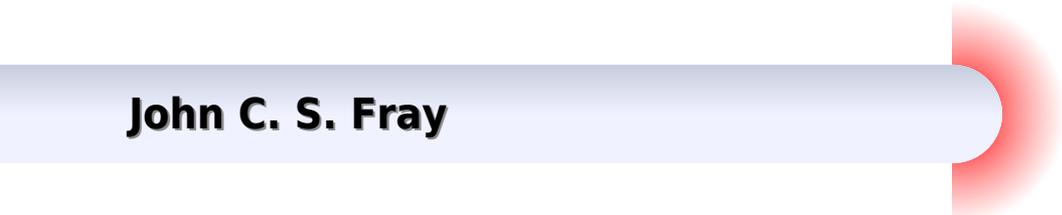


# Calciumsensing Receptor

**John C. S. Fray**



## **Calcium-sensing Receptor:**

*Calcium-Sensing Receptor* Naibedya Chattopadhyay, Edward M. Brown, 2003 Calcium Sensing Receptor provides an overview of various aspects of the calcium receptor's biochemistry, physiology and pathophysiology that is suitable both for those who have been working in the field of  $Ca^{2+}$  sensing as well as those who are new to this discipline. Calcium Sensing Receptor is the nineteenth volume published in the Endocrine Updates book series under the Series Editorship of Shlomo Melmed MD. *The Role of the Calcium-sensing Receptor (CaSR) in Parathyroid Tumorigenesis* Ana Rita Gomes, 2014

*Physiology and Pathophysiology of the Extracellular Calcium-Sensing Receptor* Enikő Kallay, 2018-07-09 Calcium is vital for human physiology; it mediates multiple signaling cascades critical for cell survival, differentiation or death, both as first and as second messenger. The role of calcium as first messenger is mediated by the G protein-coupled receptor, the extracellular calcium-sensing receptor (CaSR). The CaSR is a multifaceted molecule that senses changes in the concentration of a wide variety of environmental factors, including divalent and trivalent cations, amino acids, polyamines, and pH. In calcitropic tissues, with obvious roles in calcium homeostasis such as parathyroid, kidney, and bone, it regulates circulating calcium concentrations. Germline mutations of the CaSR cause parathyroid disorders, demonstrating the importance of the CaSR for the maintenance of serum calcium homeostasis. The CaSR has an important role also in a range of non-calcitropic tissues such as the intestine, lungs, central and peripheral nervous system, breast, skin, and reproductive system, where it regulates molecular and cellular processes such as gene expression, proliferation, differentiation, and apoptosis, as well as regulating hormone secretion and lactation. This Research Topic is an overview of the CaSR and its molecular signaling properties together with the various organ systems where it plays an important role. The articles highlight the current knowledge regarding many aspects of the calcitropic and non-calcitropic physiology and pathophysiology of the CaSR. Investigation of  $Ca^{2+}$  Signal Transduction Pathway(s) in Human Fibroblasts Shixia Huang, 1997 **Stimulus Bias at the Calcium Sensing Receptor** Anna Evelyn Cook, 2013 The calcium-sensing receptor (CaSR), a Family C G protein-coupled receptor (GPCR), is an attractive drug target due to its critical role in systemic mineral homeostasis. The CaSR is activated by a plethora of orthosteric ligands, and the action of these ligands can be modulated by an increasing number of allosteric ligands. Most notably, the positive allosteric modulator of the CaSR, cinacalcet (Sensipar, Mimpara), was the first allosteric compound for any GPCR to reach the market, currently approved for the treatment of secondary hyperparathyroidism (HPT) and primary HPT in cases of parathyroid cancer. Study of the CaSR is complicated by two unique features: chronic exposure to many endogenous ligands and that activation by its primary orthosteric ligand,  $Ca^{2+}$ , occurs over a very narrow concentration range. These two features of the CaSR present a challenge to both the initial optimization of assays to study CaSR signaling and also for the interpretation of agonism and allosteric modulation of the CaSR. Furthermore, study of the CaSR is hampered by a paucity of selective ligands. Therefore, several allosteric ligands of the CaSR were synthesized, and an allosteric receptor model was

modified to investigate the effect of ambient agonist concentrations on concentration response C R curves GPCRs do not exist solely in either an inactive or active state but rather a multitude of conformational states may be stabilised by different ligands stimulus giving rise to preferential association bias that particular intracellular coupling partners The detection of such stimulus bias at a GPCR requires that the receptor has multiple ligands and is promiscuously coupled requirements met by the CaSR Quantification of stimulus bias by allosteric ligands that is the allosteric effects on orthosteric ligand affinity and cooperativity at the CaSR in our HEK293 TREx c myc CaSR cell line was made possible by investigation across multiple signalling pathways intracellular Ca<sup>2+</sup> mobilisation ERK1/2 phosphorylation plasma membrane PM ruffling and cAMP accumulation assays and application of an allosteric receptor model The evidence herein establishes the CaSR as a prime example of a GPCR for which allosteric ligands can bias the signalling pathways activated by orthosteric ligands The current thesis has presented four novel findings First several examples of allosteric ligands engendering stimulus bias at the CaSR have been uncovered including that of a prescribed drug cinacalcet A second finding was the identification of a non interconvertible subset of CaSR with a higher affinity for NPS R568 cinacalcet NPS 2143 as evident in the PM ruffling assay Third mathematical modelling provided a parsimonious explanation for the experimentally observed changes in CaSR C R curve shape changes reflect modulation of the ambient as well as added agonist concentrations Fourth none of the allosteric modulators tested altered the signalling of Ca<sup>2+</sup> to inhibit forskolin induced cAMP production or to recruit beta arrestin1 beta arrestin2 or GRK2 likely due to weak coupling Our findings of stimulus bias at the CaSR imply that further delineation of the desired and undesired CaSR pathways for a given condition coupled with further discovery and development of biased compounds has the potential to sculpt therapeutics with greater selectivity and improved patient outcomes *In Vivo*, 2004

**Thyroid and Parathyroid Diseases** David J. Terris, William S. Duke, 2016-05-25 An up to date reference for managing thyroid and parathyroid diseases Thyroid and Parathyroid Diseases Second Edition has been revised and updated to reflect recent advances in the medical and surgical management of thyroid and parathyroid diseases This new edition serves as both a comprehensive guide to patient evaluation as well as an atlas of advanced surgical techniques for managing patients needing operative intervention Separate chapters are devoted to minimally invasive techniques and remote access robotic thyroidectomy techniques both of which have enjoyed increased application throughout the world New in the second edition A section on state of the art evidence based management of challenging parathyroid conditions such as multiple endocrine neoplasia and renal hyperparathyroidism A more detailed discussion of thyroid cancer evaluation and staging A new chapter dedicated to parathyroid cancer Nearly 200 additional full color illustrations This new edition is a valuable resource for all surgeons endocrinologists and residents seeking to expand their knowledge of thyroid and parathyroid diseases as well as seasoned clinicians who want to improve patient care and incorporate the latest surgical advancements into their practice

**The Calcium-Sensing Receptor (CaSR) as a Potential Mediator of Pollution-induced Airway Cell Responses**

Bethan Mansfield,2022      **Clinical Nephrology** ,2009-07      **Toxicological Profile for Strontium** ,2004      **Expression and function of the extracellular calcium-sensing receptor in pancreatic  $\beta$ -cells** Isidora Kitsou-Mylona,2008  
*Journal of Endocrinological Investigation* ,2005      *Annual Scientific Report* Howard Hughes Medical Institute,1995  
**The Spectrum of Renal Osteodystrophy** Tilman B. Drüeke,Isidro B. Salusky,2001 Bone deformities bone and joint diseases and growth retardation have long been of major concern to adults and children with chronic renal failure because of pain and frequently disabling consequences in terms of physical activity In recent years our understanding of the underlying causes has made major progress In addition new drugs have been developed for the treatment and prevention of the renal bone disease related to renal failure that will benefit those patients affected with these problems      *Epithelial Transport of Ions in Health and Disease* Irene Schulz,2004      *Handbook of Physiology* John C. S. Fray,1977      *CSA Neurosciences Abstracts* ,2000      **Proceedings of the National Academy of Sciences of the United States of America** National Academy of Sciences (U.S.),2007      *Renal and Electrolyte Disorders* Robert W. Schrier,1997 This edition has been updated to reflect the state of the art in the field While the text retains its hallmark clinical focus and organization new research developments in kidney function and dysfunction at the molecular level have been incorporated in virtually every chapter  
Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism Murray J. Favus,1999 Anatomy and biology of bone matrix and cellular elements Skeletal physiology Mineral homeostasis Clinical evaluation of bone and mineral disorders Disorders of serum minerals Metabolic bone diseases Genetic developmental and dysplastic skeletal disorders Acquired disorders of cartilage and bone Paget s disease Extraskeletal ectopic calcification and ossification Nephrolithiasis Dentistry

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