## Andrea H Németh

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|  | **Professor Andrea H. Németh****Titles**: Group Leader / PI / Professor of Neurogenetics**Location**: West Wing, John Radcliffe Hospital**Department**: Nuffield Department of Clinical Neurosciences**Group**: Nemeth**Webpage**: https://www.ndcn.ox.ac.uk/team/andrea-nemeth**Email**: andrea.nemeth@ndcn.ox.ac.uk |

### GMS themes:

* Genomic and –omic technologies
* Functional genomics
* Genomics of disease
* Application of genomics in the clinic (diagnostics and therapeutics)

### Research Overview

My Group is interested in understanding how gene mutations contribute to human development and disease, particularly with relevance to the central nervous system. A key area of interest is ataxia, caused by abnormal development or function of the cerebellum or its functional pathways. As a practicing clinician I have access to numerous patients and our research is often based on ideas that are derived from clinical practice. The ultimate aim is to translate our findings back into the clinic, by providing better diagnostics and better treatments for patients and their families.

The main technologies we use in the laboratory are high-throughput sequencing for diagnostics and cellular models of disease using CRISPR/Cas9 gene editing in embryonic stem cells and we have several projects using these technologies.

Project areas: Cerebellar ataxia, intellectual disability, movement disorders, next-generation sequencing, whole genome sequencing, [please include several keywords or phrases reflecting your research area and proposed projects.

Please contact directly for further information.

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Project proposal

Title: ***Missing mutations in cerebellar ataxias***

Supervisors: Prof Andrea Németh

Wet/dry lab mix (approx): 10% wet lab, 90% dry lab (partly depending on results and also on Covid)

### Description:

My group has been extensively involved in the identification of novel genes causing cerebellar ataxias and related disorders (cognitive impairment, other movement disorders, and sometimes related systemic conditions).

The main focus has been on next generation sequencing, most recently whole genome sequencing, and we were the first team in the world to identifying a novel cerebellar ataxia using this technology. Since then we have identified several others.

We have a large cohort of patients with ataxias, but despite being extensively analysed the disease causing mutations have not been identified, even when a genetic cause is the most probable. This is a very common problem and likely reflects limitations of the sequencing technologies being used, the bioinformatics pipelines currently available and our understanding of the human genome.

Some of the data is within the 100,000 Genomes Project and this remains an extremely rich source of mutations which are yet to be identified as well as our own clinical cohorts.

The specific aim of this project would be to access the data within the 100,000 Genomes and search for mutations in novel genes in this group. And additional option would be to investigate these patients using alternative sequencing technologies.

A wide variety of methods are used starting with the analysis of sequencing data and then confirming the findings using a vast array of cellular and functional methodologies, either in our own lab or with collaborators.

### Training Opportunities:

Working within the 100,000 Genomes environment, determining the links between gene mutations and human disease, improving diagnostics, identifying novel cohorts.

### Background reading / references:

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* Parolin Schnekenberg R, Perkins EM, Miller JW, Davies WI, D'Adamo MC, Pessia M, Fawcett KA, Sims D, Gillard E, Hudspith K, Skehel P, Williams J, O'Regan M, Jayawant S, Jefferson R, Hughes S, Lustenberger A, Ragoussis J, Jackson M, Tucker SJ, **Németh AH**, 2015. *De novo* point mutations in patients diagnosed with ataxic cerebral palsy. Brain. **2015**:138;1817-32.
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* Rexach J, Lee H, Martinez-Agosto JA, **Németh AH**, Fogel BL. Clinical application of next-generation sequencing to the practice of neurology. Lancet Neurol. **2019**;18:492-503.
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