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Title: Whipping GPCRs into shape for structure determination

Abstract
Over the past 15 years we have determined multiple structures of GPCRs by both X-ray crystallography and cryo-EM. For each GPCR we had to overcome the difficulties of overexpression, solubilisation, stabilisation and structure determination, as you would for any membrane protein. For X-ray crystallography, extensive protein engineering was required to form well-diffracting crystals, in parallel with judicious choices of detergent, ligand and crystallisation format (vapour diffusion or lipidic cubic phase). Different strategies also had to be devised depending on which conformational state was required for structure determination. The advent of high-resolution structure determination by single particle cryo-EM has presented new opportunities for GPCR structural biology, and structures are now being determined that would have been onerous, if not impossible, to determine by X-ray crystallography. I will present the key factors for expression, purification and structure determination that have made GPCR structures possible.