

Title (en)
SCREENING USING BIOLOGICAL TARGET MOLECULES WITH METAL-ION BINDING SITES

Title (de)
SCREENINGVERFAHREN UNTER VERWENDUNG VON BIOLOGISCHEN ZIELMOLEKÜLEN MIT METALLIONEN-BINDUNGSSTELLEN

Title (fr)
DETECTION AU MOYEN DE MOLECULES CIBLES BIOLOGIQUES POSSEDANT DES SITES DE LIAISON D'IONS METALLIQUES

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Abstract (en)
[origin: WO0150127A2] The present invention provides a molecular approach for rapidly and selectively identifying small organic molecule ligands, i.e. compounds, that are capable of interacting with and binding to specific sites on biological target molecules. The methods of the present invention are applicable to any biological target molecule that has or can be manipulated to have a metal-ion binding site. Biological target molecules are e.g. proteins, polypeptides, oligopeptides, nucleic acids, carbohydrates, nucleoproteins, glycoproteins, glycolipids, lipoproteins and derivatives thereof. More specifically, the biological target molecules include membrane receptors, signal transduction proteins, scaffolding proteins, nuclear receptors, steroid receptors, intracellular receptors, transcription factors, enzymes, allosteric enzyme regulatory proteins, growth factors, hormones, neuropeptides and immunoglobulins. A very interesting group of biological target molecules are membrane proteins such as, e.g., transmembrane protein (e.g. 7 TMs). The methods described herein make it possible to construct and screen libraries of compounds specifically directed against predetermined epitopes on the biological target molecules. The compounds are initially constructed to be bifunctional, i.e. having both a metal-ion binding moiety, which conveys them with the ability to bind to either a natural or an artificially constructed metal-ion binding site as well as a variable moiety, which is varied chemically to probe for interactions with specific parts of the biological target molecule located spatially adjacent to the metal-ion binding site. Compounds may subsequently be further modified to bind to the unmodified biological target molecule without help of the bridging metal-ion. The methods according to the invention may be performed easily and quickly and lead to unambiguous results. The compounds identified by the methods described herein may themselves be employed for various applications or may be further derivatised or modified to provide novel compounds.

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