Targeted IMmunIsation of Next Generation vaccines: towards a personalized approach of protecting risk groups from infectious diseases (TIMING)

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Note: this pitch is based on part of a project that was submitted to the NWA-ORC round 2020/21.

The problem:

Due to increasing life expectancies, the proportion of the population over 50 years of age will continue to increase over the coming decades. More frequent occurrence of (co)morbidities as well as a decline in immune function with age, a process called immunosenescence, makes this population specifically vulnerable to infectious disease and poses a major health threat to the population. Vaccination has proven to be highly effective to prevent morbidity and mortality and should ensure healthy ageing. However, vaccine effectiveness differs among individuals and between vaccines and decreases with ageing. This heterogeneity is caused by a complex interplay of physiological and immunological parameters which is thought to be influenced by differences in exposures over the life course. Currently, the associations between these exposures and the immune system's ability to control infectious diseases and mount effective vaccine responses is largely unknown. In addition, vaccine development is evolving fast and knowledge on protective immune responses and the duration thereof are limited for novel vaccine concepts. Understanding factors influencing immune responsiveness will be crucial for improvement of already existing as well as novel vaccines especially for vulnerable target groups. This is of utmost importance in an era where novel pathogen variants emerge and pose threats to a diverse and increasingly ageing population.

The challenge:

One of today's major challenges is to enhance the protection against infectious diseases in the entire society, by improving vaccine efficacy as well as uptake across all ages. This demands a more personalized approach. Here we propose to provide evidence-based knowledge to develop targeted vaccination strategies in different risk groups, including individuals with chronic diseases, cancer, undergoing therapy or otherwise experiencing disturbances in immune responses. To this end we will perform in-depth studies into underlying immunological deficits and life-time exposures that inhibit proper response to vaccination to 1) understand protective immune mechanisms, 2) develop biomarkers to identify risk groups, 3) develop strategies to improve vaccination response and 4) improve vaccination uptake. The results of the project will be an essential step in the development of targeted vaccination strategies and lead to improved protection against infectious diseases for the population at large.

The offer

The intrinsic immune capacity to deal with pathogenic challenges decays with age and renders the elderly population vulnerable to a wide array of infectious respiratory diseases. This age-related decline in immune competence does not occur at an equal pace across individuals, and leads to a large heterogeneity amongst the elderly population. Understanding heterogeneity in health status and underlying mechanisms is pertinent to optimal protection of the population from infectious diseases (Shen-Orr & Furman, 2013). Identification of measurable biomarkers may render interventions much more effective, both at the individual and population level. In this project we aim to identify novel **(bio)markers to identify groups at increased risk for infections and lower vaccination response** using existing unique longitudinal cohorts. Various markers of **biological age** have been proposed (Deelen et al., 2019; Kuo et al., 2020; Lu et al., 2019) that provide personalized readouts of an individual's rate of ageing. These markers have been designed to capture an individual's overall health status and physical capacity, and shown to predict a wide array of clinical endpoints, including mortality.

In this project, we will evaluate whether biological age markers are indicative of the intrinsic immune competence, thus marking the vulnerability to a wide array of respiratory diseases. To this end we aim to measure markers of immune competence in well described Dutch (ageing) cohorts to identify and evaluate clinical and biomarker profiles that track the age-associated decline of our immune system and subsequent susceptibility to respiratory infectious disease at old age. We welcome ideas for funding, cohorts that would be suitable to include in these analyses (with serum and potentially cells available) and collaborations to advance further synergy between this initiative on immune ageing and improving vaccination and DUSRA activities and themes.