Gata3 knockout mouse is a model for the human HDR deafness syndrome

*Van Doorninck H**, Van Looij M*/**, Van der Wees J***, Van Zanten B**, Grosveld F***, De Zeeuw C*
Departments of *Neuroscience, **ENT and ***Cell Biology, Erasmus Medical Centre, Rotterdam

The transcription factor GATA3 is expressed in several tissues including the brain and the ear. Within the ear expression is found in sensory hair cells as well as supporting cells in the cochlea, in efferent and afferent innervation neurons and in several auditory brain nuclei. Patients that carry only one functional allele of *Gata3* suffer from the hypo-parathyroidism, deafness and renal failure (HDR) syndrome. As GATA3 is expressed in both peripheral and central parts of the auditory system, it is unknown how the deafness in HDR syndrome comes about. To investigate the potential underlying peripheral and central mechanisms we have created *Gata3* mutant mice and subjected them to physiological and histological analysis. Auditory brainstem response (ABR) recordings of GATA3 heterozygous mice (+/-) and wild type littermates (wt) were made through stimulation with clicks and tone pips. As compared to wt littermates, the thresholds of *Gata3* +/- mice were elevated with about 30 dB in all age groups (1-19 month). The inner ear of *Gata3* +/- mice showed initial signs of dysmorphology as vacuoles in outer and inner hair cells. Subsequently, they showed progressive and sequential degeneration first of outer hair cells, then inner hair cells, supporting cells and spiral nerve fibres. These data strongly suggest that the deafness following *Gata3* haplo-insufficiency is caused by inner ear aberrations that lead to reduced responses of the cochlea. Further analysis showed that outer hair cells of *Gata3* +/- mice have reduced otoacoustic emissions. We do not yet know whether the loss of otoaucoustic emissions fully accounts for the observed hearing loss and therefore if other defective cell types contribute to the hearing deficiency. Current microarray experiments will study the differences in gene expression between wt and *Gata3* +/- mouse cochlea's to find the responsible target genes.

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J.Hikke van Doorninck, Dept.Neuroscience, Erasmus Medical Center, P.O.Box 1738, 3000 DR Rotterdam, t 010-4087289, e-mail j.vandoorninck@erasmusmc.nl

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