MS03-P04 | CRYSTAL STRUCTURE OF AN ANTI-TUMOUR ANTIBODY IN COMPLEX WITH A TUMOUR-SPECIFIC ANTIGEN

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When a healthy cell mutates into a cancerous cell, it exhibits altered gene expression and uncontrolled proliferation. These changes can be exploited bycancer immunotherapy for diagnostic and therapeutic purposes. One such tumour-specific antigen is the *N*-glycolyl GM3 ganglioside that is highly similar to the most common ganglioside *N*-acetyl GM3, differing only by a terminal hydroxyl group instead of a hydrogen. It is located on the cell surface of several different tumours, but not in healthy adult human cells [3] The ganglioside is recognised by a monoclonal IgG antibody named 14F7 that was developed at the Centre for Molecular Immunology in Havana, Cuba [2]. To be able to exploit the favourable properties of 14F7 it would be helpful to know precisely how the *N*-glycolyl GM3 ganglioside and the 14F7 antibody interact at a molecular level. To this end, we have generated recombinant 14F7 in scFv format, expressed the protein using a periplasmic expression system and crystallised the scFv [1]. Here, we show how the ganglioside binds to a groove created by the heavy chain CDR H3-loop.

[1] Bjerregaard-Andersen, K., Johannesen,*et al.,* (2018). Crystal structure of an L chain optimised 14F7 anti-ganglioside Fv suggests a unique tumour-specificity through an unusual H-chain CDR3 architecture. *Scientific Reports, 8*(1), 10836.
[2] Carr, A., *et al.,* (2000). A mouse IgG1 monoclonal antibody specific for *N*-glycolyl GM3 ganglioside recognized breast and melanoma tumors. *Hybridoma, 19*(3), 241-247.
[3] Malykh, Y. N. *et al.,* (2001). *N*-Glycolylneuraminic acid in human tumours. *Biochimie, 83*(7), 623-634.