Mapping Genetic Drivers of Zoonotic Capability in Avian Influenza

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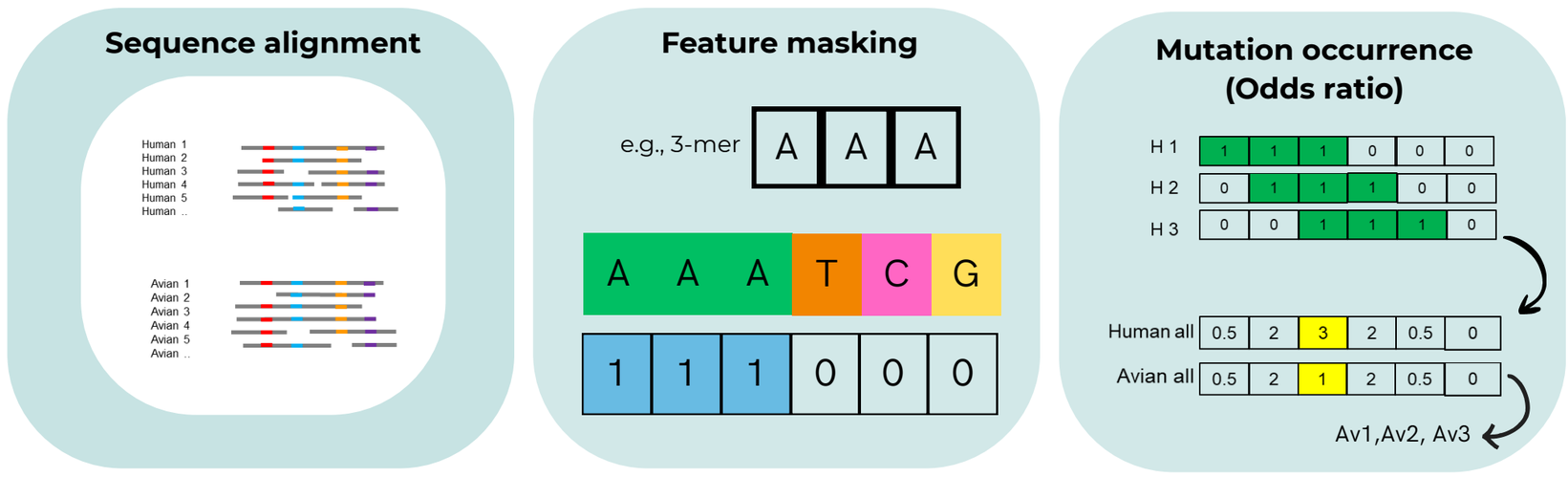
WHY SHOULD WE CARE?

- **Avian influenza** is a growing health threat to humans, as evidenced by recent events of spillover from avian species [1].
- **15 subtypes** have been recorded to be capable of infecting humans (zoonotic) so far, with **H5N2** the most recent one (April 2024) [2].
- While **human-to-human** transmission hasn't occurred yet, the virus mutates rapidly, raising concern that more transmissible strains could emerge.
- Early identification of emerging strains with zoonotic potential and underlying genetic mutations driving zoonotic capability is key to aiding the development of vaccines and therapeutics, reducing the risk of new pandemics.

WHAT ARE WE DOING?

Using whole genome sequences from avian and human hosts, the University of Glasgow has developed a **machine learning(ML) model** that predicts which new strains might be zoonotic in the future [3] (§2.9.3). The model uses genomic composition features to distinguish zoonotic from non-zoonotic sequences. UKHSA scientists are using the model outputs to identify potential mutations that may help the virus to jump from birds to humans.
This can give scientists a vital **head start** in developing vaccines and therapeutics, helping to stop the next pandemic before it begins.

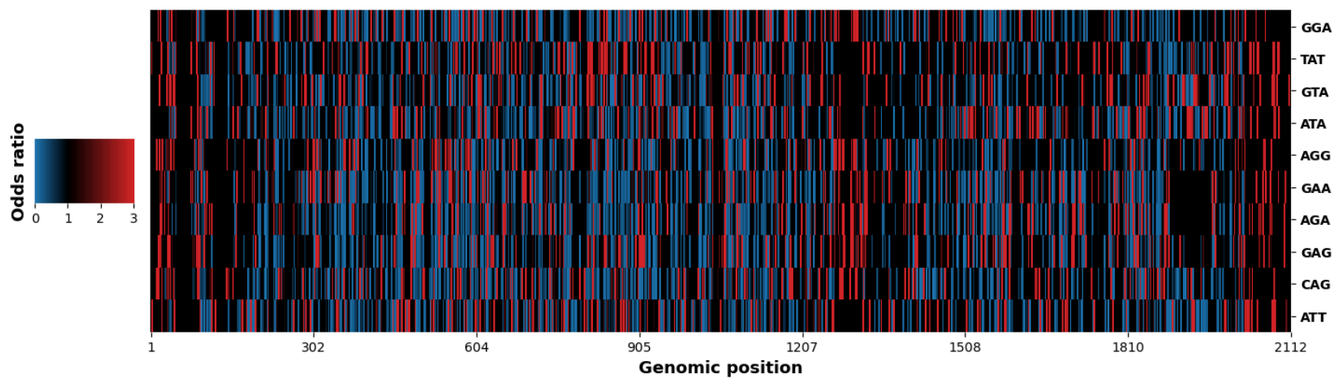
WHAT DID I DO?



I aligned the raw avian and human sequences (n = 1883 avian, 135 human) using MAFFT software and mapped the most important genetic features from the ML model (focusing on 3-mers) onto the aligned sequences using a pattern-matching approach. This produced binary-encoded sequences, where 1 represents the presence of a 3-mer within each position. I then estimated mutation likelihood by calculating the odds ratio of each 3-mer's occurrence in human vs. avian sequences. High odds ratio locations indicate regions most likely to mutate and drive zoonotic capability.

OUR FINDINGS SO FAR

HA GENE: PER-POSITION 3-MER ODDS RATIOS (ZOONOTIC VS AVIAN)



Blue <1 = avian-enriched; black ≈1 = neutral; red >1 = zoonotic-enriched; colour scale fixed to odds ratio 0–3

WHY IS THIS IMPORTANT?

- Identifying the genetic elements driving human infection and their locations in the avian influenza genome helps us prioritise **surveillance** of high-risk strains and supports the development of **vaccines** and **therapeutics**.
- Our method can **quickly screen** new sequences to identify risky strains and help develop treatments, thus reducing the risk of a new pandemic.

Please scan the QR code to review references

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