RNase L: An Antiviral Endoribonuclease With Potential Roles in Non-Alcoholic Fatty Liver Disease (NAFLD)

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INTRODUCTION

RNase L is part of the interferon stimulated, antiviral 2-5A system which results in the degradation of single stranded RNA. It has been shown in earlier work that RNase L knockout macrophages show decreased migration towards certain chemo-attractants. As a result, this research project focused on how RNase L knockout affects NAFLD progression, a disease where macrophage activity is an important mediator of inflammation and fibrosis

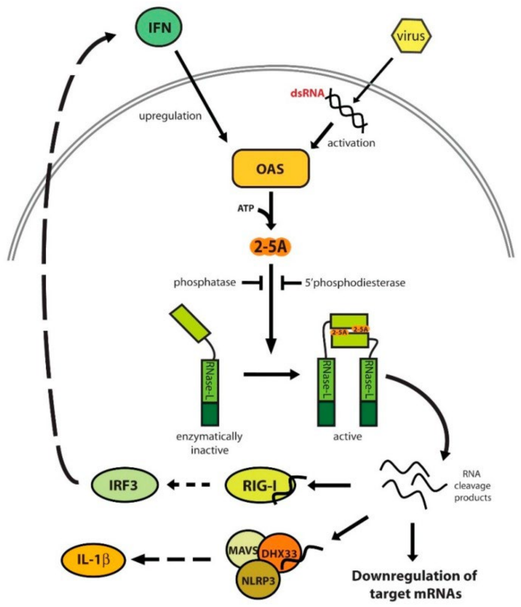

Figure 1: The 2-5A system

OBJECTIVES

The main goal of this project was to see if NAFLD progressed differently in RNase L knockout and wildtype mice. To answer this, several parameters were studied, including immune cell infiltration of the liver and expression levels of inflammatory proteins and those related to fibrosis.

METHODS

- Animal treatment
- Western blot
- IHC staining

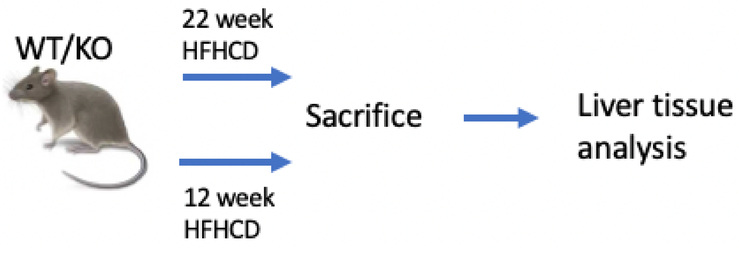

Figure 2. Experimental design

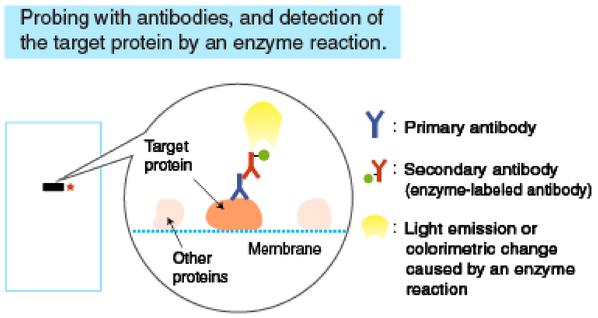

Figure 3. Western blot technique

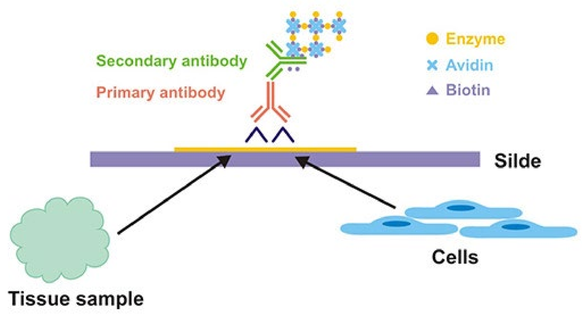

Figure 4. IHC technique

RESULTS

- Decreased expression levels of MMP9, HMGCR, and Notch2 in the knockout mice
- Decreased macrophages, CD4+, and CD8+ cells in the knockout mice

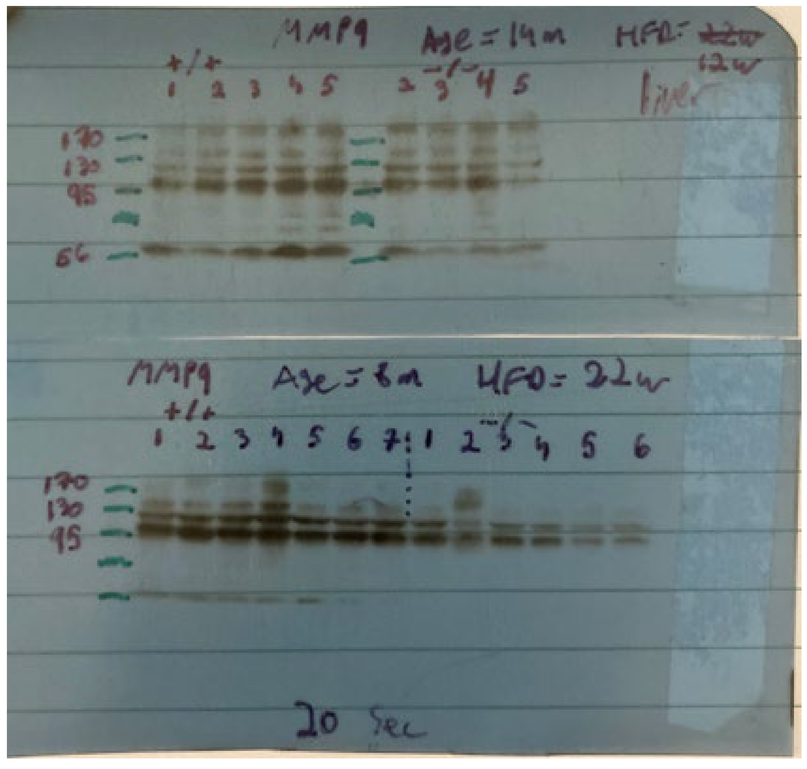

Figure 5. MMP9 western blot

CONCLUSIONS

RNase L knockout mice displayed lower expression levels of important proteins within liver tissues, including MMP9, HMGCR, and Notch2, based on western blot results. Additionally, knockout mice showed decreased numbers of macrophages, CD4+, and CD8+ cells in the liver based on IHC stains. This suggests RNase L contributes to their infiltration of the liver during NAFLD.

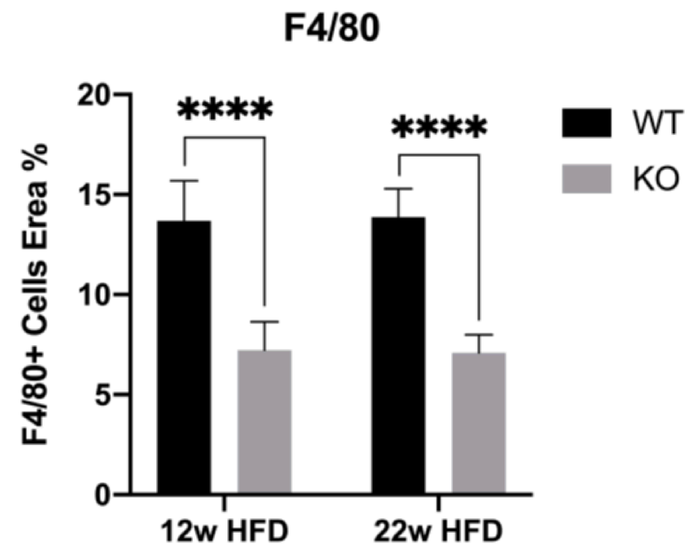

Figure 6. IHC results for macrophage marker

FUTURE WORK

Based on these results, it appears that RNase L inhibitors may be a valuable, novel therapeutic avenue in lessening the severity of NAFLD. Future studies could focus on testing the safety and efficacy of such inhibitors in mice. Additionally, the kidneys of the RNase L knockout mice were visibly a different color and size when compared to the wildtype mice. This interesting observation warrants similar tissue analysis.

References (Calibri, 40 points, bold)

Ezelle, H. J.; Malathi, K.; Hassel, B. A. The Roles of RNase-L in Antimicrobial Immunity and the Cytoskeleton-Associated Innate Response. *Int J Mol Sci* 2016, *17* (1). DOI: 10.3390/ijms17010074 From NLM.

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Acknowledgments

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