Internalization of ligand stimulated GPCRs is a proven and effective means of receptor desensitization. Although an integral part of GPCR pharmacology, quantification of receptor internalization has proven cumbersome and difficult. To overcome these challenges in monitoring cell surface receptor biology, DiscoveRx has developed a generic, fast and reliable assay for chemiluminescent detection of receptor internalization. We have applied this technique to more than 80 GPCR’s. Internalization of the receptor results in a gain of signal, enabling large signal to basal assay windows and a quantitative comparison of compound activity. In this work we demonstrate its utility in identifying strongly internalizing agonist compounds that behave as functional antagonists \textit{in vivo}, as well as weakly internalizing agonists that have prolonged \textit{in vivo} effects. More recently we have applied this technology to monitoring receptor trafficking along biosynthetic routes, in response to pharmacochaperone activity. These assays provide a simple and quantitative tool that can be used for the broad pharmacological characterisation of GPCR signalling and internalisation as an adjunct to existing methods for interrogating compound function.