ESRF	**Experiment title:** Neural Cell Adhesion Molecule, NCAM	**Experiment number**: LS-957
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Shifts: 4 and 5	**Local contact(s)**: Gordon Leonard and Andy Thompson	*Received at ESRF:*

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Report:

The neural cell adhesion molecule (NCAM) is a multifunctional glycoprotein belonging to the immunoglobulin superfamily. NCAM is involved in recognition and adhesion between cells from many tissue origins, and appears to be involved in both homophilic and heterophilic binding.

The basis for many NCAM functions is the ability of NCAM on the surface of one cell to recognize and bind to NCAM on the surface of another cell. However, the binding mechanism(s) has not yet been finally established.

Three major isoforms are expressed in brain. Two transmembrane isoforms, and one isoform attached to the membrane via a lipid-anchor. The extracellular part of NCAM in all isoforms consists of five immunoglobulin (Ig) domains and two fibronectin type three (F3) domains.

The adhesive properties of NCAM have been investigated in various research projects on a putative involvement of NCAM in cancer, where intercellular recognition/adhesion is

altered. Results indicate an inverse correlation between increased NCAM-mediated adhesion and the metastatic potential of some cancer cell lines.

We have crystallized the two N-terminal Ig domains of murine NCAM in spacegroup P21, with cell dimensions a=47.2 Å, b=122.7 Å, c=73.1 Å, β=98.3. Native data to 1.85 Å resolution have been collected at BM14.

Resolution (Å)	30-1.85 (1.92-1.85)
Average I/σ(I)	21.9 (3.4)
Redundancy	2.9
Rsym (I) (%)	4.7 (30.8)
Compl. (%)	92.6 (90.0)

Even though the structure of NCAM IgI is known from NMR, derivative data was necessary. We have tested (and collected data on) many derivative crystals, but with consistent non-isomorphy problems. Thus the collection of a full MAD-data set was needed to solve the structure.

In august 1998 we collected a full three wavelength MAD data set at BM14.

Despite a crystal mosaicity of 1.35 degrees, processing and use of the data has been straightforward.

	λ1 (peak)	λ2 (inflec.)	λ3 (remote)
Resolution (Å)	30-2.8 (2.9-2.8)	30-2.8 (2.9-2.8)	30-2.5 (2.6-2.5)
Average I/σ(I)	18.1 (4.4)	20.0 (4.2)	16.0 (2.8)
Redundancy*	2.0	1.8	1.9
Rsym (I) (%)	2.9 (10.7)	3.0 (12.1)	3.4 (16.9)
Compl. (%)	97.5 (92.8)	91.4 (84.6)	96.9 (87.0)

*no Friedel averaging

Four heavy atom sites have been localized and refined, and the 2.8 Å map arising from this solution was readily interpretable. Thus the structure is now solved. Modelbuilding and refinements are currently in progress.

With these results we have gained valuable information about NCAM homophilic binding.