NATIONAL CANCER INSTITUTE
Technology Transfer Center

Mice, Organs, and Mouse Alleles Carrying Germline and Conditional Deletions of the Zbtb7b Gene

Summary

The National Cancer Institute (NCI) seeks licensees for a mouse model of CD4+ T cell deficiency. The mice carry alleles with germline and conditional deletions of the Zbtb7b gene encoding the zinc finger transcription factor ThPOK or cKrox, essential for the development and function of CD4+ T cells.

NIH Reference Number

E-226-2022

Product Type

- Research Tools

Keywords

- CD4, Memory T Cell, Helper T Cell, Lymphocyte, Autoimmunity, Infection, Cancer, Oncology, Zbtb7b, Zinc Finger Transcription Factor, ThPOK, cKrox, Transgenic Mice, Bosselut

Collaboration Opportunity

This invention is available for licensing.

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Description of Technology

The Zbtb7b gene encodes the zinc finger transcription factor ThPOK (also known as cKrox) that promotes CD4 lineage differentiation in immature T cells. CD4+ T cells, also known as “helper” T cells, are critical for long-term immunity against pathogens as well as for promoting CD8+ “effector” T cell and effective B cell responses. ThPOK is needed for the development and functional fitness of CD4+ T cells as well as multiple aspects of the immune response to infection. As such, ThPOK offers a potential target for immune regulation. For example, increasing the activity of ThPOK may enhance the efficacy of immunization strategies against infections or cancer; diseases associated with CD4+ T cell deficiency. Alternatively, inhibitors of ThPOK could offer new ways to interfere with

CD4+ T cell activity, offering therapeutic benefit in inflammatory or autoimmune diseases such as multiple sclerosis and rheumatoid arthritis.

Researchers at the National Cancer Institute (NCI) developed mouse alleles carrying germline and conditional deletions of the Zbtb7b gene. These alleles were used to generate mice which demonstrate the Zbtb7b gene is essential for CD4+ T cell development and function. These mice can be used to study the function of ThPOK and the role of CD4+ T cells in the immune system. In addition to generating mice that are homozygous for the Zbtb7b gene deletion, the researchers generated mice that can be beneficial as experimental controls. One such mouse line is heterozygous for the Zbtb7b gene deletion; it carries one wild-type allele and one knockout allele. The other mouse line appears wild-type phenotypically but contains a “floxed” version of the Zbtb7b gene flanked by LoxP sites. It may be used to generate additional conditional deletions for the temporal and spatial regulation of gene expression. Given the importance of CD4+ T cells for the immune system, these mice are applicable to preclinical studies regarding a wide variety of human disorders.

The NCI seeks parties interested in licensing this mouse model, including the mice, organs, tissues, and other derivatives from mice carrying deletions of the Zbtb7b gene.

Potential Commercial Applications

- Research tool to study the role of CD4+ T cells in immune response
- Drug screening and evaluation
- Develop ThPOK inhibitors which could be relevant for inflammatory or autoimmune diseases
- Develop ThPOK activators which could enhance the efficacy of immunization strategies

Competitive Advantages

- Investigate the function of CD4+ T cells in vivo
- Investigate the role of the Zbtb7b gene and its protein product ThPOK in vivo
- Control the expression of the Zbtb7b gene through alleles carrying conditional deletions and/or the floxed allele

Inventor(s)

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Development Stage

- Pre-clinical (in vivo)

Publications

- Vacchio MS, et al. A Thpok-directed transcriptional circuitry promotes Bcl6 and Maf expression to orchestrate T follicular helper differentiation.

[31422869]

Ciucci T, et al. The emergence and functional fitness of memory CD4+ T cells require the transcription factor Thpok. [30638736]

- Vacchio MS, et al. A ThPOK-LRF transcriptional node maintains the integrity and effector potential of post-thymic CD4+ T cells.

[25129370]

Therapeutic Area

- Cancer/Neoplasm
- Infectious Diseases
- Immune System and Inflammation

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