s8a.m10.o5 **The BMP-2:BMP receptor IA complex: structural evidence for type I/type II receptor discrimination.** T. Kirsch, J. Nickel, W. Sebald & M. Dreyer, *Phyiologische Chemie II, Biozentrum Uni Würzburg, Am Hubland, 97074 Würzburg, Germany*.
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Bone morphogenetic proteins (BMPs) belong to the large transforming growth factor β (TGF-β) superfamily of multifunctional cytokines which control growth, proliferation and lineage specification of many cell types. BMP-2 can induce ectopic bone and cartilage formation in adult vertebrates and is responsible for central steps in early embryonal development in all animals. Signalling by these cytokines requires binding of two types of transmembrane serine/threonine receptor kinase chains with different affinities classified as type I and type II[1]. Receptor:ligand interactions in the TGF β superfamily are not one-to-one but display a certain promiscuity, i.e. some ligands are able to bind to different receptors, and some receptors are able to recognize different ligands.

Here we report the crystal structure of human dimeric BMP-2 in complex with two high affinity BMP receptor IA extracellular domains ($BRIA_{ec}$) at 2.9 Å resolution. The receptor chains bind to the "wrist" epitopes of BMP-2[2] and are in contact with both BMP-2 monomers. No contacts exist between the receptor domains. The ligand epitope comprises the mobile pre-helix/helix region in one monomer and the rigid part of the BMP "fingers" in the other monomer. The complex structure is fully consistent with biochemical data and reveals the structural basis for type I/type II receptor discrimination and the variability of receptor-ligand interactions that is observed in the BMP/TGF-β systems.

Notes

[1] Massagué, J. "TGF-beta signal transduction." Annu. Rev. Biochem. (1998) 67, 753-791.
[2] Scheufler, C., Sebald, W. & Hülsmeyer, M. "Crystal structure of human bone morphogenetic protein-2 at 2.7 Å resolution." J. Mol. Biol. (1999) 287, 103-115 .