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Preface

STIM1 structure-function and downstream signaling pathways

The critical role of calcium in biological function was first uncovered in the 19th Century by Dr. Sidney Ringer with his recognition that calcium was important to sustain muscle contraction [1]. It took more than 60 years before the critical role of Ca^{2+} in excitation-contraction coupling was clarified. The relatively slow pace of progress primarily reflected the technical challenges; current progress in understanding the generation and function of cytosolic Ca^{2+} signals has been driven by several major discoveries that have made the monitoring of cytosolic Ca^{2+} in virtually any cell type possible. In particular, the recognition by Roger Tsien that EGTA and BAPTA-based compounds exhibit high selectivity for Ca^{2+} over magnesium and protons and exhibit fluorescence changes upon Ca^{2+} binding [2] followed by his design of a non-disruptive strategy for introducing these chemical compounds into cells [3]. Currently, there are dozens of compounds available to monitor cytosolic Ca^{2+} signals in virtually any cellular compartment, with varying affinities and fluorescence properties, facilitating remarkably rapid progress in this field.

This special issue is focused upon STIM1, an ER Ca^{2+} sensor that responds to loss of ER Ca^{2+} content by forming multimers at ER-PM junctions [4], where it activates Orai Ca^{2+} channels and associates with a wide variety of different effectors [5]. This concept that loss of ER Ca^{2+} content would lead to Ca^{2+} entry across the plasma membrane was first proposed by Dr. James Putney in 1986 [6], after which, the Putney demonstrated this concept experimentally [7]. This was followed relatively shortly by direct measurements of store-operated Ca^{2+} current in lymphocytes [8], later named Ca^{2+} release activated Ca^{2+} (CRAC) current [9] as it is commonly known. However, it was not until 2005 that STIM1 was finally identified as a required component of this process, based on 2 independent selective siRNA screens [10,11]. These investigations were followed one year later with the discovery of Orai1 as the pore-forming unit of the CRAC channel [12–14]. These findings led to extremely rapid progress in our understanding of the process of store-operated Ca^{2+} entry, with over 1500 publications in this field over the last 13 years.

The first half of this special issue is focused on structure function relationships. The structure of Orai was first described in 2012 [15]; as a complex multi-domain protein, insights into STIM1 structure came in several different steps. Within this issue, Novello et al focuses on molecular insights into ER Ca^{2+} sensing by STIM1 and STIM2 [16]. Our current understanding of signaling mechanisms underlying STIM-mediated Orai activation are described in Lunz et al [17]. Yen and Lewis reported on our current understanding of STIM-Orai stoichiometry, outlining key evidences in support of 2 distinct models [18]. Finally, Nguyen et al, outlines the value of optogenetics as a novel experimental strategy for probing STIM-Orai function in live cells [19].

The second half of this special issue focuses on the role of STIM/Orai-mediated Ca^{2+} signals in changing cell function. In Nemani et al, recent progress in defining the MCU complex is reviewed, providing a context for control of bioenergetics through Ca^{2+} signals [20]. Go et al discusses EGR-mediated changes in STIM1 and other Ca^{2+} homeostasis proteins as a mechanism for the coupling of Ca^{2+} signals to physiological and pathophysiological functions [21]. Lang et al focuses on the role of SGK1 in control of Orai1 stability through the ubiquitin ligase Nedd4-2 [22]. Finally, in Berry et al, the molecular mechanisms linking STIM/Orai-mediated Ca^{2+} entry and NF-κB activation in lymphocytes are described [23].

In conclusion, we wish to thank all of the authors for their contributions to this volume. We hope that it will be useful for anyone wishing to understand the current state of the store-operated Ca^{2+} signaling field.

References

[1] S. Ringer, A further Contribution regarding the influence of the different Constituents of the Blood on the Contraction of the Heart, J. Physiol. 4 (1883) 29–42 23.
[2] R.Y. Tsien, New calcium indicators and buffers with high selectivity against magnesium and protons: design, synthesis, and properties of prototype structures, Biochemistry 19 (1980) 2396–2404.
[3] R.Y. Tsien, A non-disruptive technique for loading calcium buffers and indicators into cells, Nature 290 (1981) 527–528.
[4] J. Soboloff, B.S. Rothberg, M. Madesh, D.L. Gill, STIM proteins: dynamic calcium signal transducers, Nat. Rev. Mol. Cell Biol. 13 (2012) 549–565.
[5] R. Hooper, E. Samakai, J. Kedra, J. Soboloff, Multifaceted roles of STIM proteins, Pflugers Arch. 465 (2013) 1383–1396.
[6] J.W. Putney Jr, A model for receptor-regulated calcium entry, Cell Calcium 7 (1986) 1–12.
[7] H. Takemura, A.R. Hughes, O. Thastrup, J.W. Putney Jr, Activation of calcium entry by the tumor promoter thapsigargin in parotid acinar cells. Evidence that an intracellular calcium pool and not an inositol phosphate regulates calcium fluxes at the plasma membrane, J. Biol. Chem. 264 (1989) 12266–12271.
[8] R.S. Lewis, M.D. Cahalan, Mitogen-induced oscillations of cytosolic Ca^{2+} and transmembrane Ca^{2+} current in human leukemic T cells, Cell Regul. 1 (1989) 99–112.
[9] M. Hoth, R. Penner, Depletion of intracellular calcium stores activates a calcium current in mast cells, Nature 355 (1992) 353–356.
[10] J. Roos, P.J. Digregorio, A.V. Yeromin, K. Ohlsen, M. Lioudyno, S. Zhang, O. Safrina, J.A. Kozak, S.L. Wagner, M.D. Cahalan, G. Velicelebi, K.A. Stauderman, STIM1, an essential and conserved component of store-operated Ca^{2+} channel function, J. Cell Biol. 169 (2005) 435–445.
[11] J. Liou, M.L. Kim, W.D. Heo, J.T. Jones, J.W. Myers, J.E. Ferrell Jr, T. Meyer, STIM is a Ca^{2+} sensor essential for Ca^{2+}-store-depletion-triggered Ca^{2+} influx, Curr. Biol. 15 (2005) 1235–1241.
[12] S. Feske, Y. Gwack, M. Prakriya, S. Srikanth, S.H. Puppel, B. Tanasa, P.G. Hogan, R.S. Lewis, M. Daly, A. Rao, A mutation in Orai1 causes immune deficiency by abrogating CRAC channel function, Nature 441 (2006) 179–185.
[13] M. Vig, C. Peinelt, A. Beck, D.L. Koomoa, D. Rabah, M. Koblan-Huberson, S. Kraft, H. Turner, A. Fleig, R. Penner, J.P. Kinet, CRACM1 is a plasma membrane protein essential for store-operated Ca^{2+} entry, Science 312 (2006) 1220–1223.
[14] S.L. Zhang, A.V. Yeromin, X.H. Zhang, Y. Yu, O. Safrina, A. Penna, J. Roos, K.A. Stauderman, M.D. Cahalan, Genome-wide RNAi screen of Ca(2+) influx identifies genes that regulate Ca(2+) release-activated Ca(2+) channel activity, Proc. Natl. Acad. Sci. U. S. A. 103 (2006) 9357–9362.

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[15] X. Hou, L. Pedi, M.M. Diver, S.B. Long, Crystal structure of the calcium release-activated calcium channel Orai, Science 338 (2012) 1308–1313.
[16] M.J. Novello, J. Zhu, Q. Feng, M. Ikura, P.B. Stathopulos, Structural elements of stromal interaction molecule function, Cell Calcium 73 (2018) 88–94.
[17] V. Lunz, C. Romanin, I. Frischauf, STIM1 activation of Orai1, Cell Calcium 77 (2018) 29–38.
[18] M. Yen, R.S. Lewis, Numbers count: how STIM and Orai stoichiometry affect store-operated calcium entry, Cell Calcium (2019) in press.
[19] N.T. Nguyen, G. Ma, E. Lin, B. D'Souza, J. Jing, L. He, Y. Huang, Y. Zhou, CRAC channel-based optogenetics, Cell Calcium 75 (2018) 79–88.
[20] N. Nemani, S. Shanmughapriya, M. Madesh, Molecular regulation of MCU: implications in physiology and disease, Cell Calcium 74 (2018) 86–93.
[21] C.K. Go, S. Gross, R. Hooper, J. Soboloff, EGR-mediated control of STIM expression and function, Cell Calcium 77 (2018) 58–67.
[22] F. Lang, L. Pelzl, S. Hauser, A. Hermann, C. Stournaras, L. Schols, To die or not to die SGK1-sensitive ORAI/STIM in cell survival, Cell Calcium 74 (2018) 29–34.
[23] C.T. Berry, M.J. May, B.D. Freedman, STIM- and Orai-mediated calcium entry controls NF-kappaB activity and function in lymphocytes, Cell Calcium 74 (2018) 131–143.

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