

FIRST PERSON

First person – Aaro Salminen and Lillian Garrett

First Person is a series of interviews with the first authors of a selection of papers published in *Disease Models & Mechanisms*, helping early-career researchers promote themselves alongside their papers. Aaro Salminen and Lillian Garrett are first author on 'Meis1: effects on motor phenotypes and the sensorimotor system in mice', published in DMM. Dr Salminen is a post-doc at the Institute of Neurogenomics at Helmholtz Zentrum München, with a primary focus on modeling human neurological diseases in mice and a special interest in restless legs syndrome. Dr Garrett is part of the German Mouse Clinic and Institute of Developmental Genetics at the Helmholtz Zentrum München and interested in the behavioral and brain abnormalities associated with neurological and neuropsychiatric disease.

How would you explain the main findings of your paper to non-scientific family and friends?

Restless legs syndrome (RLS) is a common neurological disorder characterized by uncomfortable sensations in the limbs, usually at rest, with an urge to move the legs. RLS is highly hereditary and there is data from human studies suggesting that mutations in a gene called *Meis1* may be involved in causing this disorder. Thus, our goal was to reproduce the symptoms that individuals with RLS experience in a mouse model where *Meis1* is genetically modified. We showed that mutant mice were more active than the control animals in the beginning of their sleep period. This is similar to RLS symptoms in humans, which occur in the evening time. Furthermore, we established that this mutation can cause other potentially debilitating changes in behavior that, in the interests of improving quality of life, should be assessed in individuals with a *Meis1* mutation.



Aaro Salminen

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Lillian Garrett

What are the potential implications of these results for your field of research?

Most importantly, we show that knocking out *Meis1* produces an RLS-like phenotype in mice at an older age. In addition, the methods we used have the potential to point the RLS community towards better phenotyping approaches in investigating other potential RLS animal models. Moreover, the phenotypic differences that we see between these *Meis1* haploinsufficient mice and other genetic models of RLS highlight the necessity to stratify individuals with RLS according to their risk haplotypes when considering treatment options.

“Since the diagnosis of RLS is based on an interview, with no objective markers found in humans, developing animal readouts is challenging”

What are the main advantages and drawbacks of the model system you have used as it relates to the disease you are investigating?

We used heterozygous *Meis1* knockout mice in our studies. *Meis1* is the highest-confidence gene associated with RLS in humans, with its downregulation linked to development of the disease. Therefore, the main advantage is its close relation to the human disease on a molecular level. The main disadvantage is the lack of established RLS readouts in animal models. Since the diagnosis of RLS is based on an interview, with no objective markers found in humans, developing animal readouts is challenging.

What has surprised you the most while conducting your research?

Given the genetic complexity of the disorder, it was surprising that haploinsufficiency in one RLS-related gene can already lead to features reminiscent of those observed in humans.

Describe what you think is the most significant challenge impacting your research at this time and how will this be addressed over the next 10 years?

The major challenge in the development of an RLS animal model is the lack of disease-specific readouts. RLS symptoms in humans are subjective and therefore difficult to mimic in animals. Development of new animal phenotyping methods and finding a consensus within

the scientific community focusing on RLS about essential criteria for an RLS animal model will be important in the next few years.

Reference

Salminen, A. V., Garrett, L., Schormair, B., Rozman, J., Giesert, F., Niedermeier, K. M., Becker, L. Rathkolb, B., Rácz, I., German Mouse Clinic Consortium, et al. (2017). *Meis1*: effects on motor phenotypes and the sensorimotor system in mice. *Dis. Model. Mech.* **10, doi:10.1242/dmm.030080.**