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Novel Mouse Lines for Study of Cancer, Wound Healing and Stem Cell Biology

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BACKGROUND

The Dact3 protein plays an important role in oncogenesis, metastasis, wound healing and stem cell biology. Molecular signaling pathways potentially involving Dact3 include the Wnt/ β -catenin pathway, the Wnt/PCP non- β -catenin-dependent pathway, regulation of small GTPase of the Rho family, and pathways involving the Dishevelled signal transduction molecule, such as p120-catenin signaling. Dact3 may also be involved in the regulation of the TGF- β pathway. In vitro and in vivo knockdown models would be very useful for studying Dact3 function in disease but have not been reported to date.

TECHNOLOGY DESCRIPTION

UCSF investigators have generated Dact3 conditional, constitutive and partial knockout mouse lines by making a targeted mutation in the genetic locus corresponding to Dact3, a conserved homolog of the Dapper/Frodo genes originally described in *Xenopus laevis*. This mutation was designed such that the essential second and third exons of the gene are flanked by loxP sites, which allows for their excision by the Cre recombinase protein to render the allele non-functional. ES cells carrying this mutation were made by homologous recombination, and a mouse line derived from the correctly targeted ES cells was created using embryo manipulation techniques. Subsequently, through genetic crosses to a few transgenic lines of mice, several different mouse lines have been created and characterized, including a neo- version of the conditional allele, both neo+ and neo- versions of a constitutive knock-out allele, and a hypomorphic (partial knockout) allele. This invention is a valuable model that enables study of Dact3 gene's roles during development as well as postnatally by making use of Cre and Flipase to partially or fully eliminate the gene in primary tissue culture cell lines, immortalized cell lines or in mouse organs and tissues at specific developmental times by crossing to Cre and/or Flipase-expressing transgenic animals.

APPLICATIONS

- ▶ Study Dact3's role in cancer etiology, pathogenesis, metastasis and invasiveness
- ▶ Study Dact3's role in planar cell polarity pathways involved in wound healing and stem cell biology

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OTHER INFORMATION

KEYWORDS

Dact3

CATEGORIZED AS

- ▶ Medical
- ▶ Disease: Cancer
- ▶ Research Tools

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2012-119-0

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