Highly variable Receptor Binding Proteins in *Tequatrovirus* phages targeting *Escherichia coli* contribute to their host specificity

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Bacteriophages, particularly those targeting *E. coli*, are known for their specificity. The narrow host ranges of three isolated *Tequatrovirus* phages targeting *E. coli* prompted us to investigate their Receptor Binding Proteins (RBP). These proteins contain a highly variable N-terminal region that binds to its receptor during adsorption. A better understanding of the factors influencing the host range is crucial for developing phage therapy.

The serotypes and virulence factors of the strains were assessed. To identify potential RBPs, the phage genomes were annotated and progressively aligned with their 5 closest homologs. Proteins with low nucleotidic identities and situated in the tail region were further analyzed using specific models to detect depolymerase activity and potential RBPs. Finally, the 3D structure of the selected proteins were predicted and the RMSD scores were calculated.

The host range showed limited dependance on the serotype but some virulence factors like the production of capsules had an impact. In all phages, both long and short tail fibers were identified as RBPs. The distal subunit of the long tail fiber exhibited depolymerase activity and high diversity between homologous phages. The short tail fiber displayed a mild diversity and also depolymerase activity. The high RMSD score among these structures confirmed the structural variability of the RBPs.

In conclusion, although phages from the same genus have the same located RBP's, their mutations drive their specificities. The next step will be to identify the bacterial receptors and to predict the interaction between the RBP and its receptor.

Acknowledgements:

This program benefited from a financial support of Wallonia in the frame of a BioWin's Health Cluster and Wagralim's Agri-food Innovation Cluster program (Vetphage). The authors acknowledge the "Agence Régionale de Santé et d'Identification Animale" (ARSIA, Ciney, Belgium) and the Care-FEPEX (ULiège, Liège, Belgium).