ESRF	**Experiment title:** X-ray crystallographic studies on MHC class I/peptide complexes.	**Experiment number:** LS-297
Beamline: ID2-BIA (test time	**Date of Experiment:** from: 19-July-95 to: 20-July-95	**Date of Report:** 27-Feb-96
Shifts: -3	**Local contact(s):** CCD detector tests: A.P. Hamrnersley, E. Mitchell et	*Received at ESRF:* 04 MAR 1996

Names and affiliations of applicants (*indicates experimentalists):

Dr E.Y. Jones*	Lab. of Molecular Biophysics, Univ. of Oxford.
Dr D.I. Stuart	as above
Dr K. Harlos	as above
Miss K. Smith*	as above
Mr S. Reid*	as above

Report:

Data from this experiment are included in:

1. S.W. Reid, K.J. Smith, B. Jacobsen, C. O'Callaghan, H. Reyburn, K. Harlos, D.I. Stuart, A.J. McMichael, J.I. Bell and E.Y. Jones. (1996) 'Production and crystallization of MHC class I B allele single peptide complexes. *FEBS Let?*. (In the press)

and are central to:

2. S.W. Reid et *al* 'Crystal Structure of Human HLA B8 complexed with an HIV-1 Gag Peptide. (In preparation)

and

3. S.W. Reid, S. McAdam, K.J. Smith, P. Klenerman, C.A. O'Callaghan, K. Harlos, B.K. Jakobsen, A.J. McMichael, J.I. Bell, D.I. Stuart and E.Y. Jones. 'Antagonist HIV-1 Gag Peptides Induce Structural Changes in HLA B8. (Submitted)

1. Abstract (Reid et *al* 1996)

Major Histocompatability Complex Class I B alleles, HLA B8, B53 and B3501 have been cloned, expressed, refolded and crystallized in specific complexes with a number of different 8mer and 9mer peptides. For some of these crystallization was initiated by cross-seeding between different B allele complexes. All crystallize in the space group $P2_12_12_1$, with similar unit cell dimensions of approximately 52 Å x 81 Å x 112 Å contain one complex per asymmetric unit and diffract to approximately 2.0 Å resolution.

2. **Abstract (Reid et *al* in preparation)**

The major histocompatability complex (MHC) Class I proteins, of which B8 is one, are trans-membrane glycoproteins found on the surface of nearly all cells where they present short fragments of degraded proteins for scrutiny by CD8+ cytotoxic T lymphocytes (CTL). The crystal structure of an extracellular fragment of B 8 complexed to the HIV-1 Gag peptide (GGKKKYKL) has been determined to 2.2 Å resolution (data collected on an (XRII)/CCD) and compared with the structures of other Class I molecules. The main features of the peptide binding groove are subsites which accommodate the peptide anchor residue lysines at P3 and P5 in pockets complementing their size and chemistry.

3. Abstract (Reid et *al* submitted)

In the cellular immune response, recognition by cytotoxic T lymphocyte (CTL) T cell receptors (TCRs) of viral antigens presented as peptides by human leucocyte antigen (HLA) class I molecules, triggers destruction of the virally infected cell. Altered peptide ligands (APLs) which antagonise CTL recognition of infected cells have been reported- In one example lysis of antigen presenting cells by CTLs in response to recognition of a HLA B 8-restricted HIV-1 P17 (aa 24-31) epitope can be inhibited by naturally occurring variants of this peptide, which act as TCR antagonists. We have characterised two CTL clones and a CTL line whose interactions with these variants of P 17 (aa 24-31) exhibit a variety of responses. We have determined the high resolution crystal structures of four of these APLs in complex with HLA B8 to examine alterations in the shape, chemistry and local flexibility of the TCR binding surface. The variant peptides cause changes in the recognition surface by three mechanisms; changes contributed directly by the peptide, effects transmitted to the exposed peptide surface and induced effects on the exposed framework of the peptide binding groove.