Title: 'Time dependent characterization of protein profiles in different tissues induced by chronic infection with lymphocytic choriomeningitis virus´

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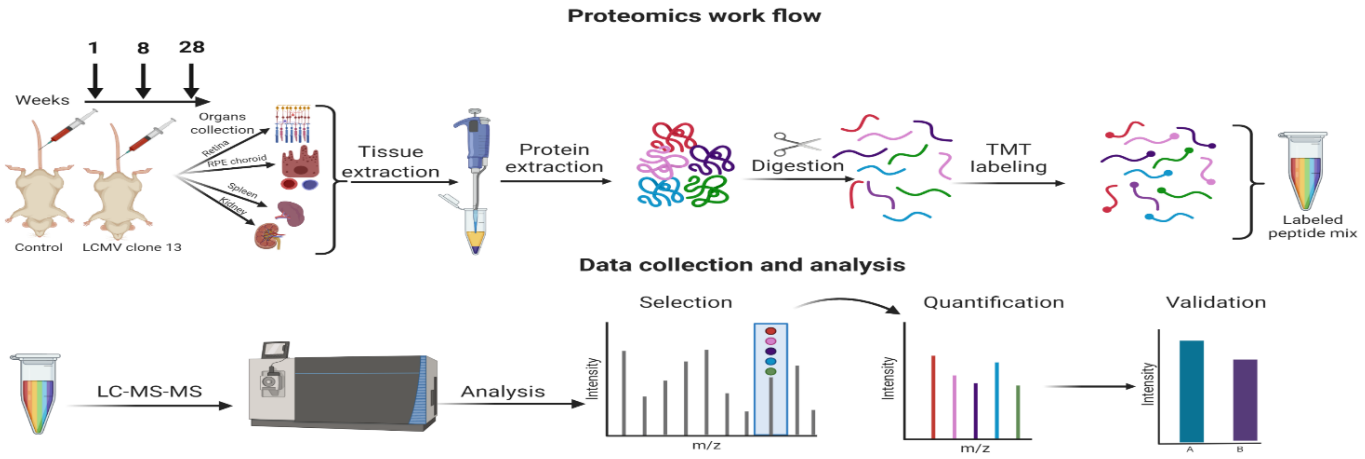

Background

We present a comprehensive discovery-based proteomic investigation of mice with chronic infection of lymphocytic choriomeningitis virus (LCMV) clone 13. To study the cellular complex protein networks in mice, we have applied a global proteome profiling and quantitative proteomics approach to improve understanding of LCMV mediated host immune interactions. We investigated infection with LCMV, which is capable of inducing a chronic infection. We followed the protein changes in a time dependent manner in the different organs and tissues. There were substantial differences in the response of various tissues to the virus.

Methods

Using high resolution liquid chromatography - tandem mass spectrometry (LC-MS/MS) and tandem mass tag (TMT) labelling, we report significant protein changes in different tissues like, retina, RPE-choroid, kidney and spleen in LCMV infected mice at 1, 8 and 28 weeks of infection. Using bioinformatics tools, we observed several protein pathways to be perturbed and associated with LCMV mediated inflammation and disease progression. Validation of the results were done using skyline based targeted proteomics**.**

Results

The effects of the infection on the cellular proteomes varied substantially between the four different tissues. In the retina at 1 week of the infection, we observed no detectable immune response, which, however, became strong at 8 and 28 weeks. Substantial degeneration of photoreceptors was observed early in the infection at 1 week. In the RPE-choroid a strong immune response was detected from week 1 and throughout to 28 weeks. No degeneration was observed initially at 1 week but substantial degeneration

was observed from 8 weeks and some degradation could be detected at 28 weeks. In kidney, a strong immune response was detected throughout the period with initial inhibition of the mitochondrial function and increased degeneration throughout the period. In spleen, no major degeneration was observed in spleen.

Conclusion

Our findings suggest that the response to a systemic chronic infection differs between neuro retina and the RPE/choroid and that the processes induced by systemic infection are not unlike those induced in non-immune privileged organs such as the kidney. Overall, our data suggest that the posterior part of the eye is not an isolated immunologic entity in spite of the existence of immune privilege.