

# Mind the gatekeeper

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## Propositions

Accompanying the dissertation

### **Mind the gatekeeper: Key role of NPC1 protein and lysosomal cholesterol in metabolic diseases and therapeutical implications**

1. Dietary supplementation with plant stanols improves lipid metabolism and reduces peripheral inflammation in a mouse model for NPC1 disease (*this thesis*).
2. Hematopoietic *NPC1* mutation, in parallel with a high fat, high cholesterol diet, shifts the profile of the host's intestinal microbiome (*this thesis*).
3. Increasing antibody levels against oxidized LDL via pneumococcal immunization reduces peripheral and neuro-inflammation and improves motor function in a mouse model for NPC1 disease (*this thesis*).
4. Vaccination with a widely used pneumococcal vaccine does not impact levels of antibodies against oxidized LDL in patients with metabolic diseases (*this thesis*).
5. The nature of metabolic diseases is complex and multifactorial. Rather than a "one size fits all" approach, it may be beneficial to consider therapeutic strategies targeting different key disease mechanisms.
6. Tools to efficiently target oxidized LDL merit more research, as they have the potential to prevent and reduce the burden of a wide array of diseases.
7. Further exploring the relationship between host genetics, diet and disease may lead to the development of more efficient diagnostic tools and personalized therapeutic strategies.
8. "Every time you take one path, you must live with the memory of the other: of a life left unchosen. Decide as seems best, one course or the other; each way will have its bitter with its sweet." — Katherine Arden
9. "The possession of knowledge does not kill the sense of wonder and mystery. There is always more mystery." — Anaïs Nin
10. "When you spring to an idea, and decide it is truth, without evidence, you blind yourself to other possibilities." — Robin Hobb
11. "Life is what we make of it. Travel is the traveller. What we see isn't what we see but what we are." – Fernando Pessoa

Inês Andreia Gonçalves Magro dos Reis

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