Published in final edited form as:

Cell Calcium. 2014 June ; 55(6): 281. doi:10.1016/j.ceca.2014.04.001.

Preface: SI Ca²⁺ signaling and secretory function

David I. Yule

University of Rochester, Department of Pharmacology and Physiology, Rochester, NY 14642

David I. Yule: David_Yule@urmc.rochester.edu

Preface

The historical importance of studies investigating Ca²⁺ signaling events in the function of secretory epithelia cannot be understated. Indeed, early studies in the exocrine glands of the pancreas and salivary glands established the important role of intracellular Ca²⁺ signals as primary regulatory events in the control of both fluid and protein secretion. These seminal studies also paved the way to establish secretory epithelia as model paradigms for investigation of both the mechanisms underlying the spatial and temporal properties of Ca²⁺ signaling events *per se*, and importantly to the role these specific characteristics play in the subsequent control over the activity of cellular effectors. This Special Issue of *Cell Calcium* provides a unique opportunity for leading authorities in the field to provide a historical perspective and to discuss the state of our current knowledge of the many and varied roles of Ca²⁺ signaling events in the control of function in a variety of secretory epithelia.

Although individual cell types have evolved specific mechanisms to control Ca²⁺ dependent secretion, several common themes shared by a majority of cells are highlighted in these articles. For example, universally the localization of both the Ca²⁺ handling machinery and downstream effectors exhibit highly polarized distributions. This ensures that agonist-stimulation invariably results in Ca²⁺ signals with tightly controlled spatial and temporal properties crucial for the appropriate activation of effectors. In the absence of voltage-gated Ca²⁺ influx, the Ca²⁺ signal often originates from specialized endoplasmic reticulum under the extreme apical plasma membrane. This initial Ca²⁺ release occurs as a function of the distribution of inositol 1,4,5-trisphosphate receptors, but is subsequently “shaped” by Ca²⁺ influx through Orai and TRPC channels and the activity of Ca²⁺ pumps and mitochondrial uptake. The characteristics of the Ca²⁺ signals are thus ideally suited to activate specific populations of ion channels, and/or the exocytotic secretion machinery. Ultimately, the fidelity imparted to the signal effectively guarantees regulated, vectoral secretion of fluid and protein. Evidently “function” tightly follows “form” in secretory epithelial cells. Given that the orchestration of exquisitely patterned Ca²⁺ signals are essential for proper physiological function, a further emerging theme is that aberrant Ca²⁺ signaling is often associated with pathology. Prominent examples in secretory tissues include disease states of

©2014 Elsevier Ltd. All rights reserved.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

the pancreas, salivary glands, liver and airways. In the case of the pancreas, a detailed understanding of the disruption of normal signaling in acute pancreatitis has already provided suggestions for novel avenues of therapeutic intervention to resolve or prevent the disease.

The secretory process is also commonly influenced by multiple signaling inputs. A particularly striking and well-established example is the interaction between Ca^{2+} signaling and the classical cAMP/PKA signaling system. Examples of “crosstalk” to influence the Ca^{2+} signaling machinery, or the activity and localization of transporters and channels important for the secretory process together with emerging ideas regarding the underlying mechanism responsible, are well documented throughout this issue.

It is clear that studies in secretory cells have contributed a great deal to our current understanding of the intricacies of Ca^{2+} signaling events and the processes controlled by this ubiquitous signal. Our intention is that this Special Edition provides a compendium of articles, which provide critical background and insight into Ca^{2+} dependent mechanisms that underlie secretion from a variety of epithelial cells and highlight important topics and areas that should be resolved as the field moves forward.