A new influenza virus which originated from the common pig influenza virus was discovered in spring 2009. This influenza virus is known as ‘swine flu’ or H1N1 and it caused the first influenza pandemic since decades. H1N1 virus has three biologically relevant proteins, hemagglutinin, neuraminidase and the matrix proteins, which are important for viral infection but also for generating protective immune responses. A target for the induction of antibody responses is the hemagglutinin protein. The lack of proofreading activity of a viral replication enzyme (RNA polymerase) and the segmented nature of the viral genome lead to the formation of ‘new’ viral pathogens. This ‘new’ variant flu protein may escape from immune recognition. Mutations may also change the quality and quantity of cellular immune responses, such as production of “hormones” of the immune systems (cytokines) i.e. interferon gamma (IFN-γ). Mutations at the position 225 of the H1N1 hemagglutinin protein have been described. A ‘new’ H1N1 virus with mutations at this position may cause severe and fatal disease associated with high IFN-γ production.

In the current project, I studied thirteen H1N1 positive nasal swab samples which were obtained from individuals who had clinical flu symptoms in Sweden with the aim to find mutations in the H1N1 hemagglutinin and matrix genes. I found fourteen mutations in the H1N1 hemagglutinin gene and two mutations in the H1N1 matrix gene. All mutations were tested for potential binding to the most frequent human major histocompatibility complex (MHC) class I alleles using a specific software (SYFPEITHI) program. Binding of flu peptides to such MHC molecules is required for immune activation. Only 5/14 mutations in the H1N1 hemagglutinin, in positions 100: proline to serine, 220: serine to threonine, 239: aspartic acid to glutamic acid, 338: isoleucine to valine and 314: proline to serine, and both mutations in the H1N1 matrix genes, in positions 23: glutamic acid to lysine and 242: lysine to Glycine showed a high binding score to MHC molecule. These results suggest that the ‘new’ (mutant) viral proteins can impact on immune cell (T-cell) recognition and activation. T-cells activation may lead to IFN-γ production in blood. Therefore, the level of IFN-γ against the H1N1 hemagglutinin and matrix proteins prior to the flu season, about two weeks after onset of symptoms and after the flu season was studied in blood from individuals who tested positive for the mutant H1N1.

The clinical symptoms of these individuals were collected using a web questionnaire. The clinical symptoms, the level of IFN-γ production and mutations in the hemagglutinin and matrix genes were studied. The results suggest that point mutations in the flu virus protein may change immune recognition and impact on clinical symptoms. These possibilities should be tested in future studies, in parallel with analysis of the genetic background of the patients, clinical symptoms and viral mutations.