Technology offer: mouse model for mutant small heat shock protein mimicking human neuropathy and myopathy

The University of Antwerp has developed a mouse model for a mutant small heat shock protein mimicking a human neuropathy and myopathy. Pharmaceutical companies having therapeutic compounds that can be validated can benefit from this mouse model.

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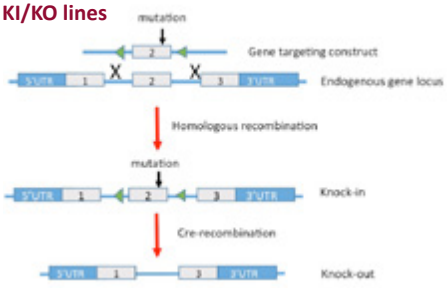
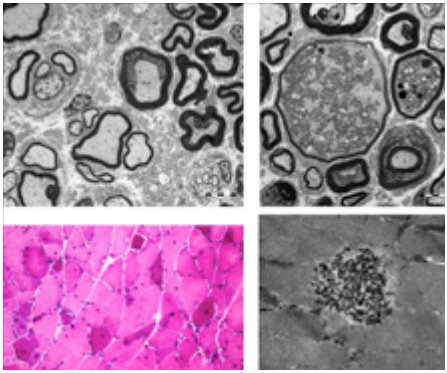
Situation before

Small heat shock proteins (HSPBs) are molecular chaperones with diverse cellular functions. Altered expression of HSPBs occurs in neurodegeneration and cancer. So far no treatment is available to delay or cure patients with neurodegenerative and neuromuscular disorders caused by mutations in the HSPBs. To delineate the molecular deficits and functional consequences of HSPB mutations, we generated a mouse model mimicking a neuropathy and myopathy phenotype. Compound screens have been performed with the aim to target HSPB expression.

Generation of the small heat shock protein KI/KO lines



Nerve and muscle pathology in the KI animals



Technology

We propose a treatment strategy that can rescue or delay neurodegeneration and myopathy. We generated a mouse model mimicking a human distal motor neuropathy by introducing a mutation in an HSPB gene (knock-in mouse). In addition we made a model in which we deleted the same gene (knock-out mouse) and these animals develop a mild myopathy. Finding drugs that can rescue or delay the neurodegeneration observed in the knock-in model, or that can result in a milder phenotype as seen in the knock-out animals, can be beneficial to treat patients affected with neuromuscular disease.

About the researchers - research group

The Peripheral Neuropathy Group gained expertise in mapping and identifying disease associated genes for inherited peripheral neuropathies. We study the effect of mutations on the normal functioning of these genes in neuronal and non-neuronal cell lines, but also in small model organisms. This information is compared to clinical, neurophysiological and neuropathological data which are essential for genotype/phenotype correlations. To unravel the disease mechanisms for sensory and/or motor neuropathies, we identify interacting transcripts and proteins through differential profiling in neuronal and non-neuronal cells, including neurons derived from induced pluripotent stem cells. We make use of mutagenesis and gene editing technologies, and perform transient and stable transformations of diverse cell lines. We apply molecular cell biology tools and phenotype small model organisms that mimic human peripheral neuropathies.

References:
Bouhy et al. Acta Neuropathol. 2018;135(1):131-148
Adriaenssens et al. Brain. 2017;140(10):2541-2549

More information

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