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To whom it may concern,

I would hereby like to report how I have utilised the grant I was lucky to receive from Linnéakademiens Forskningsstiftelse in 2017. The contribution amounted to 10 000 SEK and was requested with the aim of establishing a collaboration between the research groups of prof. Dr. Michael Lindberg (Kalmar) and Dr. Varpu Marjomäki (Jyväskylä) to study early entry and infection progression of enteroviruses.

During the first month, we focused on trying to pinpoint the host cell genes involved in the replication of coxsackievirus B2 (CVB2), a pathogen associated with myocarditis, meningitis, and diabetes. Generally, picornavirus infections are cytolytic in nature, i.e. they enter the cell, replicate, and destroy their host upon exit. However, in rhabdomyosarcoma (RD) cells, CVB2 behaves differently. Instead of activating the apoptosis-pathway and inducing cytolysis of the host cell, the virus is capable of persistent infection, producing progeny without killing the host. Previously, our group has identified a single amino acid mutation in the VP1 region of the virus that changes its replication strategy from persistence to cytolysis. Next-generation sequencing-based transcriptome analysis of the cellular genes in RD cells during CVB2 infection has shown that the gene expression of a large number of genes is very different between persistently infected, cytolytically infected and mock infected cells. Finding out which genes play a role in determining the virus's replication strategy, and if it is possible to modulate these genes in such a way that we can change a persistent infection into a cytolytic one was our next course of action. In collaboration with the group of Dr. Varpu Marjomäki we have tried to modulate the expression of one such gene called Myeloma Overexpressed Gene (MYEOV) which is implicated in cancer cell growth. Unfortunately it appears that this gene is not involved in the process of replication, and altering its expression through siRNA – treatment did not affect virus proliferation. We can therefore cross this option off the list, and we will continue to experiment with other genes.

Prior to my second visit I managed to cultivate the first known Echovirus 30B infectious clone. This pathogen is responsible for the majority of aseptic meningitis cases worldwide (a form of meningitis in which a detectable bacterial infection cannot be proven). Yet, while it causes regular global outbreaks, it has been grievously

overlooked in terms of scientific research, and there is almost no data available aside from some epidemiological studies. During my stay in Jyväskylä we used confocal microscopy to investigate early entry of the virus into the host cells, and managed to elucidate – in part – which pathway the virus uses and which cellular factors are essential for infection and proliferation. Both Dr. Marjomäki and prof. Lindberg are exceptionally fascinated by this unusually aggressive pathogen and excited about the groundbreaking work that we have performed so far. We generated a vast amount of data in a short period of time, and continue this project on two fronts (both in Jyväskylä and in Kalmar). Additionally, due to the promising results, we have also decided to send this virus to prof. Dr. Susan Hafenstein at Penn State University, Pennsylvania, whose group is at this moment in the process of constructing a structural 3D image of E30B. Thus I am hopeful that I will be able to generate a minimum of two qualitative papers – if not more – from this project.

I would once again like to express my gratitude to Linnéakademiens Forskningsstiftelse for offering me this opportunity and allowing me to establish such a valuable research connection with our colleagues in Finland.

With kind regards,

H. Vandesande, PhD – student