WG 1 (Chemical, Biological, Radiological and Nuclear materials)

High-Throughput Single-Cell Transcriptomics for the Generation of Monoclonal Antibodies Targeting Rift Valley Fever Virus

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Rift Valley fever virus (RVFV) is a zoonotic pathogen that causes significant morbidity and mortality in both humans and livestock. While veterinary vaccines exist, no licensed vaccines or therapeutics exist for human use. Neutralizing monoclonal antibodies (mAbs) represent a promising strategy for prophylactic and therapeutic interventions, particularly targeting the viral glycoproteins Gc and Gn, which contain key neutralizing epitopes.
This study aims to identify rare, potent mAbs against RVFV using high-throughput single-cell transcriptomics, facilitating the discovery of novel therapeutics for RVFV infections. Mice were immunized with live attenuated rMP-12-GFP virus and boosted with recombinant Gc/Gn antigens. Memory B cells were isolated from splenocytes via flow cytometry, and single-cell RNA sequencing (scRNA-seq) was performed using 10x Genomics technology. Bioinformatics analyses identified B cell receptor (BCR) pairs based on abundance and specificity. A panel of 23 recombinant mAbs was generated and characterized for antigen-binding affinity.
Approximately half of the generated mAbs exhibited strong and specific binding to their cognate antigen, validating the effectiveness of the single-cell sequencing approach. These findings demonstrate the feasibility of using scRNA-seq for high-throughput antibody discovery against RVFV.
Single-cell transcriptomics is a powerful tool for identifying potent neutralizing mAbs, which can be leveraged for the development of RVFV-targeted therapeutics. This methodology may also be applied to other emerging viral threats, facilitating rapid antibody-based countermeasure development. This study demonstrates the power of single-cell sequencing for rapid antibody discovery, enabling the identification of potent mAbs against RVFV. While monoclonal antibodies offer a promising therapeutic approach, challenges remain in clinical translation, including production and regulatory approval. Optimizing this strategy for other emerging viruses could enhance outbreak preparedness.

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Inhalational Exposure of Rabbits to Aerosolized Fentanyl Solutions - Experimental System Overview

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Fentanyl is a family of potent synthetic opioids legally used for anesthesia and analgesia, as well as illegally in the illicit drug trade. Fentanyl have also been used as a neutralizing agent, specifically aerosolized for inhalational exposure. As such, this family of drugs poses a severe threat from use by nefarious actors, both for incapacitation and kidnapping of civilians or soldiers, as well as for lethal attacks. We describe our approach to setting up an experimental system to perform inhalational exposures of rabbits to aerosols generated from fentanyl solutions, as a means to studying this potential threat and supplying a platform for testing treatments and countermeasures.