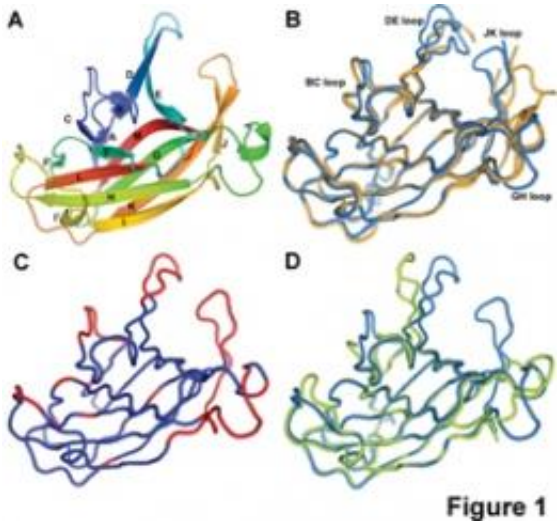
EphA4 -- the molecular transformer

October 23 2009



The structure of EphA4

(PhysOrg.com) -- EphA4 is a protein which is attached to the surfaces of many types of human cells and plays a role in a wide range of biological processes. EphA4 functions by binding to ephrin ligands, cell surface proteins which sit on opposing cells. The signalling cascades which result from this contact direct cells to move in a particular direction, to the right place in the body. This is critical in the development of the nervous system, and has also been linked with the suppression of melanoma tumours.

There are fourteen Eph receptors and eight ephrin ligands in the human genome. These are divided into two classes, A and B. Generally

receptors and ligands can only bind strongly to others in the same class, i.e. a class A receptor will bind to a class A ligand. However, this is not always the case, and one receptor in particular, Eph4A, has been known to bind to both class A and B ephrins.

Researchers from the University of Oxford have been studying the EphA4 receptor because it has the potential to be a target in the treatment of cancer. To realise this potential it is necessary to understand the mechanisms by which EphA4 binds to both class A and B ephrins on the molecular scale. They looked at the structure of EphA4 alone, and when bound to both class A and class B ephrins.

They found that when EphA4 is bound to a class A ephrin, it has a shape similar to other class A receptors, but when binding to a class B ephrin it actually changes its shape to resemble other class B receptors. This research has been published in the journal *Structure*.

“Our results show that EphA4 is a molecular transformer, able to change its shape depending on the ligand that it wants to bind. This explains how, at an atomic level, it is able to bind to both classes of ephrins. This is important in understanding how the nervous system develops, and also has potential as a future target for cancer treatments,” said Dr Thomas Bowden, University of Oxford.

More information: Structural Plasticity of Eph Receptor A4 Facilitates Cross-Class Ephrin Signaling Thomas A. Bowden, A. Radu Aricescu, Joanne E. Nettleship, Christian Siebold, Nahid Rahman-Huq, Raymond J. Owens, David I. Stuart and E. Yvonne Jones, *Structure*, 17 (10), 1386-1397, October 2009, doi:10.1016/j.str.2009.07.018

Provided by Diamond Light Source