NEWSLETTER

FLUNIVAC

AUGUST 2017

FLUNIVAC: THE ACHIEVEMENTS

OVER THE PAST YEARS, THE FLUNIVAC CONSORTIUM HAS BEEN PARTICULARLY SUCCESSFUL IN THREE MAJOR AREAS. THE FIRST AREA IS THE IDENTIFICATION AND OPTIMIZATION OF INFLUENZA ANTIGENS FOR INDUCING BROADER LEVELS OF INFLUENZA-SPECIFIC IMMUNITY, THE SECOND AREA RELATES TO THE REGULATION OF MVA GENE EXPRESSION, WHICH OPENS THE PATHWAY FOR OPTIMIZED USE IN THE FUTURE. AND THIRDLY, THE FLUNIVAC PARTNERS HAVE DEVELOPED NEW WAYS TO INFLUENCE THE MVA INDUCED ANTIGEN SPECIFIC IMMUNITY, WHICH IS IMPORTANT FOR BOTH T-CELL IMMUNITY AND ANTIBODY IMMUNITY.

FLUNIVAC consortium partners in Rotterdam, Ghent and Munich focused their collaborative research mainly on three specific virus antigens: the nuclear protein (in the aim to induce broader levels of T-cell mediated immunity against influenza), and two antibody antigens (M2e and neuraminidase). M2e is a very short membrane associated antigen of influenza A virus, and interestingly, it is based on a highly conserved amino acid sequence that allows to induce antibody responses to influenza A viruses that are cross-reactive with many strains from different subtypes.

One of the challenges associated with the shortness of M2e, however, is to optimize its presentation to the immune system.

By engineering a fusion protein with an MVA encoded glycoprotein, the FLUNIVAC partners have found a possible solution to this challenge. The glycoprotein has been modified to carry three copies of the M2e antigen in its head domain, which allows to expose the M2e antigen more prominently, leading to enhanced antibody response. Interestingly, experiments in mouse models have demonstrated that vaccination with this MVA-A56-M2e indeed protects against infection with influenza A virus. This leads to the conclusion that M2e should definitely be maintained as a highly promising candidate antigen for the development of a “universal” influenza vaccine.

Pursuing another promising research route, the FLUNIVAC partners have confirmed the nuclear protein as a very important T cell antigen, which by itself can already provide considerable levels of protection. The FLUNIVAC researchers also demonstrated that modifying this antigen – in specific ways that have been identified within the FLUNIVAC project – may enhance the T cell immunogenicity.

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FLUNIVAC: THE BASICS

THE QUEST FOR A UNIVERSAL INFLUENZA VACCINE

FLUNIVAC (InFLUenza virus UNIVersal VACcine development program) is a unique consortium of various European SMEs, universities and an industry partner, which is supported by the European Commission’s Seventh Framework Program. FLUNIVAC’s aim is to pave the way to the development of a universal influenza vaccine.

WHY IS A UNIVERSAL INFLUENZA VACCINE NEEDED?

Influenza viruses have a great capacity to mutate and change. Current flu vaccines are safe and effective, but they have to be updated annually to match the epidemic strains and occasionally there is a mismatch with the circulating virus strains. There is hence a great need for new vaccines that can induce broad immunity ideally against all manifestations of influenza in humans (seasonal, zoonotic and pandemic).

MVA: A CRUCIAL TOOL

A crucial element in FLUNIVAC’s research is a vaccine delivery platform based on MVA (Modified Vaccinia virus Ankara). This replication deficient vaccinia-derived virus is unable to form new infectious particles in humans and thus is very safe to use. It allows the construction of recombinant MVAs that express influenza virus proteins in a way that favours recognition by our immune system.

→ Thirdly, the consortium partners have demonstrated that the neuraminidase is an important addition to the hemagglutinin in order to induce virus neutralizing antibodies, suggesting that the neuraminidase can be used to enhance protective efficacy. Various versions of the neuraminidase have been tested and experiments in animal models are still ongoing, but again the project partners have succeeded in identifying antigens that provide an astonishing protective efficacy.

With regards to gene expression, the FLUNIVAC partners have tested and identified new MVA specific early-late promoters, from which a preferred candidate promoter has been selected for future vaccine construction.

The ultimate aim of the FLUNIVAC project is to select the most promising vaccine candidate from the ground-breaking research that has been performed over the past years, combining its many milestone achievements in one single candidate construct. Obviously, this would then require confirmative, pre-clinical, toxicological testing before possibly moving into a clinical evaluation. In other words, FLUNIVAC has opened up a remarkable set of promising research pathways that definitely need further exploration beyond the limited time frame attributed to the FLUNIVAC project. ■

THE FLUNIVAC CONSORTIUM

FLUNIVAC is a collaborative effort of three academic groups, four SME's and an industry partner.

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COOPERATION