

INTRACELLULAR INTERDEPENDENCE OF cGMP AND Ca²⁺

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Cyclic GMP (cGMP) and Ca²⁺ ions are key messenger molecules involved together in many physiological processes, including vision, the regulation of blood pressure, the aggregation of platelets, and the function of the heart. The intracellular level of cGMP is a result of the activities of guanylyl cyclases (GCs) and phosphodiesterases (PDEs), while the cytoplasmic concentration of Ca²⁺ ions ([Ca²⁺]_i) depends on the activities of channels, ion exchangers, and pumps. These two groups of proteins are often interdependently regulated by feedback-controlled mechanisms comprising the regulation of cGMP level by Ca²⁺ and conversely, the regulation of Ca²⁺ homeostasis by cGMP. The classic example of such interdependency is phototransduction in the retinal photoreceptors, where the change in [Ca²⁺]_i induced by light is a switch for the retina-specific GC (retGC) activity. At high [Ca²⁺]_i, retGC is inactive, and it is activated at low [Ca²⁺]_i. This regulation of retGC activity is mediated by Ca²⁺-binding proteins of the EF-hand family, referred to as GCAPs (Guanylyl Cyclase-Activating Proteins). However, it is still unknown whether this mechanism is specific only for retinal photoreceptors, since expression of genes encoding GCAP1 and GCAP2 was reported for the chicken pineal gland, GCAP1 was detected in the bovine pineal gland, and we found that GCAP1, and possibly GCAP2, are expressed in the rat pineal gland. Other mechanisms of cGMP-Ca²⁺ interdependency are mediated by cGMP-regulated protein kinases, and were described for different cell types including platelets and vascular smooth muscle cells. Our recent observations suggest that yet another mechanism linking Ca²⁺ and cGMP is present in rat macrophages.