MODIFIED ANTIBODIES AND METHOD FOR THE PRODUCTION OF SAME

Field of the Invention

The present invention relates to methods for producing non-immunogenic binding agents, in particular immunoglobulins and fragments thereof, which can be used in therapeutic methods. In particular, the methods allow a donor immunoglobulin to be modified such that it can be administered to a target species with minimal risk of neutralising antibodies being raised there against. The invention further extends to immunoglobulins produced by said methods and to their use in therapy.

Background to the Invention

Advances in recombinant DNA technology have resulted in a variety of proteins being developed for pharmaceutical applications. This has resulted in a number of protein-based drugs, which may be more generally referred to as biologics, being the subject of clinical trials or market approval. Due to their inherent properties and structures, protein-based drugs are significantly larger and more complex than more traditional small molecule organic and inorganic based molecules. In particular, the folded tertiary structure of the protein is essential to its biological function.

Antibodies are one family of proteins that are being widely developed and used in therapeutic applications in man. The popularity of antibodies in therapeutic applications has been due to their versatility in being able to specifically target virtually any desired target molecule. The majority of protein based therapeutic products are monoclonal antibodies. However one significant drawback associated with the use of monoclonal antibody-based therapies is the production of neutralising antibodies against the therapeutic monoclonal antibody when administered to a subject. These neutralising antibodies result from the immune system of the subject recognising as foreign sequences of amino acids that are present in the administered monoclonal antibody. As a result, an immune response

3. The method as claimed in claim 1 or claim 2, further comprising the step of replacing at least one constant domain of the heavy and/or light chain of the donor immunoglobulin with a constant domain of a heavy and/or light chain derived from an immunoglobulin derived from the target species.

4. The method as claimed in any preceding claim wherein the target species is a mammalian target species.

5. The method as claimed in claim 4 wherein the mammalian species is a companion animal selected from the group consisting of a dog, a cat and a horse.

6. The method as claimed in claim 4 wherein the mammalian species is a human.

7. A neutralising antibody or an antigen binding fragment thereof which is capable of specifically binding to human nerve growth factor (NGF) wherein the antibody or antigen binding fragment comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:13 or an amino acid sequence which has an identity of at least 85% thereto and/or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:14 or an amino acid sequence which has an identity of at least 85% thereto, wherein the antibody or an antigen binding fragment thereof does not contain any amino acid in any position within the framework regions of the heavy and/or light chain variable domains which would be foreign at that position in one or more immunoglobulins derived from a human, wherein the light chain variable region comprises a CDR1 sequence consisting of RASEDIYNALA, a CDR2 sequence consisting of NTDTLHT, and a CDR3 sequence consisting of HYFHYPRT and wherein the heavy chain variable region comprises a CDR1 sequence consisting of NNNVN, a CDR2 sequence consisting of GVWAGGATDYNSALK, and a CDR3 sequence consisting of DGGYSSSTLYAMDA.

8. The antibody or antigen binding fragment thereof as claimed in claim 7 wherein the light chain comprises the amino acid sequence of SEQ ID NO:25, or an amino acid sequence which has an identity of at least 85% thereto.

9. The antibody or antigen binding fragment thereof as claimed in claim 7 or claim 8 wherein the heavy chain comprises the amino acid sequence of SEQ ID NO:24, or an amino acid sequence which has a sequence identity of at least 85% thereto.