The link between ceramide transporters, innate immunity and Alzheimer’s disease

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VALORIZATION APPENDIX

Dementia imposes an enormous social and economic burden on society. Over 46 million people suffer from dementia today, and this is expected to increase to 131 million by 2050. The worldwide cost of dementia is estimated to be US $818, and projected to be a trillion dollar by 2018 (1). These statistics make finding new cures for dementia a matter of urgency and importance to the wellbeing of today’s ageing societies and countries healthcare budgets. Unfortunately, although progress has been made towards effective therapeutics, no cure for dementia is currently available. One of the reasons progress towards a cure has been slow is a lack of understanding of the fundamental disease processes.

In this thesis, I describe our research on a novel complement system activator, the ceramide transfer protein. This is the first time it has been shown that CERT is able to activate complement. Our findings with regards to CERT represent an important step in understanding the mechanisms of dementia and other diseases, in which complement activation via C1q plays an important role (such as systemic lupus erythematosus to cancer, kidney disease, organ transplantation, pregnancy disorders, multiple sclerosis and severe trauma (2–6). Modulating complement activation has potential therapeutic applications for these conditions.

The success of potential therapies for dementia depends on their specificity as well as efficiency. In the second part of this thesis, I provide an account of our research on targeting nanoparticles to the brain for drug delivery, where we attempted to identify nanoparticles with the highest specificity. We characterized a range of nanoparticle formulations to have varying specificity towards the brain, showing that this is a promising drug delivery method, albeit in need of further
Valorization appendix

development. As part of this research we also carried out toxicity tests. This type of research *in vitro* and in animals is an important first step to select therapies safe for human use. In spite of not providing clear-cut conclusions, this study is an important increment to the field, on which future research can be built.
The work described in this thesis is a combination of basic research (Chapters 1 to 3 on the role of CERT in complement activation and neurodegenerative disease) as well as research that is more directly applicable (Chapters 4 and 5 on nanoparticle targeting). While governments and other policy makers, especially in the Netherlands, understand the value of applicable biomedical research, they are less and less willing to fund basic science. Budgets are increasingly focused on applied research that has immediate, direct and tangible benefits to society. This is, in my opinion, a worrying trend since basic science is essential to long term technological advancement, prosperity and improvements to healthcare, even if it provides few short term benefits to society. This is illustrated by the way certain important discoveries in biomedical science were made, such as the green fluorescent protein and Taq DNA polymerase. The first, now ubiquitous in practically every laboratory, was discovered by researching how jellyfish glow (7). Taq DNA polymerase, essential for PCR, was discovered thermophilic bacteria, in the context of a study on the thermal control of photosynthesis (8).
Taken together, I am satisfied that the work presented here constitutes contributions to the fields of dementia research and immunology that will bring us a step closer to combating this disease. At the same time I do hope that society will arrive at the conclusion that basic research, however abstract and obscure, is an indispensable element of science.
REFERENCES