Jochen Balbach, Chem Sci J 2017, 8:3 (Suppl)
DOI: 10.4172/2150-3494-C1-010

Jochen Balbach

Martin-Luther-University Halle-Wittenberg, Germany

Conformational plasticity of the GPCR activating parathyroid hormone

The Parathyroid Hormone (PTH) from glands controls the blood calcium and phosphate level via its G-protein coupled receptors (GPCR). PTH, an 84-residue peptide, is intrinsically disordered and adopts an α-helical conformation for N-terminal residues 15-34 upon binding to the extra cellular domain of the receptor. These residues form the core cross-β structure in fast forming amyloid fibrils, which is possibly a storage form of the PTH hormone and thus a functional amyloid conformation. NMR-detected phosphorylation at the N-terminus of PTH by cell-lysate of parathyroid glands still allows hormone binding to the ectodomain but abolishes GPCR activation *in vivo*. The same inhibition can be achieved by a Zn^{2+} anthracenyl-terpyridine complex binding to the N-terminus of PTH. PTH (1-34) is already an approved drug against osteoporosis, where this Zn^{2+} coordination complex now allows to control receptor activation not by targeting the receptor itself but at the level of its agonist. The N-terminal residues of PTH thus can adopt various functional conformations depending on the local environment including binding partners, posttranslational modifications, or amyloid fibrils, and we found a conformation selective metal coordination complex to inhibit receptor activation.

Biography

Jochen Balbach has completed his PhD in Organic Chemistry at the University of Munich, Germany, before he moved to the University of Oxford, UK, and later University of Bayreuth, Germany, to develop NMR methods to follow protein folding reactions at molecular resolution. Since 2004, he is working as a Professor for Biophysics at the University of Halle, and interested in the Structural Biology of proteins mainly studied by NMR spectroscopy, the Biophysics of protein folding, and working on many systems including amyloid forming peptides and proteins, chaperones, GPCRs, ankyrin-repeat proteins, membrane shaping proteins, crystallins, and their post-translational modifications.

jochen.balbach@physik.uni-halle.de

Notes: