ORT_04 - Exploring the Interplay of CLEC5A and Zika Virus: *In Silico* and *In Vitro* Investigations

Ryann de Souza Nascimento[1]; Thiago Lazari Machado[1]; Ana Paula Dinis Ano Bom[1]; Juliana Gil Melgaço[1].
[1]Fiocruz/Bio-Manguinhos

Introduction: Arthropod-borne viruses, notably Zika virus (ZIKV), pose a grave public health threat in Brazil due to neurological conditions associated with pregnancy and newborns added to the absence of a vaccine or established treatment guidelines. Understanding the role of cellular receptors like CLEC5A in disease pathogenesis is crucial. This study investigates the interaction of CLEC5A with ZIKV to unravel infection mechanisms and aid in therapeutic development using antibodies, utilizing bioinformatics and cell culture techniques.

Objectives: Our objective was to assess the interaction and expression of CLEC5A on mononuclear immune cells with ZIKV using bioinformatics and cell culture.

Methodology: Molecular docking experiments generated receptor-protein complexes between CLEC5A (PDB ID:2YHF) and ZIKV envelope protein (PDB ID:5JHM) via ClusPro 2.0. PyMOL software facilitated visualization and prediction of binding residues, calculating root-mean-square deviation (RMSD) between ligands. *In vitro* assays utilized THP-1 cells to evaluate CLEC5A binding with ZIKV. Cells were cultured, stimulated with ZIKV (MOI=0.1), and subjected to immunophenotyping after 72 hours for flow cytometry analysis, including CLEC5A and monocyte differentiation markers.

Results: *In silico* results suggested that cluster-4 model was the best conformation for the binding form between CLEC5A and ZIKV. Binding energy (-1027.2kcal/mol) between ZIKV envelope protein and CLEC5A was comparable to that with Dengue virus (DENV) envelope protein (-999.4 kcal/mol), indicating effective interaction, consistent with documented DENV-CLEC5A interaction. Immunophenotyping revealed increased CLEC5A expression on ZIKV-stimulated cell membranes compared to controls (control:6.4% vs ZIKV:21.26%). These results align with in silico findings, enhancing understanding of ZIKV-CLEC5A interaction mechanisms.

Conclusion: Our findings suggest that blockade of the CLEC5A pathway could be a target for ZIKV therapy, as monoclonal antibody development, especially for susceptible populations, such as pregnant women. However, further in vivo studies are necessary to validate and explore clinical implications. Financial support provided by Faperj and Fiocruz.

Keywords: Zika virus; Type C lectin receptor; Interaction