

EPD/22/12 - Defining How Cilia Loss Alters The Inflammasome In Polycystic Liver Disease.

The bile ducts are biological tubes within the liver. They transport bile from the liver to the intestine, where it helps digestion. Polycystic liver disease occurs when people have mistakes in their DNA, which affects how cells make bile ducts. Instead of making tubes, these cells make large, spherical-shaped cysts. These cysts are found throughout the liver and patients with these liver cysts have a swollen stomach, live with high levels of pain and increased chance of cysts rupturing and becoming infected. Currently, there is no cure for these cysts and only by understanding how they form and grow will we be able to develop effective treatments.

Most of the DNA mistakes that cause polycystic liver disease affect a part of the cell, called the cilium, which protrudes from the top of the cell to sense the local environment. My work leading to this project has shown that when we remove cilia from bile duct cells livers develop cysts. We have found that after cilia-loss, cystic cells start communicating with immune cells, which normally make sure that your body is protected against infection.

In this project, I will study how cysts talk to immune cells. To do this, I will first develop a system where we can grow cells in a dish and introduce DNA mistakes to see how they change the cilia. I will then look to see if these DNA mistakes cause cystic cells to send out more signals that interact with the immune system.

Once I have identified whether DNA mistakes change the cilia and whether this changes which immune signals are sent out by cyst cells, I will add immune cells to dishes containing my cyst cells and determine whether the signals produced by cyst cells cause immune cells to move towards them. I will also define whether cyst cells cause changes in the immune cells that enable them to support the growth of cysts. Finally, I will use this system to test whether new medicines can be used to stop immune cells from talking to cyst cells to stop cyst growth.

By the end of this project, I hope that I will have established a system which can be used to understand how cyst cells talk to immune cells and identify new ways to prevent cyst growth. These findings will allow me to move to the next stage of my career and study cystic diseases more.