Structural characterization of the complex between TIGIT and the Fab of MK684, a novel antibody for immunotherapy

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Immunotherapy is a novel form of treatment in oncology. It contributes to efficient clearance of cancer cells by the patient immune system. This is achieved by down-regulating one of its check points. T cell immunoglobulin and ITIM domain (TIGIT) is an immune receptor which inhibits activation of T- and natural killers (NK) cells upon binding to one of its ligand, CD155 or CD112. Hence disabling the TIGIT-nediated cell signal may have therapeutic applications for cancer treatment. MK7684 is an antibody, currently in phase III of clinical trials, which was selected on the basis of its favorable profile, including high affinity and its ability to block CD155 binding by TIGIT. We have solved the X-ray crystal structure of TIGIT bound to MK7684 at a resolution extending up to 1.23Å (Figure 1), and will present the insights gleaned from the structure, in particular on the antibody mode of action.

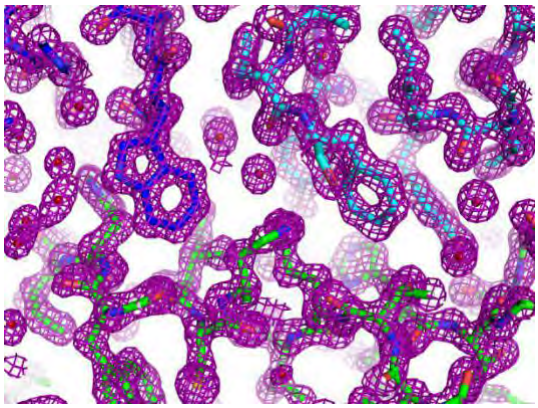

Figure 1. Electron density around the Fab-antigen interface