

Meeting abstract

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Sensitization of cAMP formation in a neuron-like cell line

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Differentiation into a nerve cell-like phenotype and growth arrest of SH-SY5Y neuroblastoma cells went along with increased cAMP formation. Both receptor-dependent as well as direct activation of adenylyl cyclase by forskolin were enhanced by at least twenty-fold. Since cAMP controls many processes in nerve cell function and development we have investigated the causal factors and mechanism of sensitization in SH-SY5Y cells. The degree of sensitization depended on pre-incubation of the cells with retinoic acid; however, maximizing the extent of sensitization required the withdrawal of serum from the culture medium. This was necessary for the cells to secrete endogenous substances into the culture supernatant. Because sensitization was blocked by inhibitors of gene transcription we surmised that the autocrine factors were relevant for sensitization and were generated by de novo protein synthesis. A gene expression screen revealed several factor candidates (including *dkk1*, *EphB2*, *NPY*, *VEGFB*); our preliminary data indicated that a combination of these may be needed to induce full sensitization. Our data further suggest that sensitization was not due to up-regulation of stimulatory G proteins or adenylyl cyclase. Rather, the immediate cause may be clustering of the catalyst and its activator G_s . This interpretation is consistent with the effect caused by altering the membrane lipid composition which enhanced and reduced cAMP formation in undifferentiated and differentiated cells, respectively.