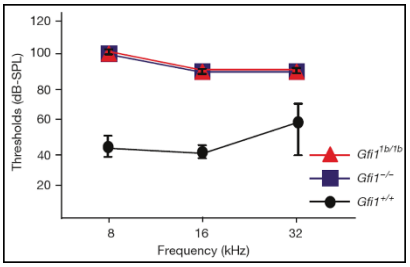
Gfi1$^{1b/1b}$-mouse model

A model for studying hearing loss

Invention

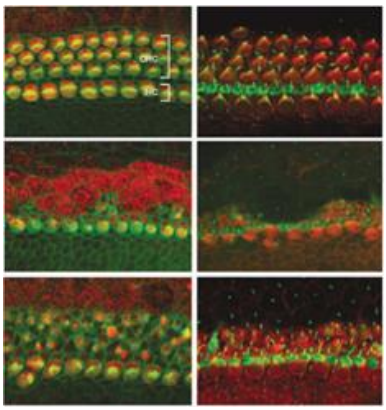
Gfi1 is a transcriptional repressor being expressed in the hematopoietic and nervous system. Loss of function leads to severe defects in hematopoiesis and inner ear development. Gfi1 is highly similar to its paralogue Gfi1b with almost identical sequences in their respective protein domains.



Evaluation of hearing capability:
Auditory brainstem response thresholds of both Gfi1$^{-/-}$ (square) and Gfi1$^{1b/1b}$ (triangle) were determined to be over 100 dB at 8 kHz, whereas wild-typ control mice (circle) were in normal range

A knock-in mouse model was created in which the Gfi1 coding region was replaced by Gfi1b.

The Gfi1$^{1b/1b}$-mice did not exhibit significant defects in the hematopoietic system as previously described for Gfi1$^{-/-}$-mice, suggesting that Gfi1b is able to rescue the loss of Gfi1-function. Interestingly, however, the Gfi1$^{1b/1b}$-mice showed significant defects in inner ear development, i.e. hair cell formation, leading to hearing loss. These results point to some interesting mechanisms on the molecular level for the differentiation and maintenance of hearing. This makes the Gfi1$^{1b/1b}$-model a valuable tool for the development of novel approaches for treating hearing loss.



Expression of hair cell markers in cochlear epithelia:
Left column: Cochlear epithelia of P0-mice was stained with antibody for myosin (red) labelling hair cells cuticular plate/cytoplasm and with phalloidin (green) labelling filamentous actin.
Right column: Respective tissue was stained with antibody for acetylated tubulin (green) labelling heir cell kinocilia and various other tubulin-based structures and with phalloidin (red)
Top: wild-type; mid: Gfi$^{-/-}$; bottom: Gfi1$^{1b/1b}$

Current Status

On behalf of the University of Duisburg-Essen, PROvendis offers access to the mouse model under a Material License Agreement. A matching mouse model of a Gfi1 point mutation, Gfi1$^{P2A/P2A}$ is available as well.

Relevant Publications

Fiolka, K., *et al.* (2006) Gfi1 and Gfi1b act equivalently in haematopoiesis, but have distinct, non-overlapping functions in inner ear development. *EMBO* Reports 7(3): 326-33.

Möröy, T. (2005) The zinc finger transcription factor Growth factor independence 1 (Gfi1). *Int. J. Biochem. Cell Biol.* 37: 541-6.

Wallis, D., *et al.* (2003) The zinc finger transcription factor Gfi1, implicated in lymphomagenesis, is required for inner ear hair cell differentiation and survival. *Development.* 130: 221-32.

Saleque, S. *et al.* (2002) The zinc-finger proto-oncogene Gfi-1b is essential for development of the erythroid and megakaryocytic lineages. *Genes Dev.* 16: 301-6.

An invention of University Duisburg-Essen.

Competitive Advantages

- Mouse model with significant defects in inner ear development
- Valuable tool for the development of novel approaches for treating hearing loss

Technology Readiness Level

1 2 3 4 5 6 7 8 9

Ready-to-market

Industries

- Pharma industry with drug discovery

Ref. No.

2960

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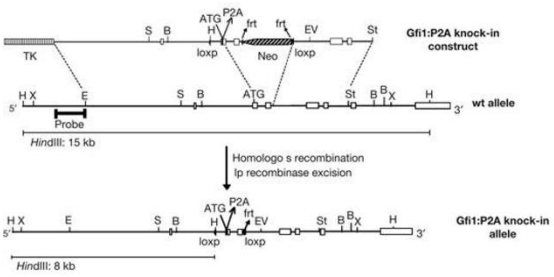
Gfi1P2A/P2A knock-in mouse model

A model to study defects in hematopoiesis and inner ear development

Invention

The Snail/Gfi1 (SNAG) family of zinc finger proteins is a group of transcriptional repressors. Gfi1 is expressed in the hematopoietic and nervous system. Consequently, mutations of Gfi1 cause defects in hematopoiesis and inner ear development. In the Gfi1$^{P2A/P2A}$ mouse strain, a point mutation has been inserted in the SNAG domain that replaces a proline at amino acid position 2 by alanine (P2A). This completely abrogates the activity of Gfi1 as transcriptional repressor.



Knock-in strategy for introducing the P2A mutation into the Gfi1 locus, taken from Fiolka et al. (2006).

Commercial Opportunities

Gfi1 and its paralogue Gfi1b have overlapping, however differential functions in hematopoiesis. Loss of Gfi1 in mice affects pre-T-cell differentiation, the development of neutrophil granulocytes and inner ear hair cells, whereas in contrast loss of Gfi1b impairs the development of erythroid cells and megacaryocytes. Therefore, Gfi1$^{P2A/P2A}$ mice can be used as a model to study and treat deafness as a consequence of defects of inner ear development as well as defects of hematopoiesis in immunological disorders.

Current Status

On behalf of the University of Duisburg-Essen, PROvendis offers access to the mouse model under a Material License Agreement.

A matching knock-in mouse model expressing the Gfi1 paralogue 1b (Gfi1$^{1b/1b}$) is available as well.

Relevant Publications

Fiolka, K., *et al.* (2006) Gfi1 and Gfi1b act equivalently in haematopoiesis, but have distinct, non-overlapping functions in inner ear development. *EMBO Reports* 7(3): 326-33.

Möröy, T. (2005) The zinc finger transcription factor Growth factor independence 1 (Gfi1). *Int. J. Biochem. Cell Biol.* 37: 541-6.

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An invention of the University of Duisburg-Essen.

Competitive Advantages

- in vivo model with significant defects of inner ear development and hematopoiesis:
- study deafness
- develop new approaches to treat deafness
- study immunological disorders

Technology Readiness Level

1 2 3 4 5 6 7 8 9

Ready-to-market

Industries

- Pharma industry with drug discovery

Ref. No.

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