Title of Project 1 : Understanding MHC-peptide binding and in silico prediction of T cell epitopes

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Short Description
The focus of our lab is on the human MHC. Our aim is to define with precision, the rules for peptide engagement with the structural HLA. We know that the ability of an antigen to stimulate T cell mediated immune responses is central to our defence against pathogens (in particular viruses), cancer and also forms the basis for successful immunization. Even when a whole organism is used it is comprised of a complex of many different proteins and sometimes elicit only weak or suboptimal responses. Identification of immunogenic T cell epitopes by current means is largely empirical and hence laborious. Our goal is to resolve the long standing problem of understanding the behaviour of a peptide with respect to its interaction with the peptide binding groove of the HLA. To approach this, we are creating a library of thousands of refolded molecules of HLA Class I alleles with known peptides and determining its interaction through binding measurements and crystallographic analysis. We will build up a series of validated MHC-peptide interactions to generate an algorithm which can be used to for selecting T cell epitopes. Applications of this information include improving tetramer design for use as diagnostic reagents and also rapid identification of vaccine epitopes that are matched to an individual or population.