Patent Claims

1. A polypeptide comprising an Fc variant of a wild-type human IgG Fc region, said Fc variant comprising an amino acid substitution at position Pro329, wherein Pro329 of a wild-type human Fc region is substituted with glycine or arginine or an amino acid residue large enough to destroy the proline sandwich within the Fc/Fcγ receptor interface, and at least one further amino acid substitution, wherein the residues are numbered according to the EU index of Kabat, and wherein said polypeptide exhibits an at least 10-fold reduced affinity to the human FcγRIIIA and a reduced affinity to the human ~~and/or~~ FcγRIIA, ~~and/or~~ FcγRI and the human C1q receptor, compared to a polypeptide comprising the wildtype IgG Fc region, and wherein the ADCC induced by said polypeptide is reduced to at least 20% of the ADCC induced by the polypeptide comprising a wild-type human IgG Fc region.

~~2. The polypeptide according to claim 1, wherein Pro329 of a wild-type human Fc region is substituted with glycine or arginine or an amino acid residue large enough to destroy the proline sandwich within the Fc/Fcγ receptor interface.~~

~~3~~2. The polypeptide according to ~~any one of~~ claims ~~1 or 2~~, wherein said at least one further amino acid substitution is S228P, E233P, L234A, L235A, L235E, N297A, N297D, or P331S.

~~4~~3. The polypeptide according to any one of claims ~~1-3~~ or 2, wherein said at least one further amino acid substitution is L234A and L235A of the human IgG1 Fc region or S228P and L235E of the human IgG4 Fc region.

~~5. The polypeptide according to any one of claims 1-4, wherein the affinity to at least one further receptor of the group comprising the human receptors Fcγl, FcγIIA, and C1q is reduced compared to the polypeptide comprising a wild-type human IgG Fc region.~~

~~6~~4. The polypeptide according to any one of claims ~~1-5~~3, wherein the polypeptide comprises a human IgG1 or IgG4 Fc region.

~~7~~5. The polypeptide according to any one of claims ~~1-6~~4, wherein the polypeptide is an antibody or an Fc fusion protein.

~~8~~6. The polypeptide according to any one of claims ~~1-7~~5, wherein thrombocyte aggregation induced by the polypeptide is reduced compared to the thrombocyte aggregation induced by a polypeptide comprising a wild-type human IgG Fc region.

~~9~~7. The polypeptide according to any one of claims 1-~~8~~6, wherein CDC induced by the polypeptide is strongly reduced compared to the CDC induced by a polypeptide comprising a wild-type human IgG Fc region.

~~10~~8. The polypeptide according to any one of claims 1-~~9~~7 for use as a medicament.

~~11~~9. The polypeptide according to any one of claims 1-~~10~~8, wherein the polypeptide is an anti-CD9 antibody, which is characterized in that the polypeptide comprising the wildtype Fc region comprises as heavy chain variable region SEQ ID NO:9 and as variable light chain region SEQ ID NO:8.

~~12~~10. The polypeptide according to any one of claims 1-~~11~~9, for use in treating a disease wherein it is favorable that an effector function of the polypeptide is strongly reduced compared to the effector function induced by a polypeptide comprising a wild-type human IgG Fc region.

~~13~~11. Use of the polypeptide according to any one of claims 1-~~12~~10 in the manufacture of a medicament for the treatment of a disease, wherein it is favorable that the effector function of the polypeptide comprising an Fc variant of a wild-type human IgG Fc region is strongly reduced compared to the effector function induced by a polypeptide comprising a wild-type human IgG Fc region.

~~14~~12. Use of a polypeptide comprising an Fc variant of a wild-type human IgG Fc region, said polypeptide having Pro329 of the human IgG Fc region substituted with glycine, and at least one further amino acid substitution, wherein the residues are numbered according to the EU index of Kabat, wherein said polypeptide exhibits a reduced affinity to the human FcγRIIIA and FcγRIIA in the manufacture of a medicament for down-modulation of ADCC to at least 20% of the ADCC induced by the polypeptide comprising the wildtype human IgG Fc region, and/or for down-modulation of ADCP.

~~15~~13. Use of a polypeptide according to claim ~~14~~12, wherein the Fc variant comprises at least two further amino acid substitution at L234A and L235A of the human IgG1 Fc region or S228P and L235E of the human IgG4 Fc region.

~~16~~14. The use according to claims ~~14~~12-~~15~~13, wherein thrombocyte aggregation induced by the polypeptide is reduced compared to the thrombocyte aggregation induced by a polypeptide comprising a wildtype human Fc region, wherein the polypeptide is a platelet activating antibody.

~~17. A polypeptide, said polypeptide having Pro329 of the human IgG Fc region substituted with Gly, wherein the residues are numbered according to the EU index of Kabat, wherein said polypeptide is characterized by a strongly reduced binding to FcγRIIIA and FcγRIIA compared to a polypeptide comprising a wildtype human IgG Fc region, for treating an individual having a disease.~~

~~18. The polypeptide according to claim 17, wherein said polypeptide comprises at least two further amino acid substitution at L234A and L235A of the human IgG1 Fc region or S228P and L235E of the human IgG4 Fc region.~~