology
- Clinical Applications
- Diagnostics
- Imaging
- Research Tools
- Therapeutics

**Intellectual Property:**

Methods for identification of sites for IGG conjugation
Issued US Patent
8,834,885
Methods for identification of sites for IGG conjugation
Issued US Patent
9,629,925
Methods for identification of sites for IGG conjugation
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**Publications:**

*Design and Application of Antibody Cysteine Variants*

*Bioconjugate Chemistry*

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External Links:
The Trout Lab at MIT
http://web.mit.edu/troutgroup/

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