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Structural and functional analysis of the binding interface of the H18N11 bat Influenza A virus and the proteinaceous receptor MHCII

Monday, September 14, 2026 9:30 AM (20 minutes)

The discovery of influenza A virus (IAV) subtypes H17N10 and H18N11 in New World bats challenged the paradigm that viral entry depends on hemagglutinin (HA) binding to sialic acid. Instead, these bat IAV use the protein receptor MHC class II (MHCII). MHCII from diverse species, including humans, mediates infection, and conserved residues within MHCII are critical for interaction with H18. Here, we structurally characterized the MHCII binding site on H18.

We purified soluble H18 homotrimers and MHCII heterodimers and demonstrated direct interaction by biolayer interferometry. Soluble MHCII efficiently blocked H18N11 infection, confirming its essential role in entry. Using hydrogen-deuterium exchange mass spectrometry and cryo-EM, we mapped the MHCII binding interface to a discrete region in the H18 head domain, distinct from the classical sialic acid binding site. Mutational analysis identified key residues required for membrane fusion triggered by the H18-MHCII interaction. Viruses carrying mutations in this interface showed severely impaired growth. Passaging of the mutant viruses led to a compensatory mutation near the binding site that restored membrane fusion and viral replication to wildtype levels.

These findings provide the first structural insights into the H18–MHCII interface and identify critical residues mediating this interaction.

Keywords

Professional status of the speaker

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Junior scientist status

No, I am not a junior scientist.

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Authors: ROBERT, Jonathan (Institute of Virology, University Medical Centre of Freiburg, Germany); OSMAN, Maria K. (Institute of Virology, University Medical Centre of Freiburg, Germany); HALWE, Nico J. (Institut für Virusdiagnostik (IVD), Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany); CALVARESI, Valeria (Department of Biochemistry, University of Oxford, UK); KOTANSKA, Anna (Structural Biology of Disease Processes Laboratory, The Francis Crick Institute, London, UK); GRADON, Jan (Structural Biology of Disease Processes Laboratory, The Francis Crick Institute, London, UK); MICHALSKI, Leon (Structural Biology of Disease Processes Laboratory, The Francis Crick Institute, London, UK); SAU, Stanley (Structural Biology of Disease Processes Laboratory, The Francis Crick Institute, London, UK); MARTIN, Stephen (Structural Biology of Disease Processes Laboratory, The Francis Crick Institute, London, UK); READING, Eamonn (Department of Chemistry, Britannia House, King's College London, London, UK); BEER, Martin (Institut für Virusdiagnostik (IVD), Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany); SKEHEL, John J. (Structural Biology of Disease Processes Laboratory, The Francis Crick Institute, London, UK); GAMBLIN, Steve J. (Structural Biology of Disease Processes Laboratory, The Francis Crick Institute, London, UK); SCHWEMMLE, Martin (Institute of Virology, University Medical Centre of Freiburg,

Germany); CIMNINSKI, Kevin (Institute of Virology, University Medical Centre of Freiburg, Germany); WROBEL, Antoni G. (Department of Biochemistry, University of Oxford, UK); REUTHER, Peter (Institute of Virology, University Medical Centre of Freiburg, Germany)

Presenter: REUTHER, Peter (Institute of Virology, University Medical Centre of Freiburg, Germany)

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