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Crystal structure of rhodopsin bound to arrestin by femtosecond X-ray laser

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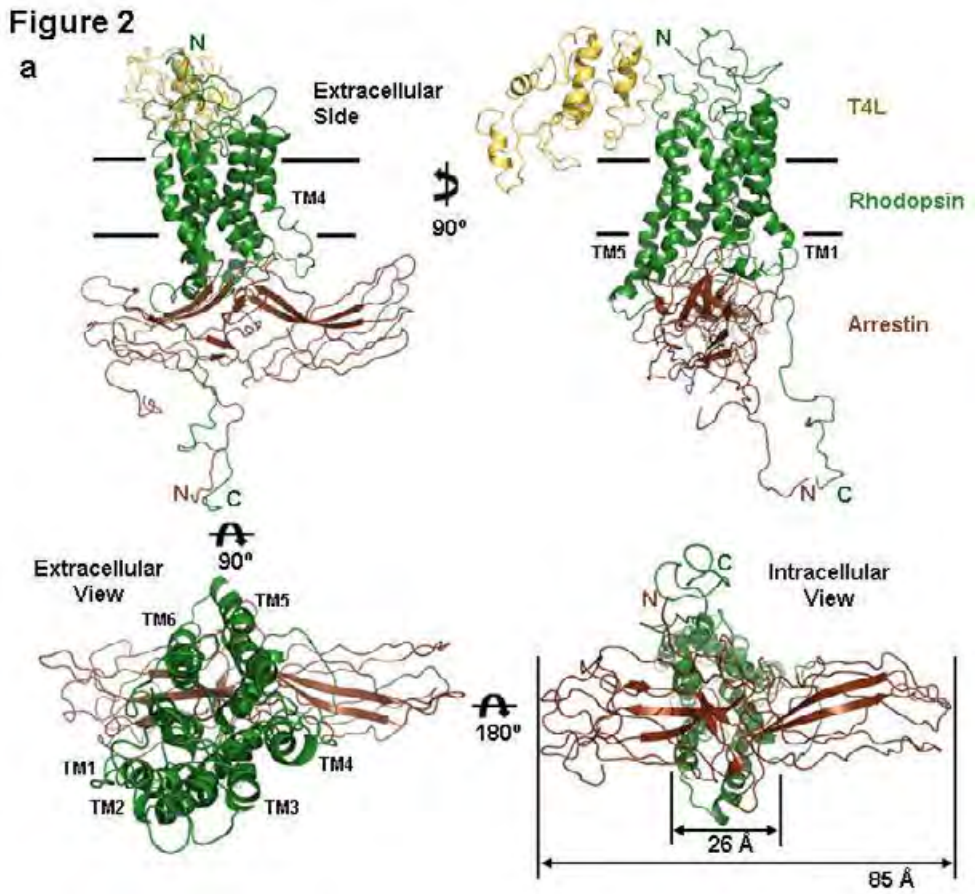
G protein-coupled receptors (GPCRs) signal primarily through G proteins or arrestins. Arrestin binding to GPCRs blocks G protein interaction and redirects signaling to numerous G protein-independent pathways. One structure of a GPCR bound to a G protein was solved, but the structure of a GPCR-arrestin complex has remained unknown despite its central role in GPCR biology. Here we report the crystal structure of a constitutively active form of human rhodopsin bound to a pre-activated form of the mouse visual arrestin, determined by serial femtosecond X-ray laser crystallography. The structure reveals that arrestin binding induces large and unexpected conformational changes at both the extracellular and intracellular sides of rhodopsin. Arrestin also undergoes dramatic rearrangements from its inactive well-ordered β-sheet structure into a more flexible molten globule-type state, allowing a snake-like movement of the first 77 arrestin residues that shortens its central crest finger loop by seven residues to accommodate the concave surface of rhodopsin. This structure provides a basis for understanding GPCR-mediated arrestin-biased signaling, reveals a new paradigm of signal transduction by a molten globule, and demonstrates the extraordinary power of X-ray lasers for advancing the frontiers of structural biology.



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