BioFactors

Editorial

Calcium signaling and disease: Preface

About 120 years have elapsed since the days of the landmark experiment by Ringer that opened the Ca^{2+} signaling area [1]. The experiment was followed by an unusually long period of incubation, after which interest and knowledge in the topic started growing exponentially, eventually establishing Ca^{2+} as a universal carrier of messages to a constantly expanding number of cell function. As knowledge advanced, it gradually became clear that Ca^{2+} has properties that set it apart from all other carriers of biological information. Among them, one could quote the auto regulatory properties of the signal and the ability of Ca^{2+} to act as both a first and a second messenger [2]. But another distinctive property gradually became evident: the ambivalence of the signal. Although it is now clear that cells would not function properly without Ca^{2+} messages, it is also clear that the messages must be delivered to cells and decoded by them, in a carefully controlled way. If cells become somehow unable to control the free concentration of Ca^{2+}, letting it increase persistently in their interior above the optimal 100–200 nM level, all Ca^{2+} controlled activities would become permanently activated, including those (e.g., proteases) that are potentially harmful to cells. Various degrees of damage, up to cell death, would inevitably ensue. Cells may activate rescue attempts: as a rule, however, they only buy time, that is, they enable cells to survive until the emergency disappears. If it does not, however, the cells are doomed.

The massive dysregulation of Ca^{2+} signaling that culminates in the death of cells is a dramatic example of the ambivalent nature of the Ca^{2+} message. The literature describing the numerous ways in which the homeostasis of Ca^{2+} may become so dramatically altered, and the molecular mechanisms by which they terminate cell life has now become impressively large. However, a number of less dramatic conditions have become known more recently, in which the Ca^{2+} signal is not altered globally and persistently to the extent necessary to rapidly precipitate cell death. It is instead altered in more specific ways that only affect individual actors in the control of Ca^{2+} signaling pathways. This is a field that is now expanding very rapidly especially because of the rapid advances in the area of genetics [3]. It will be covered in this Special Issue, which has attempted to collect essentially all what is known today on the dysfunctions of Ca^{2+} controlling systems and of Ca^{2+} signalling pathways. The articles of the issue will describe and discuss critically diseases linked to the dysfunction of membrane transporters, including channels, that control the fluxes of Ca^{2+} in and out of the cell cytoplasm, as well as diseases related to mitochondrial dysfunctions such as the neurodegenerative disorders.

It is hoped that the discussion in this contribution will expand interest, and help suggesting new work, in this very stimulating field.

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References

[1] Ringer, S. (1883) A further contribution regarding the influence of different constitutuens of the blood on the contraction of the heart. *J. Physiol.* **4**,29–43.

[2] Carafoli, E., Santella, L., Branca, D., and Brini, M. (2001) Generation, control, and processing of cellular calcium signals. *Crit. Rev. Biochem. Mol* **36**,107–260.

[3] Calcium Signalling and disease, Molecula Pathology of Calcium, Subcellular Biochemistry Vol. 45, edited by E. Carafoli and M. Brini (2007) Springer.

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