Tissue-Specific Gene Inactivation of Beta-1 Integrin

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BACKGROUND

Beta-1 integrin is a critical member of the large family of integrin proteins necessary for cell-extracellular matrix adhesion and bi-directional signaling across the cell membrane. Conventional deletion of beta-1 integrin from the mouse genome results in embryonic death soon after implantation of the blastocyst. Thus, analysis of beta-1 integrin function beyond post-implantation embryogenesis is not possible in a classic deletion model.

DESCRIPTION

Researchers at the University of California have developed a novel mouse model in which the beta-1 integrin gene can be selectively inactivated in a specific tissue, at a specific time. First, transgenic mice are created by inserting two copies of LoxP, a recognition site for Cre recombinase, within introns of the beta-1 integrin gene. Mice homozygous for this insertion are phenotypically normal and express normal amounts of the Beta-1 integrin protein. These mice can then be mated to other mice containing a gene for Cre recombinase under the control of a promoter that can drive the expression of this enzyme in a tissue-specific and/or temporal manner. Cre recombinase deletes a portion of the beta-1 integrin gene enclosed within the inserted LoxP sites, resulting in mice with selective deletion of beta-1 integrin in a tissue-specific and/or temporal manner.

APPLICATIONS

This invention may be used to analyze the functional importance of beta-1 integrin in specific tissues or cells, such as subsets of lymphocytes (e.g. T-lymphocytes), discrete cells of the vascular system (e.g. smooth muscle cells or endothelial cells), or discrete cells of the heart (e.g. atrial or ventricular cardiac myocytes).

ADVANTAGES

The advantage of the present invention over previous systems, where the beta-1 integrin gene was deleted throughout the genome, is that mice can be analyzed for beta-1 integrin function during the course of normal development or postnatally, in a specific tissue, by controlling the temporal and spatial expression of Cre-recombinase.

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OTHER INFORMATION

CATEGORIZED AS

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