Docket #: S05-018

Mouse Model for Phosphodiesterase (PDE4A) Deficiency

The mammal genome contains four cAMP-specific phosphodiesterase genes, named PDE4A-PDE4D. Major efforts in drug discovery are being devoted to identify inhibitors specific for each PDE4 gene product, the rational for this strategy being the generation of more selective pharmacological compounds with reduced side effects.
To determine the role of PDE4A in different organs and cells, we have inactivated this gene by homologous recombination in mice. This mouse model can now be used to
(a) predict the pharmacological effect of PDE4A-specific inhibitors,
(b) test the specificity of drugs targeting PDE4A at different stages of development, and
(c) identify new targets distal to PDE4 for drug development.

Applications

- This mouse model carrying an inactive phosphodiesterase gene can be used to identify substances that target phosphodiesterases.

Advantages

- The PDE4A-deficient mice allow us to directly determine the effect of PDE4A inhibition in each given tissue or organ. Furthermore, the assessment of the specificity of PDE4A inhibitors has been in the past based exclusively on cell-free assays. The mouse with a null PDE4A gene allows one to dissect the side effects of PDE4A inhibitors under development.

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