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Study of HLA-C Binding Stability in HIV-1 Infection and in Cognitive Disorders

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MHC-I is an heterotrimeric complex composed by HLA-C/ β 2-microglobulin/peptide. The different HLA-C variants can be grouped into stable and unstable clusters based on their binding stability to β 2-microglobulin. The presence of unstable HLA-C molecules increases β 2-microglobulin release. It is known that patients affected by AIDS Dementia Complex (ADC), a very severe neurological condition of HIV-1 infection, present high level of β 2-microglobulin in the cerebrospinal fluid. We observed a higher frequency of unstable HLA-C alleles in ADC patients. We demonstrated that, upon HIV-1 infection, HLA-C molecules associate with HIV-1 virions, increasing viral infectivity. In addition, HIV-1 virions produced in the presence of unstable HLA-C variants are more infectious. We aimed to evaluate how each HLA-C variant affects the ADC onset in HIV-1 infected patients. To assess the contribution of each HLA-C variant in the modulation of HIV-1 infection, CRISPR/Cas9 was used to generate 293T HLA-C^{-/-} packaging cells. The different HLA-C alleles were transfected in 293T HLA-C^{-/-} cells, to develop different cell lines expressing a specific HLA-C allotype. The different cell lines will be used to produce HIV-1 pseudo typed viruses to be tested in infectivity assays conducted on TZm-bl cells. Furthermore, to assign a stability score to each HLA-C variant, based on their dissociation rate from β 2-microglobulin, each HLA-C expressing cell line will be treated with an acid wash, to study the kinetic of β 2-microglobulin dissociation from HLA-C. These analyses will be fundamental to clarify the relationship between HLA-C binding stability, HIV-1 infection progression and the development of HIV-1 related neurocognitive diseases.

Biography:

Simona Mutascio received a Master of Science in Cellular and Molecular Biology in 2015 at the University of Rome Tor Vergata, Italy. In 2016 she started her Ph.D in Applied Life and Health Sciences at the University of Verona, Italy, in the molecular biology laboratory directed by Prof. Donato Zipeto. Her Ph.D thesis project is focused on the development of new cell models using CRISPR/Cas9 technique, to study the involvement of specific proteins in tumorigenesis, neurological disorders, and in the modulation of HIV-1 infectivity.