Abstract

Magnesium is the most abundant divalent cation in mammalian cells, with multiple roles that are essential for cellular function. Disrupted homeostasis of this metal has been associated with various pathologies including age-related diseases, neurodegeneration, and cancer. However, detailed understanding of the mechanisms by which intracellular Mg$^{2+}$ concentrations are regulated and their role in human health is still lacking, hampered by the paucity of efficient tools for the detection of this ion in the complex environment of the cell. Research in our group focuses on the development of molecular sensors for the study of Mg$^{2+}$ by live-cell microscopy techniques, seeking to shed light on fundamental aspects of magnesium biology. We have developed new fluorescent indicators and cellular labeling techniques for the visualization of Mg$^{2+}$ with improved selectivity and subcellular resolution, which have enabled the study of magnesium dynamics in mitochondria and the uncovering of Mg$^{2+}$ fluctuations in early stages of apoptosis. Furthermore, our studies have revealed that complex binding schemes leading to the formation of ternary complexes may cause some common indicators to co-report on various intracellular species, challenging the interpretation of fluorescent imaging experiments conducted to date. In light of these results, new approaches for the study of magnesium speciation in the cell and new directions in metal sensing by optical methods will be discussed.

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