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New adjuvant G3/DT induces protective T cell response with a split-virion influenza vaccine

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Background: Vaccination has become a major medical success since its introduction by Jenner 1780, even if he neither discovered nor invented smallpox vaccine in a strict sense. However he was the first to apply scientific methods (although unethical with today's standard) to prove the concept of vaccination, using a less harmful ('attenuated') virus strain - cowpox. This eventually led to the global extinction of smallpox.

Today attempts to use the same basic concept to conquer influenza are struggling with the added complexity of hypervariability. CDC issued a warning already in December 2014 that the profile of influenza viruses currently circulating (with A/H3N2 predominating) do not match with the corresponding strain in this year's vaccine. This later turned out to be true and the flu 2015 was severe. There was no protection against 97 % of the virus strains, 40 % higher mortality in England, 7 % of all mortality in USA in December due to influenza and about 1000 persons succumbing to flu in Sweden this season.

Aim: This raises the question whether it is possible to construct a vaccine that gives a heterotypic protection. In 1998 a paper was published on this subject. ISCOM H1N1 influenza vaccine protected mice against H2N2 influenza strain challenge. A commercial vaccine (Pandemrix®) was issued in 2010 and gave a longer lasting immunoprotection, apparently due to the use of squalene as an adjuvant. Unfortunately a strain of influenza was selected that later turned out to cause narcolepsy in predisposed individuals, esp children. This could not have been anticipated and not even tested beforehand, due to the rarity of the condition, even if it was increased about 3-fold.

Methods: A further development of ISCOM is now under investigation under the name of G3/DT®. It was shown that a vaccine H1N1 A/California/7/2009 (H1N1pdm09) protected against a lethal challenge with antigenically distinct H1N1 A/PR8/34 in a mouse model. It was also shown that the adjuvanted vaccine gave a high level of protective antibodies. Also influenza A virus-specific CD8+ T lymphocytes were induced and might in fact be responsible for the heterotypic response.

Conclusions: Due to the problem with adjuvanted vaccines so far no such influenza vaccine has been licensed in the US. To meet the above problem of non-matching strains we believe it is of great interest to investigate whether adjuvanted vaccines might address this problem and be advantageous for protection against yearly flu infection.

It might also be of interest in the context of other infections to investigate the role of an adjuvanted immune response.

Biography

Jan Fohlman has completed his PhD and MD from Freiburg, Linköping, Uppsala University and has been working as a consultant in infectious diseases for >30 years, now at Dept of Research and Development Region Kronoberg, Växjö, working closely with Linnaeus Univeristy. He is a board member of 3Diva AB, a recently started vaccine development company. He has published more than 100 papers in reputed journals and has been serving as a referee for multiple journals.

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