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Microbial platform for vaccine production for low and medium income countries (LMICs): 2 case studies

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MICROBIAL PLATFORM FOR DENGUE VACCINE PRODUCTION FOR LOW AND MEDIUM INCOME COUNTRIES (LMICs)

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There is a growing public health need for effective preventive interventions against dengue disease. Not only are the number of cases increasing as the disease spreads to new areas, but explosive outbreaks are occurring. It is estimated that more than 40% of world population is at risk of dengue infection. Dengue disease is the most common mosquito-borne disease, transmitted by the bite of the female *Aedes aegypty* mosquito and caused by four distinct but closely related viruses, termed serotypes 1-4 (DENV1-4). The infection can be asymptomatic or a self-limited, acute febrile disease ranging in severity. Recovery from one serotype gives lifelong immunity to that particular strain, though a second infection by a different serotype can lead to dengue haemorrhagic fever (DHF), which has 2.5% mortality rate (*Figure 1*).
Additionally Dengue effects disproportionately LMICs, where the probative costs have slowed the development and distribution of prophylactics. Currently control measures rely on targeting mosquito vectors. However, the effectiveness of the applied techniques is often questionable [1,2]. Equally, up to now, there is only one licensed dengue vaccine, Dengvaxia® (CYD-TDV), which has been shown to have some limitations, namely the lower efficacy against serotype 2 as well as lower protective efficacy in children under 9 years old and dengue-naïve individuals, in whom it increases the risk of hospitalization and severe dengue [3]. Therefore, a safe, effective and affordable dengue vaccine against the four strains would represent a major therapeutic outcome for the control of the disease and could be an important tool for reducing dengue morbidity and mortality [2]. For this reason, the development of alternative cost-effective platform for the delivery of a multicompetent Dengue vaccine would constitute a major therapeutic outcome.
The focus of this study, carried out in collaboration with PT Bio Farma, Indonesia, is to create a platform for dengue production, which can be afforded and used by LMICs. The platform being developed uses yeast *Pichia pastoris*, a versatile and potentially cost-effective factory for the production of Virus-Like-Particles (VLP) for four dengue virus serotypes as a vaccine candidate. We are investigating the upstream design space to optimize both quantity and quality of the dengue vaccine prototypes (DENV1-4 vaccine). We will focus our presentation on reporting the optimisation of the upstream processing design space for the production of the serotypes, also we will report on both the quantity and the quality of the desired product, before purification steps.
Furthermore, we will share our experience on how international industrial-academic partnership can successfully develop tools and technologies to de-risk scale-up and enable rapid response.

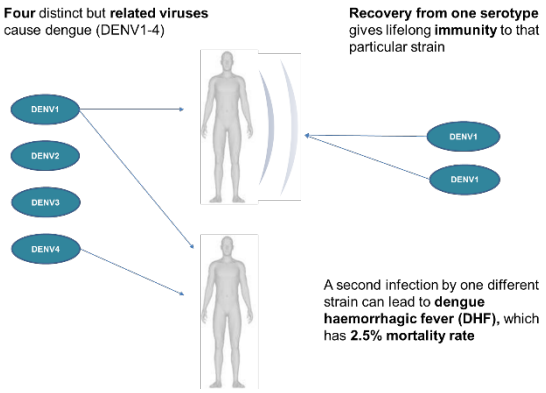

Figure 1: Dengue disease progression

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2. https://www.who.int/denguecontrol/disease/en/, assessed 7th January 2020
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