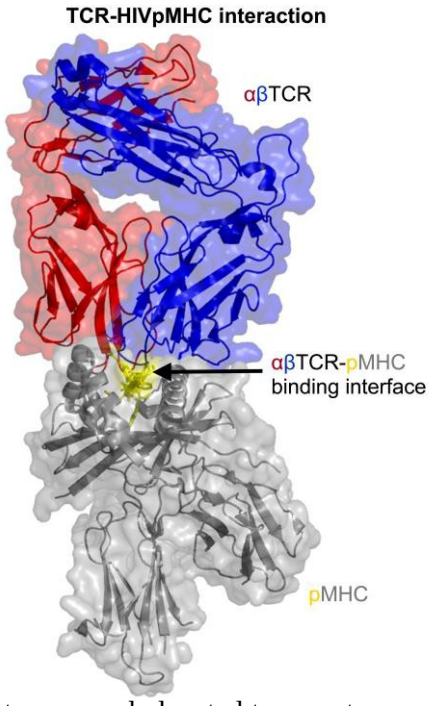
Molecular basis of HIV immune escape from T-cells

David Cole

School of Medicine, Cardiff University



The T-cell antigen receptor (TCR) mediates T-cell destruction of virally infected cells through the recognition of viral proteins (p) presented by major histocompatibility complexes (MHC) molecules at the cell surface. However, HIV can rapidly mutate its genome during replication, changing the sequence of these viral proteins and enabling evasion from T-cell attack. The molecular mechanisms that allow HIV to escape from T-cells are poorly understood.

In order for T-cells to activate, the TCR-pMHC interaction must be of sufficient specificity and duration. Mutations in HIV are predicted to have two consequences for this recognition. First, changes in viral proteins might reduce or abrogate MHC binding, so no stable viral pMHC molecules are presented at the cell surface. Second, these changes might inhibit the interaction between the TCR and pMHC, so that the T-cell can no longer activate.

To investigate the escape mechanisms utilized by HIV, we have assessed the relative stability of pMHCs containing a series of mutated HIV proteins by observing the differences in the CD spectra at room and elevated temperatures. Furthermore, we have generated X-ray crystal structures and conducted biophysical investigations of the interaction between a TCR and these mutant pMHCs. These data have implications for understanding the nature of HIV evasion from T-cells, and for the development of new HIV vaccines.

Email corresponding author: ColeDK@cardiff.ac.uk