Adenosine kinase

Adenosine kinase (AdK; EC 2.7.1.20) is an enzyme that catalyzes the transfer of gamma-phosphate from Adenosine triphosphate (ATP) to adenosine (Ado) leading to the formation of Adenosine monophosphate (AMP). In addition to its well-studied role in controlling the cellular concentration of Ado, AdK also plays an important role in the maintenance of methylation reactions.

Adenosine is tightly controlled through its metabolic enzyme adenosine kinase, which exists in a cytoplasmic (ADK-S) and nuclear (ADK-L) isoform.

Gebril et al. recently discovered that ADK-L contributes to adult hippocampal neurogenesis regulation. Although the cerebellum is a highly plastic brain area with a delayed developmental trajectory, little is known about the role of ADK. Here we investigated the developmental profile of ADK expression in C57BL/6 mice cerebellum and assessed its role in developmental and proliferative processes. We found high levels of ADK-L during cerebellar development, which was maintained into adulthood. This pattern contrasts with that of the cerebrum, in which ADK-L expression is gradually downregulated postnatally and largely restricted to astrocytes in adulthood. Supporting a functional role in cell proliferation, we found that the ADK inhibitor 5-iodotubercidin reduced DNA synthesis of granular neuron precursors in a concentration-dependent manner in vitro In the developing cerebellum, immunohistochemical studies indicated ADK-L is expressed in immature Purkinje cells and granular neuron precursors, whereas in adulthood, ADK is absent from Purkinje cells, but widely expressed in mature granule neurons and their molecular layer processes. Furthermore, ADK-L is expressed in developing and mature Bergmann glia in the Purkinje cell layer, and in astrocytes in major cerebellar cortical layers. Together, our data demonstrate an association between neuronal ADK expression and developmental processes of the cerebellum, which supports a functional role of ADK-L in the plasticity of the cerebellum. Significance statementThe role through which adenosine metabolism functions in the developing and adult cerebellum is poorly understood. Here we investigated the expression and possible function of ADK during cerebellum development. We report that ADK-L expression is associated with cerebellar development and linked to neural progenitor cell proliferation in vitro In contrast to the cerebrum, the adult cerebellum maintained high levels of both isoforms of ADK (L and S) [1)]

1)
Gebril H, Wahba A, Zhou X, Lai T, Alharfoush E, Bloom ED, Boison D. Developmental role of adenosine kinase in the cerebellum. eNeuro. 2021 Apr 14:ENEURO.0011-21.2021. doi: 10.1523/ENEURO.0011-21.2021. Epub ahead of print. PMID: 33863781.