

A ROLE FOR ANTIZYME INHIBITOR 2 IN THE BIOSYNTHESIS AND CONTENT OF SEROTONIN AND HISTAMINE IN MOUSE MAST CELLS

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Polyamines (putrescine, spermidine and spermine; PAs) are essential for the majority of living cells. Antizymes and antizyme inhibitors are key regulatory proteins of PA levels by affecting ornithine decarboxylase and PA uptake. In addition to PAs, mast cells (MC) synthesize and store in their granules histamine (Hia) and serotonin (5-HT), which are critical for their function. Our previous studies have indicated a metabolic interplay among PAs, Hia and 5-HT in this cell type. For instance, we showed that PAs affect Hia synthesis during early stages of IL-3-induced bone marrow cell differentiation into bone marrow derived MCs (BMMCs) and demonstrated that PAs are present in MC secretory granules and are important for granule homeostasis, including Hia storage and 5-HT levels. A few years ago, a novel antizyme inhibitor (AZIN2) was described whose expression is restricted to a few tissues and cell types including brain, testis and MCs. In MCs, it was recently proposed that AZIN2 could act as a local regulator of PA biosynthesis in association with 5-HT-containing granules and with 5-HT release following MC activation. To gain insight into the role of AZIN2 in the biosynthesis and storage of 5-HT and also Hia, we have generated BMMCs from both wild-type and transgenic mice with severe *Azin2* hypomorphism, and have analyzed the content of PAs, 5-HT and Hia, and some elements of their metabolisms. Spermine and 5-HT levels were reduced in *Azin2* hypomorphic BMMCs compared with wild-type controls, whereas the amount of Hia was increased. Accordingly, the level of tryptophan hydroxylase 1 (the key enzyme for 5-HT biosynthesis) was reduced and the amount of enzymatic activity of histidine decarboxylase (the enzyme responsible for Hia biosynthesis) was increased in *Azin2* hypomorphic BMMCs. Taken together, our results show evidence that AZIN2 has an important role in the regulation of 5-HT and Hia biosynthesis and storage in MCs

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