B14R HOMOLOGY ACROSS VIRAL GENOMES & PROTEINS WITHIN THE POXVIRIDAE FAMILY

Anthony Tu, Hari Parthasarathy, Parshawn Gerafian, Quin Lamothe

RESEARCH ABSTRACT

Smallpox, caused by the variola virus, was one the most devastating diseases of the past few centuries of human history, with a mortality rate of 30-40% in its most virulent forms. Its potency came not only from its highly contagious nature – it was capable of spreading rapidly through respiratory droplets, direct contact, and surfaces – it was also able to induce other diseases as a byproduct (most notably diabetes and osteomyelitis). Though formally eradicated in the 1980s through global vaccination campaigns leveraging other Poxviridae viruses (cowpox and monkeypox being the most used candidates), recent news indicates the potential re-emergence of smallpox has reignited strong interest in further understanding the molecular mechanisms and interactions leading to its virality.

This study focuses on comparative analyses of the B14R gene and hypothetical protein encoded via the viral genomes of monkeypox, cowpox, vaccinia, and variola. These proteins interact with the IKBKB pathway, and the NF-kappa B inhibitor, which plays an important role in immune signaling and inflammation, lending to osteomyelitis and Type II diabetes.

By examining the relationship of genetic sequences, protein structures and functional differences, we endeavor to understand the differences in viral modulation of host immune responses. We are fundamentally interested in investigating how the difference in structure of similar proteins across the different viral genomes leads to changes in pathogenicity and virulence between species, and how it contributes to the poxvirus-induced predisposition to other diseases.

RATIONALE AND OBJECTIVES

Our focus on the Variola **B14R** (Gene ID: 1486544, NC_001611.1 (163090..163539)) gene stems from the need to understand the molecular basis of varied Poxviridae member species pathogenicity. These proteins are known to interact with host signaling pathways, potentially influencing disease outcomes. A comparative analysis of these proteins across four key poxviruses — **Monkeypox** (NC_063383.1), **Cowpox** (NC_003663.2), **Vaccinia** (NC_006998.1), and **Variola** (NC_001611.1)—could reveal critical variations that contribute to disease predisposition.

The **primary objectives** of this study are

1. To identify and compare sequence variability of the genes encoding B13R and B14R across the different Poxviridae viral genomes
2. To identify and compare structural and functional variations in B13R and B14R proteins through Alphafold, and simulate the docking patterns of said proteins.
3. To explore how these variations may influence interactions with the IKBKB pathway and integrin receptors.
4. To provide insights into the mechanisms underlying poxvirus-induced diseases, such as diabetes and other-related conditions.

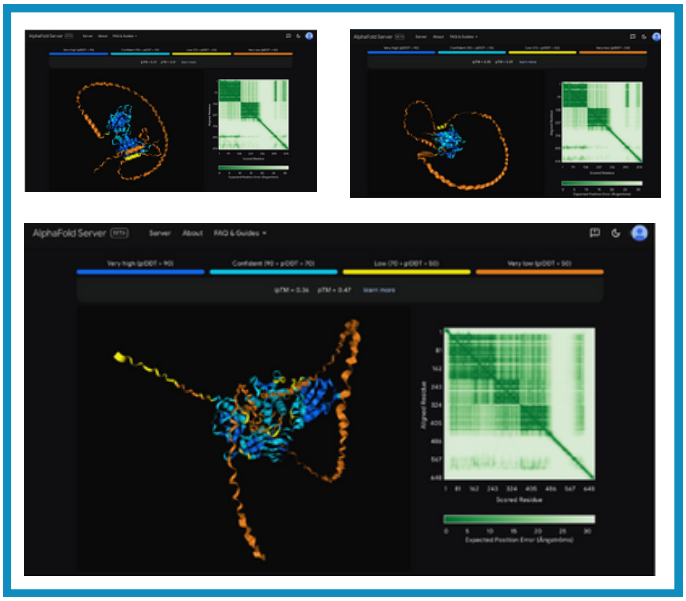

Figure 1: Alphafold Outputs for B14R Docking to IRF Receptors across Variola (Top Left), Monkey Pox (Top Right), and Vaccinia (Center)

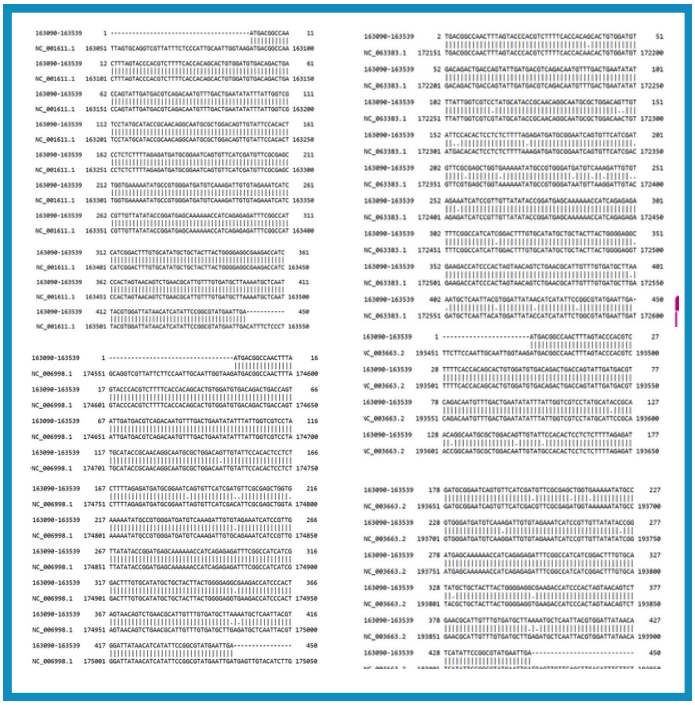

Figure 2: Pairwise Alignment Results for Variola B14R-{Monkeypox (NC_063383.1), Cowpox (NC_003663.2), Vaccinia (NC_006998.1), and Variola (NC_001611.1)}

METHODOLOGY

Genomic sequences Variola B14R (Gene ID: 1486544, NC_001611.1 (163090..163539), Monkeypox (NC_063383.1), Cowpox (NC_003663.2), Vaccinia (NC_006998.1), and Variola (NC_001611.1), were retrieved from the NCBI and analyzed using JBrowse's Synteny alignment tool, as well as EMBL-Needle to identify conserved and variable regions. Variola B14R was aligned with Monkeypox, Cowpox, Vaccinia, and Variola genomes. Structural modeling through Alphafold was employed to predict how sequence variations (number of amino acids, mutations, etc.) might impact protein folding patterns (helices, clustering, etc.) and how that may impact the protein function and docking interactions with the IKBKB pathway and NF-kappa B factor.

RESULTS & FINDINGS

Through bioinformatic analysis the conservation of Variola B14R (Gene ID: 1486544, NC_001611.1 (163090..163539)) was established between the Monkeypox (NC_063383.1), Cowpox (NC_003663.2), Vaccinia (NC_006998.1), and Variola (NC_001611.1) genomes. Sequence homology was evidenced by JBrowse synteny, as well as pairwise alignments of >95% percent identity. The strongest docking with predicted between Variola B14R and Human IRF protein, lending to the hypothesis that the high pathogenicity and virulence of this virus is related to its ability dock strongly to host cell immune receptors to modulate host immune responses.

RESULTS & FINDINGS

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