Contribution ID : **34** Type : **Oral**

Understanding CD4+ TCRs recognition of a single HIV epitope presented by multiple HLA class II molecules

Friday, 23 November 2018 11:45 (15)

Human Immunodeficiency Virus (HIV) is a major health issue. With 2 million people newly infected per year, there is an urgent need to develop an HIV cure. Without treatment, HIV infection leads to the progressive disruption of the immune system leading to AIDS, and the occurrence of multiple opportunistic infections. Surprisingly, a small fraction of HIV-infected individuals (< 0.5%) can spontaneously control HIV replication in the absence of antiretroviral therapy. These patients, named HIV controllers show signs of a particularly efficient cellular antiviral response, which control the virus.

The role of CD8+ T cells in HIV has been extensively studied; however the role of CD4+ T cells remains unclear, due to the elimination of those cells upon infection. In HIV controller individuals the count of CD4+ T cells stays high, as they are able to control the viral load. These individuals provide a unique opportunity to study the immune system in the context of HIV infection.

We recently identified a CD4+ T cell population specific from HIV individuals exhibiting a highly biased TCR repertoire recognizing an immunodominant capsid epitope (Gag293). Those T cells were of high affinity and polyfunctional, as well as able to recognise the Gag293 presented by diverse molecules called HLA.

Using structural and functional approaches, our work published in Science Immunology[1] revealed for the first time how a single TCR can recognise so many different HLA molecules, and the role of the HIV epitope in driving this recognition. We provided the first functional and structural basis of the role of CD4+ TCRs in HIV infection in the context of HIV controller individuals, offering new avenues to develop immunotherapeutic approaches.

Primary author(s) : Dr FARENC, Carine (Biomedicine Discovery Institute, School of Biomedical Sciences, Monash University, Clayton, Victoria, Australia)

Co-author(s) : Dr GALPERIN, Moran (Pasteur Institute, Viral Pathogenesis Unit, Paris, France); MUKHOPADHYAY, Madhura (Pasteur Institute, Viral Pathogenesis Unit, Paris, France.); JAYASINGHE, Dhilshan (Biomedicine Discovery Institute, School of Biomedical Sciences, Monash University, Clayton, Victoria, Australia); Prof. ROSSJOHN, Jamie (Biomedicine Discovery Institute, School of Biomedical Sciences, Monash University, Clayton, Victoria, Australia); Dr GRAS, Stephanie (Biomedicine Discovery Institute, School of Biomedical Sciences, Monash University, Clayton, Victoria, Australia); Dr CHAKRABARTI, Lisa (Pasteur Institute, Viral Pathogenesis Unit, Paris, France.)

Presenter(s) : Dr FARENC, Carine (Biomedicine Discovery Institute, School of Biomedical Sciences, Monash University, Clayton, Victoria, Australia)

Session Classification : Parallel Session 12

Track Classification : Structural Biology