In WO 2008/031532 an anti-drug antibody assay is reported. The detection of a therapeutic antibody in an experimental animal is reported in WO 2006/066912. In US 5,332,665 species specific, high affinity monoclonal antibodies are reported.

Summary

Herein are reported at first a conformational epitope on antibodies of the immunoglobulin class G of humans and chimpanzee that is not present in commonly used experimental animals. At second are reported non-cross-reactive anti-human IgG antibodies and anti-chimpanzee IgG antibodies binding to this epitope. At third are reported assays using these antibodies.

As reported herein is an antibody binding to human or chimpanzee IgG (immunoglobulin of subclass G) and not binding to canine and marmoset IgG.

In one embodiment the antibody is not binding to canine, Rhesus-monkey, marmoset, baboon, and cynomolgus IgG. In another embodiment the antibody is specifically binding to human and chimpanzee IgG. In a further embodiment the K_D-value for binding to a human or chimpanzee IgG is 10^{-9} mol/l or less determined by surface plasmon resonance and the K_D-value for binding to canine, Rhesus-monkey, marmoset, baboon, and cynomolgus IgG is 10^{-6} mol/l or more. In one embodiment the K_D-value for binding to a human or chimpanzee IgG is of from 10^{-9} mol/l to 10^{-13} mol/l. In another embodiment the K_D-value for binding to canine, Rhesus-monkey, marmoset, baboon, and cynomolgus IgG is not determinable via surface plasmon resonance. In one embodiment the antibody is a monoclonal antibody.

As reported herein is an antibody specifically binding to an IgG1 (immunoglobulin of subclass G1) that comprises a kappa light chain constant domain.

In one embodiment the antibody is further binding to an IgG2. In also an embodiment the antibody is further binding to an IgG4. In another embodiment the antibody is not binding to an IgG3. In one embodiment the antibody is not binding to an IgG1 that comprises a lambda light chain constant domain. In one embodiment the antibody is a monoclonal antibody.

The herein reported antibodies obtained from cell lines DSM ACC3006 (M-1.3.2), DSM ACC3007 (M-1.5.8), and DSM ACC3008 (M-1.7.10) show a reduced cross-

reactivity compared e.g. to antibody M-R10Z8E9 produced by cell line DSM ACC2708, bind to different epitopes in the Fab-region, are not influenced by a neighboring glycosylation site, and can be mixed in an immunoassay for the determination of Fab therapeutic antibodies as the binding sites of each of the antibodies is present only once in the Fab-fragment.

Individual aspects as reported herein are the cell lines DSM ACC3006, DSM ACC3007, and DSM ACC3008 as well as the respective antibodies obtained from the cell lines and the use of these antibodies in an immunoassay.

In one aspect, there is provided cell line DSM ACC3006, or DSM ACC3007, or DSM ACC3008. In another aspect, there is provided an antibody obtained from one of the cell lines reported herein. In another aspect, there is provided use of an antibody as reported herein in an immunoassay.

As reported herein is a kit comprising

a) an antibody obtained from cell line DSM ACC3006, or DSM ACC3007, or DSM ACC3008, or DSM ACC2708 in biotinylated form,
b) an antibody obtained from cell line DSM ACC3006, or DSM ACC3007, or DSM ACC3008, or DSM ACC2708 in digoxygenylated form.

As reported herein is a method for detecting a therapeutic antibody in a sample obtained from an experimental animal comprising the steps of

a) providing the sample to be analyzed,
b) incubating the sample with an antibody binding to the same epitope as an antibody as reported herein,
c) optionally incubating the sample with a reagent appropriate for the selective detection of total, active or antigen-bound therapeutic antibody, and
d) correlating the complex formed in (b) or (c) to the concentration of the therapeutic antibody, optionally via a calibration curve.

In another aspect, there is provided a method for detecting a human or humanized antibody in a sample obtained from an experimental dog, rhesus-monkey, marmoset, baboon, cynomolgus comprising the steps of

a) providing the sample to be analyzed,

b) incubating said sample with an antibody as reported herein,

c) optionally incubating said sample with a reagent appropriate for the selective detection of total, active or antigen-bound human or humanized antibody, and

d) correlating the complex formed in (b) or (c) to the concentration of said human or humanized antibody.

As reported herein is a method for immunologically determining a therapeutic antibody in a sample obtained from an experimental animal using an antigen bridging immunoassay comprising a capture antibody and a tracer antibody, wherein the capture antibody and the tracer antibody are both independently selected from antibodies binding to the same epitope as an antibody as reported herein.

In another aspect, there is provided a method for immunologically determining a human or humanized antibody in a sample obtained from an experimental dog, rhesus-monkey, marmoset, baboon, cynomolgus using an antigen bridging immunoassay comprising a capture antibody and a tracer antibody, characterized in that said capture antibody and said tracer antibody are both independently selected from antibodies as reported herein.

In one embodiment the immunoassay is a sandwich immunoassay. In another embodiment the conjugation of the antibody to its conjugation partner is performed by chemically binding via N-terminal and/or ε-amino groups (lysine), ε-amino

groups of different lysines, carboxy-, sulfhydryl-, hydroxyl- and/or phenolic functional groups of the amino acid backbone of the antibody and/or sugar alcohol groups of the carbohydrate structure of the antibody. In a further embodiment the capture antibody is immobilized via a specific binding pair. In one embodiment the capture antibody is conjugated to biotin and immobilization is performed via immobilized avidin or streptavidin. In still another embodiment the tracer antibody is conjugated to the detectable label via a specific binding pair. In one embodiment the tracer antibody is conjugated to digoxygenin and linking to the detectable label is performed via an antibody against digoxygenin. In another embodiment the therapeutic antibody is a Fab. In one embodiment the experimental animal is selected from the group comprising the members of the families of marmosets and tamarins, old world monkeys, dwarf and mouse lemurs, gibbons and lesser apes, true lemurs, as well as crossings thereof. In one embodiment the experimental animal is selected from dog, Rhesus-monkey, marmoset, baboon and cynomolgus. In one embodiment the experimental animal is a Macaca monkey. In a further embodiment the antibody binding to the therapeutic antibody and not binding to the immunoglobulin of the experimental animal is an antibody as reported herein. In one embodiment the therapeutic antibody is a human or a humanized antibody. In a further embodiment the human or humanized antibody is a monoclonal antibody. In one embodiment the total therapeutic antibody is detected, in another the active therapeutic antibody is detected, and in a further the therapeutic antibody is detected which is bound to its antigen.

As reported herein is the use of an antibody which is binding to a therapeutic antibody and not binding to the immunoglobulin of an experimental animal for determining the concentration of total, active, or antigen-bound therapeutic antibody in a sample obtained from an experimental animal whereby the antibody is binding to the same epitope as an antibody as reported herein. In another aspect, there is provided use of an antibody which is binding to a human or humanized antibody and not binding to the immunoglobulin of an experimental dog, rhesus-monkey, marmoset, baboon, cynomolgus for measuring the concentration of total, active, or antigen-bound human or humanized antibody in a sample obtained from an experimental dog, rhesus-monkey, marmoset, baboon, cynomolgus whereby the antibody is an antibody as reported herein. In one embodiment the antibody is an antibody as reported herein.

As reported herein is an antibody composition comprising a mixture of the antibody produced by the cell line DSM ACC3006, the cell line DSM ACC3007, the cell line DSM ACC3008, and/or the cell line DSM ACC2708.

In another aspect, there is provided an antibody composition, characterized in comprising a mixture of antibodies produced by the cell line DSM ACC3006, the cell line DSM ACC3007 and the cell line DSM ACC3008.

In another aspect, there is provided use of an antibody composition as reported herein in a method as reported herein. In another aspect, there is provided use of an antibody as reported herein in a method as reported herein.

In another aspect, there is provided an antibody binding to human or chimpanzee IgG and not binding to canine and marmoset IgG, characterized in that the K_D-value for binding to a human or chimpanzee IgG is 10^{-9} mol/l or less and characterized in that the antibody is obtained from one of the cell lines DSM ACC3006, DSM ACC3007, or DSM ACC3008.