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Autotaxin(ATX) is an exo-nucleotide pyrophosphate and phosphodiesterase (NPP) which stimulates tumor cell motility at low nanomolar concentration. We compared the expression of ATX in normal breast and tumor tissues and linked the differential expression of ATX with the invasiveness of breast cancer cells. Cellular ATX mRNA expression was more than 3times higher in breast tumor cells. Breast cancer cells with high invasive and/or metastatic capacity such as MDA-MB 435S and MDA-157 showed relatively higher ATX expression. Overproduction of ATX in MCF7 cells incerased the cell migration response to ATX as a chemoattractant. Takem together, these data suggest that cellular expression of ATX is correlated with growth and invasiveness of breast tumor cells.

[PA1-66] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Homo-or hetero-dimerization of muscarinic receptor subtypes are not mediated by protein-protein interaction through intracellular and C-terminal regions.

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A number of cell surface receptors including G-protein coupled receptors (GPCRs) mediate their actions via dimerization which alters the ligand-binding, signaling and properties of the receptors. GPCR dimerization have shown to occur by various mechanisms such as disulfide linkage, transmembrane domain-involved (noncovalent) interaction or direct interaction through C-terminal tails. Muscarinic receptors which are members of GPCRs may also be arranged in dimeric or oligomeric complexes but their mechanisms are not clear. Here we examined whether muscarinic receptors form homo-oligomer or heteromer by direct protein-protein interactions among the same subtypes or different subtypes using yeast two hybrid system. Each cytoplasmic loop and C-terminal cytoplasmic tail of human muscarinic (hm) receptor subtypes, hm1, hm2 and hm3, were cloned into vectors of two hybrid system and examined direct protein-protein interactions between cytoplasmic domains. We also cloned extracellular loops and N-terminal to reveal the interactions between extracellular loops. No detectable interactions were observed in all Hm/Hm receptor sets tested. These results indicate that the hm1, hm2 and hm3 receptors do not interact directly through hydrophilic intracellular and C- terminal tail domains to form dimer or oligomer. N-terminal of Hm2 also showed no interaction with any extracellular domain. Our study raises the possibility that interactions for dimerization of muscarinic receptors may occur indirectly or require proper conformation or subunit formation.

[PA1-67] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Natural resistance-associated macrophage protein 2(DMT1/DCT1) expression is associated with pH-dependent Lead uptake in astrocytes.

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Nramp2, also known as DMT1 and DCT1, is a 12-transmembrane(TM) domain protein responsible for dietary iron uptake as well as metal ions such as lead, manganese, zinc, copper, nickel, cadmium, and cobalt. In duodenal cells iron transport by Nramp2 occurs by a proton-dependent mechanism. Metal ion overload is toxic and leads to neurodegenerative diseases in CNS. Astrocytes may play a role in the scavenger of toxic divalent heavy metal ions in CNS. The process of lead uptake by Nramp2 was not reported in astrocytes.