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(54) MULTIPURPOSE ANTIBODY DERIVATIVES

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(56) **References Cited**

U.S. PATENT DOCUMENTS

5,648,237 A * 7/1997 Carter

FOREIGN PATENT DOCUMENTS

WO WO 94/09131 * 4/1994
WO WO 99/37791 * 7/1999

OTHER PUBLICATIONS

Muller et al., FEBS Letters 422259-64, 1998.*
Tutt et al., The journal of Immunology 147:60-69, 1991.*
Chester et al., TIBTECH 13:296, 1995.*
Huston et al., Methods in Enzymology 203:46-88, 1991.*
Paul, Fundamental immunology, Raven Press, p. 299-300, 1993.*

Hennie R. Hoogenboom, *Mix and match: Building manifold binding sites*, Nature Biotechnology, vol. 15, Feb. 1997, pp. 125-126.

H. Perry Fell et al., *Genetic Construction and Characterization of a Fusion Protein Consisting of a Chimeric F(ab')* with Specificity for Carcinomas and Human IL-2, *The Journal of Immunology*, vol. 146, No. 7, Apr. 1, 1991, pp. 2446-2452.

F. Duncane et al., *Genetically engineered colorimetric antibody*, *Protein Engineering*, vol. 6, No. Suppl., 1993, p. 87.

Eini Nyssönen et al., *Efficient Production of Antibody Fragments by the Filamentous Fungus Trichoderma reesei*, *Bio/Technology*, vol. 11, May 1993, pp. 591-595.

Mark A. Nedelman et al., *Rapid Infarct Imaging with a Technetium-99m-Labeled Antimyosin Recombinant Single-Chain Fv: Evaluation in a Canine Model of Acute Myocardial Infarction*, *The Journal of Nuclear Medicine*, vol. 34, No. 2, Feb. 1993, pp. 234-241.

D.C. Anderson et al., *Enhanced in Vitro Tumor Cell Retention and Internalization of Antibody Derivatized with Synthetic Peptides*, *Bioconjugate Chem.*, vol. 4, 1993, pp. 10-18.

* cited by examiner

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(57) **ABSTRACT**

The present invention relates to a class of molecules specified as novel multipurpose antibody derivatives. This class of molecules is created by heterodimerization of two constituting components. Heterodimerization is obtained by the specific heterotypic interaction of a chosen VH-CH1 combination of immunoglobulin domains, with a chosen VL-CL combination of immunoglobulin domains. The appropriate VH and VL domains in the VHCH1 and VLCL context, a binding specificity can be constituted by the heterodimerization scaffold itself. One or both of the comprising VHCH1 and VLCL chains can thus be extended at either the N- or the C-terminus or both with other molecules, such as a toxin polypeptide, an enzyme, a hormone, a cytokine, a signaling molecule, or a single chain linked Fv fragment with the same or a different specificity.

16 Claims, 14 Drawing Sheets