2016Joint Usage and Research Report

Title of Research Project		Dynamic Changes in the Liver Highlight Metabolic Reprogramming in Chronic Viral Hepatitis
Applicant	Institution	Research Center of Molecular Medicine of the Austrian Academy of Sciences (CeMM), Vienna, Austria
	Job title and name	Predoctoral Fellow Alexander Lercher, MSc
Visiting researcher	Name	Alexander Lercher
Purpose of the Research Project (approx. 250 words)		Viral infections represent major challenges for human health. It is well established that the innate phase of infections, such as type I interferon (IFN-I) signaling plays a crucial role in early viral hepatitis and contributes to the establishment of chronic viral infections. In a systems biology approach, we integrated transcriptomic, proteomic and metabolomic changes in the liver to find distinct metabolic changes that might serve as specific footprints for different phases of infection. These central metabolic nodes indicate potential novel targets for therapeutic intervention in chronic viral infection and hepatitis.
Development of the Research Project and Results (approx.. 850 words)		The chronic murine infection model of lymphocytic choriomeningitis virus (LCMV) is a benchmark model of immunology and has led to many seminal discoveries. LCMV Cl13 establishes a chronic viral infection and causes T cell mediated hepatitis. To identify IFN-I-mediated in hepatocytes metabolic changes we combined the LCMV model with a cell-specific Ifnar1 targeted mouse model. Hepatocyte-specific interference with IFN-I signaling identified central metabolic nodes that are specifically modulated by IFN-I. Clustering of these IFN-I regulated nodes in hepatocytes identified genes that are specifically regulated in the innate phase and such that remain changed throughout the chronic phase of infection. Major changes could be observed in amino acid and fatty acid related pathways that are also major metabolic processes in hepatocytes. Next steps will include a targeted metabolomics approach to

	metabolite changes in liver tissue in this model system. This will help to pinpoint metabolic footprints that are dependent on IFN-I signaling in hepatocytes. Knowing metabolic signatures that are mediated by a certain cytokine or specific for different phases of infection will impose a new opportunity for therapeutic intervention that are not restricted to viral infections.
Publication *Enter the names of conference or journal and its vol. No. where the above work was presented.	【Conference, symposium, workshop etc.】 Conference on Infection, Immunity, Cancer and Inflammation, Institute of Genetic Medicine, Hokkaido University, Sapporo, Japan.
	【Journals】