Modulation of cytosolic Ca^{2+} signalling by cADPR independent of ryanodine receptors

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The intracellular second messenger, cyclic ADP-ribose (cADPR) regulates Ca^{2+} release from internal Ca^{2+} stores in a wide range of cells, where it is thought to promote Ca^{2+} liberation through ryanodine receptors. However, there is evidence suggesting that cADPR may also modulate SERCA pump activity. We examined this hypothesis by using *Xenopus* oocytes, which lack ryanodine receptors, to study the effects of cADPR on Ca^{2+} transients evoked by photoreleased IP_3 and by influx through plasma membrane channels.

Oocytes were injected either with Ca^{2+} indicator (Fluo-4) and caged-IP_3; or with these compounds plus caged-cADPR. Ca^{2+} transients evoked by photoreleased IP_3 showed no change in amplitude with concomitant photorelease of cADPR, but their decay rate was accelerated. Moreover, this change in kinetics appears to result from modulation of Ca^{2+} sequestration rather than a direct action on IP_3R because the decay of signals evoked by transient Ca^{2+} influx through nicotinic receptor/channels expressed in the oocyte membrane was similarly accelerated.

Our results suggest that cADPR acts through multiple pathways to regulate cellular Ca^{2+} signalling via actions on both Ca^{2+} release channels and sequestration mechanisms.

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