MS02-1-7 Structural characterization of SARS-CoV-2 spike derived peptides presented by the Human Leukocyte Antigen A*29:02
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Abstract
The rapid emergence of SARS-CoV-2 out of Wuhan China in late 2019, has resulted in the current COVID-19 pandemic which has crippled social and economic development worldwide. With over 6.2 million deaths, significant efforts are being made to generate a viable treatment option. It has been well established that T cells destroy cells infected with a virus. These T cells also produce long lasting immunity through the maintenance of memory cells which can recognize future viral invasion.
Activation of T cells is achieved through the Human Leukocyte Antigens (HLA) surface molecule on infected cells. These HLA molecules present viral peptides to T cells that are then able to recognize these as antigens. However, due to the highly polymorphic nature of HLA molecules, it remains unclear how different peptides bound to the vast number of HLA molecules affect the stimulation of the adaptive immune response.
This project focuses on a single HLA, that is HLA-A*29:02, found in approximately 3% of the world population. Here we have structurally characterise a peptide and its Omicron mutated homologue derived from the spike protein. Using X-ray crystallography to solve the structure of a purified peptide complex, we have gained deeper insights into how viral mutation in the Omicron variant is capable of abrogating T lymphocyte recognition by destabilising the bound peptide.
We have solved the first structure of HLA-A*29:02 showing how it present viral peptide, and used stability assay to determine the impact of mutations on peptides presentation to T cells. Overall, this research has furthered our understanding of how our own immune system responds to these antigens. It may also help to develop long lasting therapies such as vaccines which stimulate T cell activation.