DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Live cells produce exosomes - tiny bubbles, which can travel long distances in the body and which can be taken up by other cells. Since these vesicles often contain information which may change function and behaviour of those “recipient cells”, exosomes are considered one of the ways in which cells communicate.

We want to look at this communication during infection at body barriers, such as in the skin and mucosa. The majority of cells which are present there are so called “epithelial cells” - these form the lining of the gut, in the respiratory tract or bladder and create a top layer of our skin. Epithelial cells provide the first line defence against invading pathogens such as bacteria, fungi or viruses. We believe that during infection these cells produce exosomes and send the alert message across to the sentinel immune cells (populations which are called “dendritic cells” and “Langerhans cells”), which can then become activated. Activated cells promote a response against the pathogen, mediated by effector cells (T lymphocytes). We think that in this case, the message which is contained in the “bubbles” is provided by an enzyme, called PLA2, which helps sentinels generate specific molecules (new antigens) recognised by the T cells if presented to them on the surface of the sentinel cell, sitting within a protein called CD1a.

We will investigate this basic mechanism of cell communication using the skin as our model, as we can source both the epithelial cells (in this case these are called “keratinocytes”) and the immune cells from the same person. This is much easier with the skin as we can get leftover skin fragments from plastic surgeries, while it would be much more difficult in the case of trying to obtain cells from the gut or bladder. We will carry out experiments to understand how PLA2 is produced and if infection can increase its amount in exosomes, how the cells get activated and how exosomes target the sentinel cells. Since exosomes are very tiny (around a 100nm across) we will also look at them, using so called “super-resolution microscopy”, a technique which enables us to see details much smaller than it was ever possible even with the most advanced microscopes. This technology is ground breaking and was awarded a Nobel Prize in 2014. We will also look into atopic dermatitis (or “eczema”), a disease where keratinocyte function is defective, increasing the chance of those patients to have skin infections.

While we will be using skin samples for experiments, if we discover the mechanism responsible for production of exosomes and immune cell activation in this model, we will be able to understand how exosomes circulating between other type cells and the cells of the immune system everywhere in the body (not only at body barriers) help us clearing the invading pathogens. This, in the future, should help us to create new drugs for long and widespread infections, which will stimulate this communication and will not be antibiotics, so bacteria will not become resistant to them.