A Genetic Model for Deoxycytidine Kinase Deficiency

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BACKGROUND

Production and maintenance of a balanced pool of deoxyribonucleoside triphosphates (dNTPs) for DNA synthesis is of critical importance for cell division. Cellular dNTP pools are generated by two biosynthetic pathways: *de novo* synthesis and deoxyribonucleoside salvage. Amongst salvage pathway enzymes, deoxycytidine kinase (dCK) has unique properties: it provides cells with all 4 dNTPs required for DNA synthesis (dATP, dCTP, dGTP, dTTP) and activates many pro-drugs that are widely used in cancer, autoimmunity and viral infections such as gemcitabine, fludarabine and cladribine. dCK is highly expressed in hematopoietic/lymphoid cells and is also overexpressed in lymphoid malignancies and in some solid tumors. These properties make dCK an attractive therapeutic and imaging target.

INNOVATION

Researchers at UCLA have generated a novel deoxycytidine kinase (dCK) conditional knockout mouse to better understand the function of the deoxyribonucleoside salvage pathway and identify new therapeutic targets for immune disorders and cancer.

APPLICATIONS

- Develop new therapeutics for cancer and autoimmune disorders
- Identify and characterize agents that bind deoxycytidine kinase and/or modulate its activity
- Identify biological processes in which dCK plays a critical role
- Indentify small molecule dCK inhibitors

STATE OF DEVELOPMENT

The deoxycytidine kinase (dCK) conditional knockout mouse has been generated and validated.

RELATED MATERIALS

- Nucleoside salvage pathway kinases regulate hematopoiesis by linking nucleotide metabolism with replication stress. J Exp Med. (2012)
- Requirement for deoxycytidine kinase in T and B lymphocyte development. Proc Natl Acad Sci U S A. (2010)

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OTHER INFORMATION

KEYWORDS

Research tool, mouse model, deoxycytidine kinase, dCK, knockout mouse, immune disorders, deoxyribonucleoside salvage, cancer

CATEGORIZED AS

- **Research Tools**
  - Animal Models

RELATED CASES

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