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Poster Sessions

Drug development targeting histamine *N*-methyltransferase

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Brain histamine has a role as a neurotransmitter in the regulation of various physiological functions. Previous studies revealed the involvement of histamine depletion in several neurological disorders, leading to the development of new drugs targeting brain histamine system. Histamine *N*-methyltransferase (HNMT), a histamine metabolizing enzyme, had a great impact on brain histamine concentration, assuming that HNMT inhibition can increase histamine and have a therapeutic effect on various brain diseases. Here, we aimed to reveal the HNMT functions and find new HNMT inhibitors to activate brain histamine system and improve brain functions.

First, we phenotyped HNMT knockout mice. HNMT deficiency increased the amount of brain histamine, indicating the essential role of HNMT in brain histamine. Next, we constructed high-throughput screening (HTS) system to find HNMT inhibitors. Six thousands compounds were applied to the system and 9 compounds (A-I) were selected as candidates. Direct administration into hypothalamus and systemic administration of compound G could increase extracellular histamine. These results demonstrated that compound G was a potential candidate as a new HNMT inhibitor.