

P011 Development of a non-imaging, homogenous assay format for analysis of arrestin recruitment as a detection method for generic GPCR screening

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Most approaches for GPCR screening involve detection of second messengers in cell-based assays, which differ depending on the receptor coupling mechanism. A generic approach is highly desirable for primary screening, and much interest has focused on β -arrestin for this purpose, particularly with the availability of imaging methods to follow arrestin-GFP fusion proteins. We have developed a generic cell-based screening approach using a modified form of enzyme fragment complementation (EFC) that allows researchers to detect GPCR interactions with β -arrestin. In this approach, the GPCR of interest is expressed with a short C-terminal peptide tag in a clonal cell background expressing a β -arrestin-EA fusion protein. The peptide tag has a weak affinity for the EA fragment, and complementation is only possible when β -arrestin binds to an activated GPCR and brings the two EFC components together. Data will be presented for Gi, Gs and Gq-coupled GPCRs analyzed with this novel screening approach.