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Meeting abstract

Fluorescence resonance energy transfer (FRET) sensors

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The principle of "fluorescence resonance energy transfer" (FRET) has been exploited in cell biology to demonstrate the interaction of two proteins in living cells. FRET is highly specific and sensitive and allows for the online recording of events that modulate the interaction. We here demonstrate that FRET-based sensor molecules represent an alternative in monitoring receptor-dependent signalling. We have used a sensor for the second messenger cAMP to assess cellular formation of cAMP and to follow receptor activity and its desensitization with sufficient temporal resolution. Compared to standard biochemical means of determining cAMP, which require a large number of cells, the sensor records transient events localized in single cells. We show in primary neurons that cAMP formation triggered by the A_{2A} adenosine receptor occurs in a manner similar to that observed in established models from cell culture. Another way to apply FRET in signal transduction research is in determining the conformational change of signalling proteins. One example is SAP102 (synapse associated protein of 102 kDa) and its binding partner mPINS (mammalian partner of inscuteable). Both proteins are known to form intramolecular bonds and therefore exist in an "open" and "closed" conformation which presumably reflects different activity states in a signalling pathway. For instance, binding of mPINS to the heterotrimeric G protein α subunit $G\alpha_i$ leads to an open conformation. With the use of constructs, where the conformationally active protein regions are tagged with FRET-partner fluorophores, we show that a G protein-coupled receptor may impinge on the folding of these proteins. This may provide a tool to scan for receptors capable of activating an effector as specific as mPINS.