to predict pharmacological properties, stoichiometry and possible degradation products of the therapeutic or diagnostic agent captured by the bispecific antibody.

In addition, currently used conjugates can not be applied for most therapeutic agents since conjugation often results in reduced or eliminated activity of the therapeutic agent or in undesired alterations of the binding capabilities of the antibody.

Therefore there is a need for a well-defined, efficient and specific delivery platform for therapeutic and diagnostic agents with effective release of the payload at the target that can be broadly applied.

Summary ~~of the invention~~

The present ~~invention~~disclosure relates to a complex of
a) a bi-specific antibody specific against digoxigenin and a target protein, comprising a first antigen-binding site that binds to digoxigenin and a second antigen-binding site that binds to a target protein, and
b) digoxigenin wherein the digoxigenin is conjugated to a therapeutic or diagnostic agent selected from the group consisting of a peptide, a small compound, a radioactively labeled small compound, and an imaging reagent.

In one aspect, there is provided a complex of

a) bi-specific antibody specific against digoxigenin and a target protein, comprising a first antigen-binding site that binds to digoxigenin and a second antigen-binding site that binds to a target protein, and

b) digoxigenin wherein the digoxigenin is conjugated to a therapeutic or diagnostic agent selected from the group consisting of a peptide, a small molecule, a radioactively labeled small molecule, and an imaging reagent, wherein said antigen-binding site specifically binding to digoxigenin comprises as heavy chain variable domain SEQ ID NO 3 with the mutations S49A, I57A and A60P and as light chain variable domain SEQ ID NO 5.

In one embodiment the bi-specific antibody is characterized in comprising

a) a monospecific bivalent antibody consisting of two full length antibody heavy chains and two full length antibody light chains whereby each chain is comprising only one variable domain,

b) two peptide-linkers,

c) two monospecific monovalent single chain antibodies each consisting of an antibody heavy chain variable domain, an antibody light chain variable domain, and a single-chain-linker between said antibody heavy chain variable domain and said antibody light chain variable domain;

Another embodiment of the ~~invention~~disclosure is the use of the complex according to the ~~invention~~disclosure for delivery of a therapeutic or diagnostic agent to a target cell or tissue.

In another aspect, there is provided a complex as defined herein for use in the delivery of a therapeutic or diagnostic agent to a target cell or tissue.

Another embodiment of the ~~invention~~disclosure is the use of the complex according to the ~~invention~~disclosure for targeted cancer therapy.

Another embodiment of the ~~invention~~disclosure is the use of the complex according to the ~~invention~~disclosure for targeted radiotherapy.

In another aspect, there is provided~~Another embodiment of the invention is~~ the complex as defined herein~~of any of claims 1-14~~ for targeted cancer therapy.

In another aspect, there is provided~~Another embodiment of the invention is~~ the complex as defined herein~~of any of claims 1-14~~ for targeted radiotherapy.

In another aspect, there is provided~~Another embodiment of the invention is~~ the use of the complex as defined herein~~of any of claims 1-14~~ for the manufacture of a medicament for targeted cancer therapy.

In another aspect, there is provided~~Another embodiment of the invention is~~ the use of the complex as defined herein~~of any of claims 1-14~~ for the manufacture of a medicament for targeted radiotherapy.

Another embodiment of the ~~invention~~disclosure is the use the according to the ~~invention~~disclosure for imaging of cells or tissues.

In another aspect, there is provided the complex as defined herein for use in the imaging of cells or tissues.

In another aspect, there is provided~~Another embodiment of the invention is~~ a composition comprising the complex as defined herein~~according to the invention~~. In one embodiment the composition is a diagnostic composition. In one embodiment the composition is a pharmaceutical composition.

Another embodiment of the ~~invention~~disclosure is the use of the pharmaceutical composition in targeted cancer therapy.

Another embodiment of the ~~invention~~disclosure is the use of the pharmaceutical composition in targeted radiotherapy.

Detailed description of the invention

The invention provides methods for producing the bispecific antibodies or antibody fragments, as well as methods for using them, in particular their use as a delivery platform for therapeutic and diagnostic agents, as well as pharmaceutical compositions and diagnostic tools comprising said antibodies.

Preferred embodiments include bi-specific antibodies or antibody fragments against a target protein and digoxigenin, comprising a first antigen-binding site that binds to digoxigenin (referred to as "Dig" or "DIG") and a second antigen-binding site that binds to a target protein. Said binding sites of the bi-specific antibodies or antibody fragments are referred to as "<target protein>" (or shortly, "<target>") and "<Dig>", respectively.

Further this invention relates to monoclonal bi-specific antibodies and antibody fragments that comprise a first antigen-binding site that binds to digoxigenin and a second antigen-binding site that binds to a target protein, DNAs that encode such antibodies and antibody fragments, and vectors for expressing the DNAs. Preferably, said bi-specific antibodies are humanized and chimeric antibodies.

One embodiment of the invention is a bispecific antibody binding to digoxigenin and a target protein comprising a first antigen-binding site that binds to digoxigenin and a second antigen-binding site that binds to a target protein, comprising