Claims

1. The use of an allosteric inhibitor binding site consisting of either SEQ ID NO. 1 or a sequence presenting at least 70%, 80%, 90% or 95% of homology with SEQ ID NO.1, to screen for non-polymeric small compound inhibitors of FGFR, said inhibitors having a molecular weight of less than 1000 D.

2. A method for identification of a putative allosteric inhibitor binding site in the extracellular domain of a FGFR, comprising the screening for the presence of frustrated domains in said extracellular domain using a protein secondary structure prediction program, to identify those domains, or fragments thereof, in said extracellular domain that are prone to undergo β-sheet to α-helix transitions, or that have a structure predicted by said protein secondary structure prediction program that is in contradiction with the real structure, as determined by crystallization and X-ray diffraction, and selecting the domains, or fragments thus identified for further screening to confirm the function of the putative inhibitor site by designing compounds such as small molecules, small peptides, peptidomimetics, antibodies or nanobodies that bind to the site and of which the allosteric inhibitory function can be tested.

3. The method of claim 2 wherein the inhibitory function of the allosteric binding site is selective inhibition of downstream signaling pathways.

4. A method for identification of a non-polymeric small compound allosteric inhibitor of a RTK binding to an allosteric inhibitor site in the extracellular domain of a tyrosine kinase receptor comprising

• contacting an allosteric binding site of a RTK with the small compound allosteric inhibitor candidate compound, and

• comparing the changes in the state of at least two different reporters induced by two different downstream pathways dependent upon the activation/inhibition of said tyrosine kinase receptor,

wherein said non-polymeric small compound inhibitor has a molecular weight of less than 1000 D.

5. A method according to claim 4 wherein an allosteric inhibitor is identified when, in presence of a ligand binding to the ligand binding domain of the receptor, at least one downstream pathway is inhibited whereas at least one other downstream pathway is unaffected.

6. A method according to claim 4 or 5, wherein the tyrosine kinase is an FGFR.

7. A method according to claim 6, wherein the FGFR is chosen from one of FGFR-1, FGFR-2, FGFR-3 or FGFR-4.

8. A method for identification of an allosteric inhibitor of a RTK, according to any of claims 4 to 7, wherein the said two different downstream pathways correspond to the ERK1/2 signalling pathway and the PLC_γ signalling pathway.