Canada where morbidity rates remain high. In a small isolated community, the rate of tuberculosis is 60 times higher than that of the average Canadian Aboriginal population. Previous research demonstrated that significant differences exist in the frequency of cytokine gene polymorphisms maintained by distinct Aboriginal and Caucasian populations in Manitoba. The Dené are a discrete Aboriginal cultural group and recent analysis has shown that this group maintains a high frequency of cytokine gene polymorphisms (TNFa, IL-6, IFNg, IL-10, TGFb) related to an effective Th2 immune response but a less effective Th1 response to infectious diseases. In addition, the Dené have a high frequency of gene polymorphisms in the Vitamin D Receptor gene which may in part, contribute to their susceptibility to tuberculosis. This presentation will describe the analysis of a panel of purported tuberculosis-susceptibility genes (Vitamin D Receptor and cytokine SNPs) from a northern Canadian Dené cohort. The Dené have a unique history and prehistory in relation to other northern Canadian Aboriginal populations and as a result they have preserved their cultural identity and along with that, their distinct immunogenetic profile that is well adapted to a specific pathogen environment.

(18) Malaria *Plasmodium* agent induces alteration in the head proteome of their *Anopheles* mosquito host

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Host behavioural changes induced by parasites that increase the likelihood of parasite transmission has long captured the interest of parasitologists and behavioural ecologists. For instance, in pathogens - insect vector systems, several studies support the idea that pathogen manipulates the behaviour of their vectors, such as feeding behaviour, in a way that increase the contact with the vertebrate host and hence favour the parasites' transmission. Despite increasing evidence of such behavioural changes, the underlying mechanisms causing infected vectors to act in ways that benefit pathogen transmission remain enigmatic in most cases. Here, 2D difference gel electrophoresis coupled with mass spectrometry were employed to analyse and compare the head proteome between malaria (*Plasmodium berghei*) infected mosquitoes and uninfected mosquitoes (*Anopheles gambiae*). This proteomics approach detected 12 protein spots in two cohorts of mosquitoes with altered levels in the head of sporozoite infected individuals. These proteins were subsequently identified using mass spectrometry and functionally classified as metabolic, synaptic, molecular chaperone, signalling, and

cytoskeletal proteins. Our results indicate an altered energy metabolism in the head of sporozoite infected mosquitoes. Some of the up/down regulated proteins identified such as synapse associated protein, 14-3-3 protein, and calmodulin have previously been shown to play critical roles in the central nervous sytem of invertebrates and vertebrates. Furthermore, a heat shock response (HSP 20) and a variation of cytoarchitecture (tropomyosins) have been evidenced. These proteins shed light on potential molecular mechanisms underlying behavioural modifications and offer new insights into the study of intimate interactions between *Plasmodium* and its *Anopheles* vector.

(19) The ORF2 Glycoprotein of Hepatitis E Virus Retro-Translocate from the endoplasmic reticulum to the cytoplasm and down-regulates NF-□B activity in human hepatoma cells

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Keywords: retro-translocation, NF-□B, ER stress, ERAD pathway, I□B□ ubiquitination, ORF2 protein of Hepatitis E virus.

NF-□B is a key transcription factor that has been implicated to play a crucial role in host survival during infection by pathogens. Therefore, it has been a priority of many pathogens to manipulate the cellular NF-□B activity in order to create a favorable environment for their survival inside the host. In this report, we provide evidence for a novel mechanism of inhibition of NF-□B activity, which is mediated by the major capsid (ORF2) protein of the Hepatitis E virus. Heterologous expression of the ORF2 protein in human hepatoma cells was found to inhibit I□B□ ubiquitination by interfering with the assembly of the $SCF^{\square TRCP}$ complex, thus resulting in stabilization of the cellular I□B□ pool, with a concomitant reduction in the activity of NF-□B and its downstream targets. NF-□B inhibitory activity exhibited by the ORF2 protein was found to depend on its ability to retro-translocate from the endoplasmic reticulum (ER) to the cytoplasm, where it was observed to be stably present. Further, retro-translocation of the ORF2 protein was dependent upon the glycosylation status of the protein, mediated in a p97 dependent pathway and independent of ubiquitination of the former. The ORF2 protein, therefore, exploits the ER associated degradation pathway to gain access to the cytoplasm, where it interferes with the I□B□ ubiquitination machinery, leading to inhibition of host cell NF-□B activity.

(20) Development of a Novel Immunome-Based *Candida* Vaccine

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