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Ataxia and Dystonia: from individual genes to networks and disease mechanisms

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Ataxia and Dystonia:

from individual genes
to networks and disease mechanisms

Miaozhen Huang

university of
 groningen

umcg

**Ataxia and Dystonia:
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The research presented in this thesis was performed at the Department of Genetics, and Expertise Center Movement Disorders Groningen, Department of Neurology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands.

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university of
 groningen

Ataxia and Dystonia: from individual genes to networks and disease mechanisms

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. C. Wijmenga
and in accordance with
the decision by the College of Deans.

This thesis will be defended in public on

Monday 25 October 2021 at 11.00 hours

by

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born on 9 January 1992
in Guangdong, China

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Paranymphs

Michiel Fokkens

Yanni Li

To my dear mother

致亲爱的妈妈

Propositions

1. Rare functional variants in the voltage-gated calcium channel *CACNA1H* are hypothesized but not definitely linked to Writer's cramp. (This thesis)
2. The key to pervasive Purkinje cell degeneration and cerebellar ataxia very likely resides in the unique intracellular characteristics of these neurons compared to other cells in the cerebellum. (This thesis)
3. Tissue-specific gene co-regulation networks are an effective method to identify not-yet-exposed gene functions and their corresponding biological pathways. (This thesis)
4. Synaptic plasticity is a key biological pathway in the shared pathogenesis of ataxia, dystonia and depression. (This thesis)
5. The cerebellum regulates motor coordination and motor function, but it may also play a role in mood processing. (This thesis)
6. With next-generation sequencing, the identification of novel genetic variations in disease genes is relatively easy, but proving causality often remains difficult and requires several layers of evidence. (This thesis)
7. Dysregulated calcium signaling appears to be a potential common theme in the pathogenesis of dystonia. (This thesis)
8. *"Knowledge is power"*.
— Francis Bacon, 1597.
9. *"A handy tool makes a handy man"*.
(工欲善其事，必先利其器).
— Analects of Confucius, Chapter XV: Weil Ling Kung (551–479 BCE).
10. *"It was the best of times, it was the worst of times"*.
— Charles Dickens, A Tale of Two Cities (1812-1870).

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