The eye as a miRror

Summary

"The eye as a miRror: targeting microRNAs in ocular pathologies" is a doctoral work performed by Quentin Roblain from February 2017 to January 2021 in collaboration between the University of Liège, Belgium (under the supervision of Prof. Dr. Agnès Noël) and Maastricht University, The Netherlands (under the supervision of Prof. Dr. Stephane Heymans). The main goal of this doctoral work was to evaluate the biological implication of microRNAs during age-related macular degeneration (AMD) and diabetic retinopathy (DR).

Vision impairment and blindness affect 2.2 billion individuals worldwide. Despite causing no direct death, vision impairment increases by a factor 3 the risk of being involved in a vehicle collision, the likelihood of suffering from depression and being unemployed. It also doubles the risk of having a fall while walking. AMD and DR are two vision-threatening eye disorders which are currently treated by intravitreal delivery of anti-VEGF drugs. However, patients exhibit great discrepancies in response to this treatment, and no cure for AMD and DR are available. MicroRNAs, a class of non-coding RNAs, have diverse biological functions during development, normal physiology and pathophysiology. These molecules could thus eventually be promising therapeutic targets in eye pathologies. In this work, the biological implication of microRNAs during AMD and DR was evaluated. In **Chapter 1**, every notion needed for a comprehensive reading of subsequent chapters is introduced, reviewed and summarized, microRNAs being the common thread between sections. Thus, a focus is made on their biology, their implication in the developing and adult eye, as well as in the pathological eye and finally, their role in microglia cells. In **Chapter 2**, the suitability of ZSF1 rat model as a model of DR is evaluated. Despite showing hyperglycemia an increased arteriolar tortuosity, the ZSF1 rats failed to develop further diabetic retinopathy. A potential genes network is next highlighted, possibly preventing ZSF1 rats from developing DR. In **Chapter 3**, an expression profile of microRNAs in human and mouse samples and their potential as biomarker or therapeutic target in DR is made and discussed. In **Chapter 4**, specific overexpression of miR-142-3p is revealed in CNV lesion of a mouse model of choroidal neovascularization. Implication of miR-142-3p in activation of microglia cells both *in vitro* and *in vivo* is next demonstrated. Finally, in **Chapter 5**, a global discussion of the present work is made, as well as suggestions of perspectives that might be considered for a better understanding of microRNAs implication in AMD and DR.

In conclusion, this doctoral work presents biological contributions of microRNAs in two eye pathologies, namely age-related macular degeneration and diabetic retinopathy. These findings extend the current knowledge on AMD and DR pathophysiology, and may contribute to the development of novel therapeutic strategies.