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Comparative Immune Responses to Pathogenic and Non-Pathogenic Mammarenaviruses in Human and Reservoir-Derived Antigen-Presenting Cells

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Mammarenaviridae is a genus of ambisense RNA-viruses, with members that cause viral hemorrhagic fever, namely Lassa virus (LASV) and Lujo virus (LUJV) and members that have not been associated with disease, such as
Mopeia virus (MOPV). LASV infection results in 5000 to 10,000 deaths annually in sub-Saharan Africa, and LUJV has a case-fatality rate of up to 80%. The Natal multimammate mouse (Mastomys natalensis, NMM) has been identified as a natural reservoir of LASV and MOPV. However, these animals do not show clinical signs upon infection. In humans, LASV targets dendritic cells (DCs) and macrophages (MΦs), among other cells, and induces activation and maturation of DCs, but downregulates interferon response and fails to induce robust T-cell responses.
Given the lack of pathology of LASV infection in NMM, and the pivotal role of DCs and MΦs in the disease development in humans and non-human primates, the purpose of our study is to compare the immune profile of human and NMM-derived DCs and MΦs responses LASV, LUJV and MOPV infection. We differentiated DCs and MΦs from bone-marrow cells isolated from adult NMM or human monocytes and infected them with LASV, LUJV or MOPV. We sampled cells and supernatants at 2 days post-infection. As controls for the activation of the innate immune response in these cells, we stimulated the cells Sendai virus (SeV). We performed a characterization of immune profile of the cells the cells,
measured the transcript levels of immune-related genes and quantified viral loads. We describe the comparative immune-profile resulting of the infection with pathogenic vs. non-pathogenic Mammarenaviruses, in human and in a natural reservoir species. This gives us insights on the mechanisms of pathogenesis in humans and protection for the natural reservoir species. This highlights the importance on the insights on the immune mechanism that lead to a non-pathogenic infectious phenotypes and the relevance for natural reservoir's further studies.

Keywords

Mammarenavirus, Antigen-presenting cells, Host-pathogens interaction, innate immunity,
Natural reservoir

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Professional Status of the Speaker

PhD Student

Junior Scientist Status

Yes, I am a Junior Scientist.

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