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MICROBIAL PLATFORM FOR VACCINE PRODUCTION FOR LOW- AND MEDIUM-INCOME COUNTRIES (LMICS): 2 CASE STUDIES

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Vaccination is critical for the prevention and control of infectious-disease outbreaks, being of paramount importance to global health, they are a key component of primary health care and an indisputable human right. Yet far too many people around the world have insufficient access to vaccines. The limited availability and affordability of vaccines to resource low-income countries has created a need for solutions that will ensure effective, affordable vaccine production technology. With potential for more pandemics, the urgency to expand vaccine range has become even more evident.

We will present a collaborative project between UCL and PT Bio Farma in which we have developed platforms to manufacture two novel immunization candidates, a recombinant virus-like-particles vaccine against Dengue disease (case study 1) and a recombinant protein vaccine against COVID-19 disease (case study 2). Both vaccines will have a social and economic impact by reducing the number of cases, and the overall mortality and morbidity.

Dengue is an emerging mosquito-borne viral infection with increasing reports of outbreaks and can be in tropical and sub-tropical areas, with Southeast Asia and the Western Pacific being the most seriously affected zones. A total of 3.8 billion people is potentially at risk, and in a scenario of global warming, this can increase to 6 billion people by 2080. To date, there is one commercialized vaccine (Sanofi-Pasteur) but is restricted to individuals aging from 9-45 years, who have been previously infected with the virus. The COVID-19 pandemic has sum approx. 400 million cases and 6 million deaths worldwide since it was first reported in 2019. Even though the production and delivery of a vaccine has significantly increased over time, the affordability, accessibility, and acceptability at individual and country levels is still a major limitation.

The work performed consisted in the establishment of a cost-effective manufacturing processes to be implemented in Indonesia, which is classified as a lower-middle income country (World Bank 2021). *Pichia pastoris* (*Komagataella phaffii*) was used as a host in both vaccine manufacturing processes, since it is one of the most promising candidates for expression of heterologous proteins in vaccines development. It combines the speed and ease of highly efficient prokaryotic platforms with some key capabilities of mammalian systems. We have increased production yields, by employing scale down methodologies, and scaled-up production of the COVID-19 vaccine at the partner company. To ensure high product quality, we have simplified vaccine purification using affinity chromatography and developed alternative biophysical characterisation methods for the dengue vaccine prototype.

We have successfully demonstrated the versatility of using *K. phaffii* platform in the manufacturing of soluble vaccines (S1 SARS-CoV-2 RBD antigen) as well as the production of nanoparticles (dengue virus like particles, VLPS). Overall, these two case studies, will act as a foundation for the establishment and development of COVID-19 and dengue vaccine for industrial production, enabling Indonesia to be self-sufficient in a pandemic situation.