ADAM Gene Expression in The Adult CNS and Genetic Aberrations in Cancer Cells

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ABSTRACT

ADAM metalloprotease-disintegrins share a common modular structure of functional domains for proteolytic, cell adhesion, and signaling interactions. The metalloprotease domain of oughly half of the known ADAMs contain an intact consensus metzincin catalytic site, and they are thus thought to function as active metalloproteases. The types of interactions mediated by ADAMs are expressly conspicuous in the CNS. However, the information of ADAM functions in the adult CNS remains fragmentary while the neural ADAM research has mainly been focused at the neural development. Nevertheless, ADAMs are emerging as a major CNS metalloprotease family, implicated in, e. g., alpha-secretase processing of amyloid precursor protein (APP), proteolytic activation of cytokines and growth factors, and ectodomain shedding of cell surface receptors. An important prerequisite for exploration of individual ADAMs is detailed knowledge of their expression in the CNS. Here, an update on CNS ADAM gene expression will be presented, including a novel potentionally proteolytic ADAM. Their dual potential to mediate both proteolysis and cell-cell contacts raises also the question about the involvement of ADAMs in the pathobiology of malignancy. Indeed, ADAMs have been associated with several types of cancer. Here, novel data on genomic rearrangements and aberrant pre-mRNA splicing of ADAM15 will be presented, suggesting that one of the impairments in the genetic machinery in cancer cells may be at the level of post-transcriptional processing.

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