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Theme Topic on "Cell Receptors and Signaling"

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Editorial

The Special Issue "Cell Receptors and Signaling"

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This special issue of The Annual Review of Biomedical Sciences (ARBS) brings together a collection of reviews covering distinct aspects of cellular receptor function and signaling, written by a team of authors whose major focus is unraveling the complexities of conversion of extracellular signals into intracellular signals, via cell surface receptors. The Theme Topic "Cell Receptors and Signaling" (http://arbs.biblioteca.unesp.br/index.php/arbs/issue/view/11) includes six contributions, covering discussions about structure, mechanism of action, function and clinical relevance of different cell surface receptors. Altogether, the data point out to important concepts for different receptors and cell/tissue systems which can certainly have impact in terms of screening and discovery of novel mechanisms for clinically validated targets.

The volume starts with a detailed and interesting historical overview of the cholinergic system written by Dr. Alexander G. Karczmar; from the early anatomical studies and application of medicinal plants with cholinergic properties, by shamans, hunters, medicine men and mystics, to the latest discussion of the contribution of muscarinic acetylcholine receptor, members of the G protein-coupled receptor (GPCR) superfamily, to behavioral, psychological and mental function (Karczmar, 2009). Dr. Karczmar is Professor Emeritus of Pharmacology at Loyola University Medical Center, USA, and has devoted more than 6 decades of his life studying various aspects of the cholinergic nervous system.

Next, aspects of the general structure and function of GPCRs, a large and diverse family of membrane proteins whose members participate in the regulation of most cellular physiological processes, is reviewed in detailed by Dr. Laerte Oliveira from Universidade Federal de São Paulo, Brazil (Oliveira, 2009). Emphasis is given on the relationships between structure and function of the family AGPCR, or rhodopsin-like receptors, which represents the most numerous of GPCR families comprising several

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known receptors, including receptor for bioamines, glycoprotein hormones, peptides, opsins and odorant receptors, among others. Dr. Oliveira, an important contributor of the GPCR database [(GPCRDB), http://www.gpcr.org/7tm], presents the paradigma shifts currently occurring in GPCR research, discussing the importance of residue conservation and special motifs in the structure of these proteins. The use of multiple sequence alignment and 3D structures for the analysis of residue conservation and mechanisms of receptor activation is also reviewed.

More details and a critical analysis of the contribution of GPCRs mediating the sense of smell are also presented in this ARBS Theme Topic volume by Dr. Betina Malnic (Universidade de São Paulo, Brazil) and Adriana Mercadante (Universidade Federal do Paraná, Brazil) (Malnic & Mercadante, 2009). The general organization of the main and accessory olfactory systems, the structures of the receptor group in each of these organs and their signaling pathways are reviewed. The authors outline in details interesting aspects of how odorants bind to these receptors, leading to the activation of specific heterotrimeric G-protein, Golf, linked to adenylyl cyclase III. An overview of the mechanisms involved in the smell discrimination of a broader range of volatile molecules is also herein accomplished.

Since the first cloning of GPCR gene sequences over two decade ago, many new members of GPCR family have emerged. Because their ligands have not been identified, the physiological relevance of these "orphan" receptors remains to be defined. Discovery of endogenous molecules that target known or orphan GPCRs may have enormous economic and therapeutic impact. In this ARBS Theme Topic volume, Dr. Andrea Heimann (Proteimax Co., Brazil) and Dr. Emer S. Ferro (Universidade de São Paulo, Brazil) present an overview of the recent advances in the methods for the identification of novel biologically active peptides, with potential ability to activate GPCRs (Heimann & Ferro, 2009). The authors also address recent approaches based on conformational-sensitive antibodies capable to discriminate between active or non-active states of GPCRs, a promising new tool to drug discovery or screening of mechanism of action.

Another interesting aspect of cell surface receptors is their ability to crosstalk to intracellular receptors, inducing finely orchestrated changes in signaling events that link these receptors to different cell functions and, during abnormal cross-talk, to several human diseases. In this ARBS Theme Topic volume, Dr. Christopher Gregory (Clinsys Clinical Research, USA; University of North Carolina, USA) reviews the current understanding of the functional relevance of kinase signaling pathways downstream of epidermal growth factor (EGF) receptor family of tyrosine kinases to prostate cancer cell lines, xenograft tumor models, and prostate cancer patients (Gregory, 2009). The consequences of the biological crosstalk between EGFR and androgen receptor pathways is also discussed, with emphasis on the potential contribution of targeting these signaling pathways to drug development and future applications in therapeutic programs for patients with castration-resistant prostate cancer. Overall, the review provides a good example of how basic science can provide the foundation and knowledge to solve specific clinical questions, translating basic research findings into therapeutic application.

In the closing chapter, Báez-Saldaña, Ingrid Fetter-Pruneda, Gabriel Gutiérrez-Ospina and collaborators from Mexico (Universidad Nacional Autónoma de México, Universidad Michoacana de San Nicolás de Hidalgo and Instituto Nacional de Pediatría) outline how the information approaching the brain in the form of electrochemical codes is translated into biochemical, epigenetic and genetic events which, in turn, contribute to brain plasticity (Báez-Saldaña et al., 2009). In fact, a growing body of reports has indicated the importance of epigenetic events to cell surface receptor and, consequently, to cell function. Here the authors discuss this topic in the context of the involvement of cell surface receptor and downstream signal transduction on neuronal plasticity induced by daily live activity, including exercise or cognitive tasks, such as learning new tricks or memorizing new routes, emphasizing the potential role of epigenetic chromatin remodeling in promoting changes in the organization of neuronal networks and brain gene expression.

Collectively, this ARBS Theme Topic volume covers important aspects of the complex status of research in cell receptor and signal transduction, showing that the present and future challenges of how researchers conduct receptor drug discovery and development remain high. We are grateful to those who contributed to "Cell Receptors and Signaling", including the authors, reviewers, and colleagues, especially to Dr. Gilson Volpato (Editor-in-Chief, ARBS).

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