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Universal pandemic and seasonal Influenza vaccine design: directing the antibody repertoire

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Seasonal Influenza vaccines have a variable and limited breadth of protection primarily due to the dominant dependence on the induction of hemaglutination inhibiting (HAI) antibodies. HAI antibodies bind to the head of the hemaglutinin (HA) molecule. We discovered somatically mutated antibodies of the VH1-69 lineage to the stem of the HA molecule shortly after influenza vaccination. These antibodies were broadly protective against influenza group A1, A2 and B viruses, in case of influenza A due to virus neutralization (fusion inhibition) and in case of B viruses due to antibody-dependent cellular cytotoxicity (ADCC). Comparing the CR9114 epitope (Dreyfus et al, Science 2012) with epitopes of HIV and HCV binding to antibodies of the VH1-69 lineage, attachment to the antigen is largely defined by a conserved hydrophobic CDR2 region.

Subsequently we developed a HA stem trimer with the capability to tightly bind to a Fab of CR9114. The paratope of CR9114 was shown to bind to the HA stem trimer in a similar way (CDR3 & CDR2 dominance) as to full length HA. The HA stem trimer protected mice completely against both H1N1 and H5N1. In cynomolgus monkeys, the HA stem trimer reduced fever following H1N1 challenge and elicited broadly reactive stem-directed antibodies. These data provide proof-of-concept for design of an universal influenza vaccine based on directing the antibody repertoire.

Biography

Jaap Goudsmit is Global Head of the Janssen Prevention Center, a Center of Excellence launched at the start of 2015 within Janssen Research & Development, part of the Pharmaceutical Companies of Johnson & Johnson. In this role, he is responsible for driving the development and implementation of innovative strategies for disease prevention, focusing on the chronic, non-communicable illnesses that are on the rise in our aging populations. He joined the Janssen R&D Senior Leadership Team on January 1, 2015.

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