The PathHunter™ β-arrestin Assay is a revolutionary assay for monitoring GPCR activation following ligand stimulation, without an imaging instrument, fluorescent protein tag or radioactivity. Instead, the assays detect GPCR activation through movement of β-arrestin to an expressed GPCR of interest, using Enzyme Fragment Complementation (EFC) technology. The GPCR of interest is expressed with a short C-terminal peptide tag in a clonal cell line expressing a β-arrestin-inactive β-galactosidase (β-gal) fusion protein. The peptide tag has a weak affinity for the inactive β-gal fragment and only complements to form active β-gal when β-arrestin binds to the activated GPCR. This approach has been used with over 50 GPCR's and offers a range of benefits including simple single-addition assay format, signal amplification resulting in large assay windows and robust performance. Data will be presented for Gs, Gi and Gq coupled receptors.