Structure Watch

UNRAVELLING CLASS B GPCRS

Structural studies of the transmembrane domain (TMD) of G protein-coupled receptors (GPCRs), which can largely be classified as class A, class B or class C, have mainly focused on class A receptors. Two papers now present crystal structures of the TMD of class B GPCRs. Hollenstein *et al.* solved the structure of the TMD of human corticotropin-releasing factor 1 receptor (CRF1R), in complex with a small-molecule agonist, at 3 Å resolution. Siu *et al.* solved the structure of the TMD of the glucagon receptor, the amino-terminal domain of which was replaced by a thermally stabilized protein, at 3.4 Å. The authors compared the position of the seven transmembrane helices in their structures with the position of these in representative class A GPCRs. The positioning of helices TM6 and TM7 at the extracellular face of class A and class B GPCRs differed; this changes the relative position of helices TM6 to TM5 and TM1 to TM7 in class B structures and widens what is thought to be the peptide binding cavity. Differences were also observed between the CRF1R and glucagon receptor structures, in particular in the upper segments of TM6 and TM7. These structures provide a model for all class B GPCRs and reveal several features of these receptors against which novel drugs could be designed.

ORIGINAL RESEARCH PAPERS Hollenstein K. *et al.* Structure of class B GPCR corticotropin-releasing factor receptor 1. *Nature* **499**, 438–443 (2013) | Siu, F. Y. *et al.* Structure of the human glucagon class B G-protein-coupled receptor. *Nature* **499** 444-449 (2013)
FURTHER READING Sexton P. M. & Wootten, D. Structural biology: meet the B family. *Nature* **499**, 417–418 (2013)

BRASSINOSTEROID RECEPTOR ACTIVATION

Brassinosteroids are hormones that are important for plant growth, development and immune responses. They are sensed by the transmembrane receptor kinase BRASSINOSTEROID INSENSITIVE 1 (BRI1) when they bind to its extracellular Leu-rich repeat (LRR) domain. Brassinosteroid binding to BRI1 is known to induce conformational changes that create a platform in BRI1 for co-receptor binding. Somatic embryogenesis receptor kinases (SERKs; which are also receptor kinases with LRR ectodomains) have been implicated in mediating brassinosteroid signalling, and their size and membrane localization makes them BRI1 co-receptor candidates. This study reveals that BRI1 and SERK1 interact to activate BRI1 signalling. The authors solved the crystal structure of a ternary complex formed by BRI1, the LRR ectodomain of SERK1 and the hormone at 3.3 Å resolution. Their findings indicate that the SERK1 LRR domain forms an integral part of the ligand-binding pocket of the receptor and thus that BRI1 and SERK1 interact in a ligand-dependent manner. Therefore, the activation of the cytoplasmic kinase domain of BRI1, the underlying mechanism of which was unclear, involves BRI1–SERK1 heterodimerization following extracellular hormone binding at the cell surface.

ORIGINAL RESEARCH PAPER Santiago, J., Henzler, C. & Hothorn, M. Molecular mechanism for plant steroid receptor activation by somatic embryogenesis co-receptor kinases. *Science* http://dx.doi.org/ 10.1126/science.1242468 (2013)