The crystal structure of a murine TCR bound to an allogeneic MHC molecule, J.B. Reiser\textsuperscript{a}, C. Darnault\textsuperscript{b}, A. Guimezanes\textsuperscript{b}, C. Grégoire\textsuperscript{b}, T. Mosser\textsuperscript{c}, A.-M. Schmitt-Verhult\textsuperscript{d}, J.C. Fontecilla-Camps\textsuperscript{e}, B. Malissen\textsuperscript{f}, D. Housset\textsuperscript{g} and G. Mazza\textsuperscript{h}. J. Biol. Chem. 279, 1166-1172.

Keywords: viruses, immunology.

The T lymphocytes (or T cells) are the main actors of the cellular immune response and protect the organism against pathogens such as viruses and intracellular bacteria, and some kind of cancer. To achieve this goal, the T lymphocytes are able to recognize peptide fragments derived from foreign proteins and presented at the surface of infected cells by a Major Histocompatibility Complex (MHC) coded protein, the MHC molecule. For the recognition of a peptide antigen by a T cell, three main partners have been identified: for the antigen presenting cell, the membrane anchored MHC molecule and its bound foreign peptide (pMHC), and for the T lymphocyte, a specific membrane bound Ig like receptor (TCR for T-Cell Receptor). One hundred TCR engaged in complexes with foreign peptides bound to self-MHC molecules, is enough to induce a cascade of signals which eventually activates the specific T cell clone, leading to its proliferation and the death of infected cells.

During the 90s, several crystallographic studies of MHC molecules, TCR and TCR/peptide/self-MHC complexes performed by different groups all over the world allowed to define a general mode of TCR-pMHC interaction\textsuperscript{1,2,3}. However, due to the intrinsic variability of the TCR, the structural basis for its specificity remains to be elucidated.

The aim of our project is to establish the structural basis of TCR cross-reactivity for several peptides and MHC molecules. On the one hand, the TCR binding degeneracy is essential to insure that at least one T-cell clone, among the large but finite repertoire, reacts with anyone of the millions of putative foreign peptides. On the other hand, TCRs can productively bind intraspecies allelic variant of self-MHC molecules, and consequently govern graft rejection and graft-versus-host disease.

We will present the crystal structure of a complex involving the murine BM3.3 TCR and a naturally processed octapeptide (pBM1) bound to the H-2K\textsuperscript{b} allogeneic MHC molecule. This structure shows that the TCR/p-alloMHC complex shares the same general binding mode of the TCR/p-selfMHC complexes. However, the peptide “read-out” as well as the details of the MHC footprint differ markedly from the previously determined TCR/pMHC complexes\textsuperscript{1,2,3}.