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Investigations into the reduced effectiveness of the H1N1pdm09 component of the live attenuated influenza vaccine

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Decreased effectiveness of the influenza A(H1N1)pdm09 strains (A/California/7/2009 and A/Bolivia/559/2013) included in live attenuated influenza vaccines (LAIV) have been observed in recent years. Multiple hypotheses have been suggested as potential explanations for this reduced effectiveness compared with inactivated influenza vaccines (IIV). The most frequently cited hypotheses include poor replicative fitness of the A(H1N1)pdm09 LAIV strains, vaccine–virus interference in the quadrivalent formulation, reduced LAIV replication due to preexisting anti-influenza immunity from prior influenza vaccinations, and poor thermostability of A(H1N1)pdm09 LAIV strains. We have systematically evaluated each of these hypotheses and initiated a multifaceted scientific investigation in to the causes of the recently observed reduced effectiveness of LAIV. Laboratory studies show that A/ California and A/Bolivia strains have reduced replication in a human alveolar cell line, primary human nasal epithelium air-liquid cultures. Data suggests that the underlying mechanism for this is likely to be multi-factorial. For example, the pdm09H1N1 LAIV strains have reduced binding to α2,6-linked sialic acid receptors (the primary receptor for influenza viruses in the human upper respiratory tract) and increased neuraminidase activity. Finally, ferret studies confirm that LAIV which replicate well in tissue culture are more effective in protecting from wild type influenza virus challenge.

Biography

Helen Bright is an Immunologist with over 20 years' experience in the biopharmaceutical industry. She has a degree in Microbiology from the University of Newcastle upon Tyne and a PhD in RSV Vaccine Research. She is currently a Principal Scientist at Medimmune, responsible for the research, selection and development of vaccine strains for the seasonal and pandemic live attenuated influenza vaccine. Previously, she successfully led anti-viral, immune modulation and vaccine discovery projects at GSK and Pfizer. She has been a Reviewer for the MRC Infection and Immunity Board and a Journal Referee.

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