

P017 RII binding to AKAP450 lowers the activation threshold of anchored PKA

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Centrosomes are major microtubule-organizing centers. During S phase, the cell duplicates its centrosome and, as prophase begins, the two daughter centrosomes separate and move to opposite positions in the cell. AKAP450 is localized at the centrosome and functions as a ‘multiscaffolding’ protein by simultaneously associating PKA with other kinases, phosphatases and phosphodiesterases.

We generated CHO clones stably expressing a GFP-tagged PKA that acts as a cAMP sensor. The stable clones show a clear targeting of the fluorescent probe at the centrosome area. When challenged with a cAMP raising agent (forskolin) such cells show a larger fluorescence change at the centrosome than in the cytosol, indicating a higher sensitivity to cAMP of the AKAP450-anchored probe as compared to free probe or probe anchored to other AKAPs. We propose a new mechanism by which anchoring to AKAPs can locally modulate PKA activation. This mechanism may be relevant in the PKA-mediated control of cell cycle progression.