



**I bastoncelli retinici come cellule altamente
specializzate nella fotorecezione : individuazione e
caratterizzazione del metabolismo del cADPR
(Italian Edition)**

Andrea Fabiano

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Cyclic ADP-ribose (cADPR) is a second messenger modulating intracellular calcium levels. We have previously described a cADPR-dependent calcium signaling pathway in bovine rod outer segments (ROS), where calcium ions play a pivotal role. ROS ADP-ribosyl cyclase (ADPR-cyclase) was localized in the membrane fraction. In the present work, we examined the properties of the disk ADPR-cyclase through the production of cyclic GDP-ribose from the NAD⁺ analogue NGD⁺. The enzyme displayed an estimated K_m for NGD⁺ of 12.5 ± 0.3 μM, a V_{max} of 26.50 ± 0.70 pmol cyclic GDP-ribose synthesized/min/mg, and optimal pH of 6.5. The effect of divalent cations (Zn²⁺, Cu²⁺, and Ca²⁺) was also tested. Micromolar Zn²⁺ and Cu²⁺ inhibited the disk ADPR-cyclase activity (half maximal inhibitory concentration, IC₅₀ 5.1 and 3.6 μM, respectively). By contrast, Ca²⁺ ions had no effect. Interestingly, the properties of the intracellular membrane-associated ROS disk ADPR-cyclase are more similar to those of the ADPR-cyclase found in CD38-deficient mouse brain, than to those of CD38 or CD157. The novel intracellular mammalian ADPR-cyclase would elicit Ca²⁺ release from the disks at various rates in response to change in free Ca²⁺ concentrations, caused by light versus dark adaptation, in fact there was no difference in disk ADPR-cyclase activity in light or dark conditions. Data suggest that disk ADPR-cyclase may be a potential target of retinal toxicity of Zn²⁺ and may shed light to the role of Cu²⁺ and Zn²⁺ deficiency in retina

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