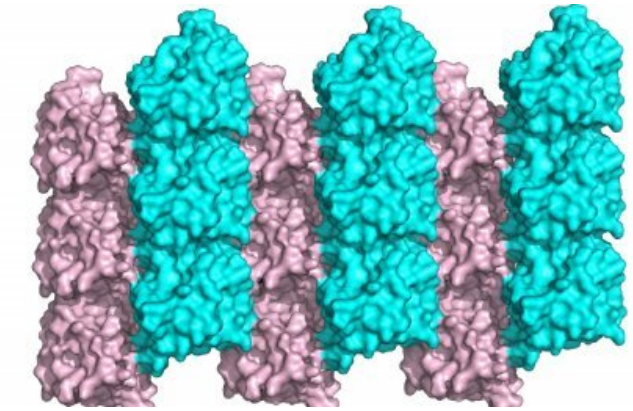
Drug target pathway could unlock treatments for diabetes, cancer and COVID

11 May 2021



The protein studied, MyD88, is a key signalling molecule in innate immunity pathways.

Scientists have visualized and investigated a key molecular pathway that could one day help treat inflammation, diabetes, cancer, infectious diseases and potentially even COVID-19.

The international collaboration, featuring University of Queensland researchers, isolated and studied the MyD88 molecule and found the missing link between immune cell receptors and the body's inflammation response.

UQ's Professor Bostjan Kobe said that he and his colleagues noticed, a few years ago, a gap in understanding what activated inflammation within the body.

"Our immune system triggers inflammation as a protective measure when pathogens or bacteria enter our bodies, but sometimes this defense goes awry and can worsen how our body copes with the disease," Professor Kobe said

"We knew that signals sent from the receptors on the surface of immune cells led to inflammation in the body but didn't understand how this occurred at a molecular level.

"Now we've scrutinized and visualized an incredibly important protein called MyD88.

"This is a key signaling molecule in immunity pathways; its job is to pass a message from the immune cell receptors for the body to trigger an immune response.

"While immunity is clearly needed to fight against pathogens, sometimes the immune system can trigger falsely or hyperactivate an inflammatory response even once the pathogen is gone."

By better understanding how to block this pathway, researchers could be able to treat diseases like rheumatoid arthritis, diabetes, cancer and even COVID-19.

Griffith University's Dr. Thomas Ve said the research was achieved thanks to advancements in molecular visualization and analysis technology.

"Just a few years ago, 'conventional' techniques such as X-ray crystallography weren't able to study these types of proteins," Dr. Ve said.

"We've had to develop and utilize some cutting edge technology, in this case microcrystal electron diffraction and X-ray free electron lasers.

"This is one of the first times microcrystal electron diffraction has been used to determine a new protein structure in this way.

"And this was one of the first comparisons of these emerging structural biology techniques.

"In the end, both of these incredible technologies gave us the world's first clear image of this critical inflammatory target."

The research has been published in *Nature*

Communications.

More information: Max T. B. Clabbers et al. MyD88 TIR domain higher-order assembly interactions revealed by microcrystal electron diffraction and serial femtosecond crystallography, *Nature Communications* (2021). DOI: 10.1038/s41467-021-22590-6