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Meeting abstract



# A membrane network of receptors and enzymes for adenine nucleotides and nucleosides

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Most cells express more than one receptor plus degrading enzymes for adenine nucleotides or nucleosides, and cellular responses to purines are rarely compatible with the actions of single receptors. Therefore, these receptors are viewed as components of a combinatorial receptor web rather than self-dependent entities, but it remained unclear to what extent they can associate with each other to form signalling units. $P2Y_1$, $P2Y_2$, $P2Y_{12}$, $P2Y_{13}$, $P2X_2$, $A_1$, $A_{2A}$ receptors and NTPDase1 and -2 were expressed as fluorescent fusion proteins which were targeted to membranes and signalled like the unlabelled counterparts. When tested by FRET microscopy, all the G protein-coupled receptors proved able to form heterooligomers with each other, and $P2Y_1$, $P2Y_{13}$, $A_1$, $A_{2A}$, and $P2X_2$ receptors also formed homooligomers. P2Y receptors did not associate with P2X, but G protein-coupled receptors formed heterooligomers with NTPDase1, but not with NTPDase2. The specificity of prototypic interactions ($P2Y_1$/$P2Y_1$, $A_{2A}$/$P2Y_1$, $A_{2A}$/$P2Y_{12}$) was corroborated by FRET competition or co-immunoprecipitation. These results demonstrate that G protein-coupled purine receptors associate with each other and with NTPDase1 in a highly promiscuous manner. Thus, purinergic signalling is not only determined by the expression of receptors and enzymes but also by their direct interaction within a previously unrecognized multifarious membrane network.

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