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Universal influenza vaccines: Prevention of infection against matched and mismatched strains

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Annual vaccination against seasonal Influenza A and B virus subtypes with well-matched inactivated virus (INV) vaccines are highly effective against upper respiratory tract (URT) Influenza infection and induced disease. Protection against infection is thought to be mediated principally by neutralizing antibodies targeting the receptor binding site (RBS) of the hemagglutinin globular head (HA1). Immune pressure on HA1 results in antigenic drift, necessitating worldwide surveillance with subsequent WHO recommendations on strain selection for manufacture of forthcoming seasonal influenza vaccines. The development of Universal Influenza Vaccines (UIV) that could protect against matched as well as drifted or mismatched strains would provide significant improvement over standard of care (SOC). Additionally, a target product profile that also offers long-lasting immunity would be a substantial advantage of current annual vaccination practices, potentially enabling year-round manufacture. UIV that induce both breadth and durability across multiple influenza seasons would be paradigm shifting for the Influenza field and offer significant health care benefits. As part of our universal influenza vaccine program, and using the H1 subtype as our proof of concept (POC), we have built both consensus-based, computationally optimized broadly reactive antigens (COBRAs), as well as designs displaying dominant epitope patterns, through Structural Mapping of Antigenic Repertoires (SMARt). These prototype designs have been demonstrated to fold properly, have the ability to bind conformation-specific mAbs(HA1 & HA2) as well as agglutinate red blood cells. Prototype H1N1 HA proteins were presented on virus-like particles (VLPs), tested in-vivo, and determined toelicit broadly cross-neutralizing functional antibody responses, protect against viral challenge and prevent transmission in pre-clinical mouse and ferret models. This is the first report describing the induction of universal, broadly-reactive, protective immunity against H1N1 isolates using a consensus-based HA strategy focusing on the globular head.

Biography

Harry Kleanthous has over 20 years industry experience in the research & development of recombinant live attenuated and subunit-based vaccines against viral and bacterial pathogens. He joined Sanofi Pasteur as US Head of Discovery Research in 2008 with responsibility for evaluating and developing novel viral vaccine platforms and delivering novel targets to the Development pipeline. Previously, he was Vice President of Research at Acambis Inc. (formerly OraVax) with responsibility for developing a new exploratory portfolio. His research interests are in the field of replication-defective viral vaccine platforms, targeting Influenza, Flaviviruses and Herpes viruses, as well as their use for foreign antigen delivery. Prior to joining industry, he was a scientific investigator at academic teaching hospitals and the Health Protection Agency (Colindale) in the UK, where he developed his expertise in the area of infectious diseases and molecular epidemiology. He obtained his PhD in the field of Molecular Microbiology from the University of London.

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