ESRF	**Experiment title**: **Crystal Structure of the Cytostatic Cytokine Oncostatin M**	**Experiment number**: LS-1128
Beamline: BM14	**Date of experiment**: from: 1998 to: 1999	**Date of report**: 01/09/00
Shifts: 3	**Local contact(s)**: Vivian Stojanoff	*Received at ESRF:*

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Report:

Background: The cytokine Oncostatin M (OSM) inhibits growth of certain tumour-derived cells, induces proliferation in other cell types (for example haemangioblasts) and is a mediator of inflammatory responses. Its mechanism of action is through specific binding to the gp130 and LIFR or OSMR receptor systems at the cell surface to form an active signalling complex.

Results: MAD data collected at the ESRF facilitated the structure determination of hOSM. As a result we have published the refined structure of hOSM along with mutagenesis data, which map the receptor binding epitopes of the molecule. The structure was determined to a resolution of 2.2 Å and conforms to the haematopoietin cytokine up-up-down-down four-α-helix bundle topology. The site 2 epitope, responsible for gp130 binding, is centred around Gly 120 which forms a ‘dimple’ on the surface of the molecule located on helices A and C. The site 3 motif, responsible for LIFR and OSMR binding, consists of a protruding Phe 160/Lys 163 pair located at the start of helix D.

Conclusions: The data allowed functional dissection of the receptor binding interfaces to atomic resolution. Modelling suggests that gp130 residue Phe 169 packs into the site 2 ‘dimple’ in an analogous fashion to structurally equivalent residues at the growth hormone/growth hormone receptor interface implying certain key features may underlie recognition across the whole cytokine/receptor superfamily. Conversely, detailed comparison of the available structures suggests that variations on a common theme dictate the specificity of receptor-ligand interactions within the gp130 family of cytokines.