

Dengue and Chikungunya viruses sensing by immune system

Mindaugas Paužuolis

Dengue (DENV) and Chikungunya (CHIKV) viruses which are transmitted by *Aedes* mosquitos cause potentially lethal disease in humans. For example, DENV infects 80 million people each year in Africa, South America and South East Asia causing mortality and significant loss in productivity. Due to increases in global temperatures, the mosquitos carrying these viruses will be able to survive in a wider geographical area, potentially infecting a larger number of people.

When DENV infects cells, specialized receptors get activated in a host cell. Activation of these receptors through virus-specific molecules triggers an immune response, whereby cells trigger the release signalling molecules known as cytokines in an attempt to limit the infection. It has been shown that known that a protein called toll-like receptor 2 (TLR2), which is a key mediator of the innate immune response, is activated in response to infection by a variety of human viruses including measles and hepatitis C. Therefore we were curious about a potential role for this protein in DENV infection.

Preliminary studies in our laboratory showed that TLR2, expressed at high levels on cells targeted by DENV, was able to sense the virus. My project aimed to elucidate the mechanism of TLR2 activation by DENV following infection. I showed that DENV is recognized by TLR2 and causes activation of a protein called NF- κ B, a potent mediator of the TLR2-activated immune response. All four serotypes of DENV, as well as immature viral particles, activated the transcription factor. This sheds some light on the recognition of DENV by the immune system during infection.

In contrast to DENV, CHIKV causes a milder disease. However, for older people CHIKV infection can lead to development of long term joint pain and disease similar to arthritis. This is a result of aberrant activation of monocytes, a type of white blood cells. Their infiltration into tissues surrounding joints has been postulated to play a role in severe arthralgia that could lead to arthritis. Monocytes are one of our main sentinel cells. These cells are present in all tissues and are the first line of defence in an immune response to invading pathogens. Based on their phenotype and function monocytes can be separated into three different subgroups: classical monocytes, intermediate and non-classical monocytes. CHIKV has been shown to infect monocytes but it is unknown if CHIKV infects all monocytes or a specific subgroup.

The aim of my project was to assess the effect of CHIKV infection on isolated human blood cells and infection in monocytes subsets. The data showed that CHIKV infection increased the overall level of viability of blood cells, but not monocytes. CHIKV also caused an expansion of intermediate monocyte subset. Further studies are needed to assess whether the expansion of intermediate monocytes contribute to the development of arthritis like disease caused by CHIKV infection. Overall, this study contributes to the understanding of how CHIKV infection modulates the immune response.