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## Preface

As our understanding of *G protein-coupled receptor (GPCR) signal transduction* continues to grow, we cannot help but be struck by the emerging complexity and the ability of this receptor superfamily to continually surprise us as new facets are discovered. At the level of the GPCR itself, we are only now beginning to glimpse how receptors might behave in vivo and many fundamental questions still lack definitive answers. For example, are all GPCRs functionally dimeric and how informative are the available crystal structures with respect to the true conformational repertoires of GPCRs? At the post-receptor level, the diversity of signal transduction mechanisms regulated by GPCRs continues to expand. This, of course, includes G protein-independent signaling, leading some to question the appropriateness of the term “GPCR” and suggesting “7TM receptor” may be a better term, dissociating the receptor from an automatic assumption of G protein association and activation. Indeed, how important is G protein-independent GPCR signaling within the cell? Does such signaling extend beyond the recruitment of  $\beta$ -arrestin and the formation of molecular signaling scaffolds? From a pharmacological perspective, much in the GPCR landscape has changed in recent years. The concepts of inverse agonism, protean agonism, and functional selectivity have all required reappraisal of the simple receptor-G protein-effector hierarchy that we have previously viewed in linear terms. Perhaps the greatest change in GPCR research has been the rapid assimilation of the concept of the receptor as allosterically regulated switches allowing (pharmacological) modulation of ligand affinity and the efficacy of receptor-coupling to signaling pathways.

In preparing this third edition of *Receptor Signal Transduction Protocols*, we have attempted to be mindful of the constant evolution of the GPCR field and to deal with methods that allow researchers to address many of these important issues. This has involved the thorough revision of some core chapters, a complete rewriting of others to encompass new technological developments since the publication of the first and second editions, and the commissioning of chapters to expand on previous coverage. We, therefore, see the current edition very much as a companion to previous editions. We are enormously grateful to all our authors, new and old, for generally living with our deadlines and providing excellent and comprehensive methods, as well as the essential “tricks of the trade” that are often needed to troubleshoot new techniques. Finally, we thank the Series Editor, John Walker, for again giving us this opportunity to complement previous editions with a new volume in the *Methods in Molecular Biology* series.

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