Extended Data Fig. 1: Comparison of receptor binding site residues in diverse H5 HAs.
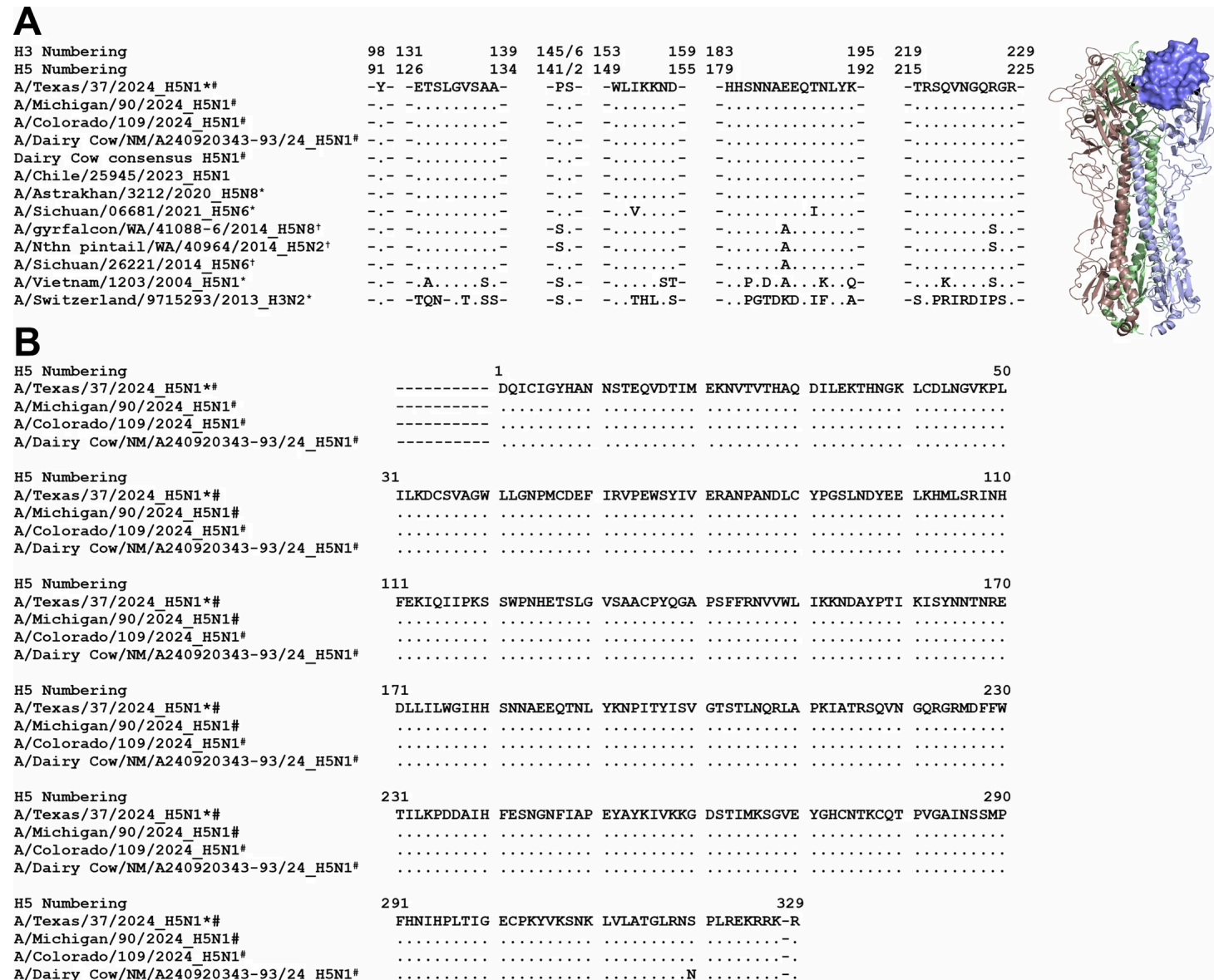
From: [Transmission of a human isolate of clade 2.3.4.4b A(H5N1) virus in ferrets](#)

A

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H3 Numbering                              98 131       139 145/6 153    159 183          195 219       229
H5 Numbering                              91 126       134 141/2 149    155 179          192 215       225
A/Texas/37/2024_H5N1*#                    -Y- -ETSLGVSAA-   -PS- -WLIKKND-  -HHSNNAEEQTNLYK-   -TRSQVNGQRGR-
A/Michigan/90/2024_H5N1#                  -.- -.........-   -.-  -.......-  -..............-   -..........-
A/Colorado/109/2024_H5N1#                 -.- -.........-   -.-  -.......-  -..............-   -..........-
A/Dairy Cow/NM/A240920343-93/24_H5N1#     -.- -.........-   -.-  -.......-  -..............-   -..........-
Dairy Cow consensus H5N1#                 -.- -.........-   -.-  -.......-  -..............-   -..........-
A/Chile/25945/2023_H5N1                   -.- -.........-   -.-  -.......-  -..............-   -..........-
A/Astrakhan/3212/2020_H5N8*               -.- -.........-   -.-  -.......-  -..............-   -..........-
A/Sichuan/06681/2021_H5N6*                -.- -.........-   -.-  -..V....-  -.........I....-   -..........-
A/gyrfalcon/WA/41088-6/2014_H5N8†         -.- -.........-   -S.- -.......-  -......A.......-   -.......S..-
A/Nthn pintail/WA/40964/2014_H5N2†        -.- -.........-   -S.- -.......-  -......A.......-   -.......S..-
A/Sichuan/26221/2014_H5N6†                -.- -.........-   -.-  -.......-  -......A.......-   -..........-
A/Vietnam/1203/2004_H5N1*                 -.- -.A.....S.-   -S.- -.....ST-  -..P.D.A...K..Q-   -...K....S..-
A/Switzerland/9715293/2013_H3N2*          -.- -TQN-.T.SS-   -S.- -..THL.S-  -..PGTDKD.IF..A-   -S.PRIRDIPS.-
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B

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H5 Numbering                                        1                                                50
A/Texas/37/2024_H5N1*#                    ---------- DQICIGYHAN NSTEQVDTIM EKNVTVTHAQ DILEKTHNGK LCDLNGVKPL
A/Michigan/90/2024_H5N1#                   ---------- .......... .......... .......... .......... ..........
A/Colorado/109/2024_H5N1#                  ---------- .......... .......... .......... .......... ..........
A/Dairy Cow/NM/A240920343-93/24_H5N1#      ---------- .......... .......... .......... .......... ..........

H5 Numbering                              31                                                        110
A/Texas/37/2024_H5N1*#                     ILKDCSVAGW LLGNPMCDEF IRVPEWSYIV ERANPANDLC YPGSLNDYEE LKHMLSRINH
A/Michigan/90/2024_H5N1#                    .......... .......... .......... .......... .......... ..........
A/Colorado/109/2024_H5N1#                   .......... .......... .......... .......... .......... ..........
A/Dairy Cow/NM/A240920343-93/24_H5N1#      .......... .......... .......... .......... .......... ..........

H5 Numbering                              111                                                       170
A/Texas/37/2024_H5N1*#                     FEKIQIIPKS SWPNHETSLG VSAACPYQGA PSFFRNVVWL IKKNDAYPTI KISYNNTNRE
A/Michigan/90/2024_H5N1#                    .......... .......... .......... .......... .......... ..........
A/Colorado/109/2024_H5N1#                   .......... .......... .......... .......... .......... ..........
A/Dairy Cow/NM/A240920343-93/24_H5N1#      .......... .......... .......... .......... .......... ..........

H5 Numbering                              171                                                       230
A/Texas/37/2024_H5N1*#                     DLLILWGIHH SNNAEEQTNL YKNPITYISV GTSTLNQRLA PKIATRSQVN GQRGRMDFFW
A/Michigan/90/2024_H5N1#                    .......... .......... .......... .......... .......... ..........
A/Colorado/109/2024_H5N1#                   .......... .......... .......... .......... .......... ..........
A/Dairy Cow/NM/A240920343-93/24_H5N1#      .......... .......... .......... .......... .......... ..........

H5 Numbering                              231                                                       290
A/Texas/37/2024_H5N1*#                     TILKPDDAIH FESNGNFIAP EYAYKIVKKG DSTIMKSGVE YGHCNTKCQT PVGAINSSMP
A/Michigan/90/2024_H5N1#                    .......... .......... .......... .......... .......... ..........
A/Colorado/109/2024_H5N1#                   .......... .......... .......... .......... .......... ..........
A/Dairy Cow/NM/A240920343-93/24_H5N1#      .......... .......... .......... .......... .......... ..........

H5 Numbering                              291                             329
A/Texas/37/2024_H5N1*#                     FHNIHPLTIG ECPKYVKSNK LVLATGLRNS PLREKRRK-R
A/Michigan/90/2024_H5N1#                    .......... .......... .......... .......-.
A/Colorado/109/2024_H5N1#                   .......... .......... .......... ........-.
A/Dairy Cow/NM/A240920343-93/24_H5N1#      .......... .......... .........N ........-.
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(**A**) Sequence residues that comprise the TX/37 HA receptor binding site (RBS) aligned with HA sequences from this and a previous study[44], as well as with a recent bovine A(H5N1) virus sequence that reported both human and avian receptor binding[18]. Alignments with amino acid positions (H3 and H5 numbering) are indicated above the alignment. Conserved residues are indicated as dots. The position of the RBS on the HA is illustrated on the TX/37 structural model. The HA is illustrated as a cartoon, while the receptor binding site residues listed in the alignment are shown as a surface representation. Figure was generated using PyMol 2.5.5. *Current data. †HAs with published glycan array binding results. #Isolates associated with dairy farm outbreaks including dairy cow isolate consensus sequence. (**B**) Full alignment of the HA for all viruses associated with dairy farm outbreaks included in A.

[Source Data](#)