

University of Groningen

## Exploring the mechanisms underlying the phenotype of MCAD deficiency with Systems Medicine

Martines, Anne-Claire

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2019

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Martines, A-C. (2019). *Exploring the mechanisms underlying the phenotype of MCAD deficiency with Systems Medicine: from computational model to mice to man*. [Groningen]: Rijksuniversiteit Groningen.

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

*Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.*

# STELLINGEN

behorende bij het proefschrift:

## Exploring the mechanisms underlying the phenotype of MCAD deficiency with Systems Medicine

### From computational model to mice to man

1. MCKAT strongly contributes to positive flux control at high substrate concentrations in an isolated, closed-system of rodent mitochondrial fatty-acid oxidation (mFAO) *in silico*. – *This thesis*
2. Particularly pathways containing reactions with CoA- and/or NADP(H) as reactants could play an important role in the phenotype of MCAD-KO mice. – *This thesis*
3. In fasted MCAD-KO mice, cold exposure induces hepatic acyl-carnitine homeostasis, lipid profile remodeling and the use of hepatic amino acids as an alternative fuel source. – *This thesis*
4. CPT1-promiscuity could be an MCAD-deficiency-specific vulnerability that needs to be investigated further *in silico* and *in vivo*. – *This thesis*
5. Asymptotology in MCAD-deficient individuals with loss-of-function MCAD-encoding gene mutations might be a result of efficient medium-chain acyl-carnitine excretion and mFAO flux-increasing adaptation in mFAO protein levels. – *This thesis*
6. Differentiated MCAD-KO HepG2 cells will provide a very practical *in vitro* system to investigate the interplay of the mFAO pathway with surrounding pathways and to validate computer simulations. – *This thesis*
7. The universe is under no obligation to make sense to you. – *Neil deGrasse Tyson*
8. Conformity is the jailer of freedom and the enemy of growth. – *John F. Kennedy*
9. Vulnerability is the birthplace of innovation, creativity and change. – *Brené Brown*
10. Love is a better teacher than duty. – *Albert Einstein*

**Anne-Claire M.F. Martines**

Groningen, 10 juli 2019