# SPOROMALVAC

The enduring goal of an effective vaccine against malaria constitutes a crucial component of efforts to eliminate this devastating disease. So far, vaccine candidates against the hepatic stages of Plasmodium infection have shown most success, with whole-sporozoite (Wsp) vaccines standing out as the sole strategy consistently shown to convey durable sterile immunity against malaria.

PfWsp vaccines, relying on the use of attenuated sporozoites (spz) of P. falciparum (Pf), are the most commonly employed approach to Wsp vaccination, albeit carrying the risks inherent to the use of the most virulent species of human-infective Plasmodium. The host lab recently established an alternative approach to Wsp malaria vaccination, based on the use of non-pathogenic rodent P. berghei (Pb) parasites genetically engineered to express antigens of their Pf counterparts. The proof-of-concept of this immunization strategy was firmly established by a wide array of pre-clinical data that warranted the clinical evaluation of a first PbWsp vaccine candidate, currently underway.

Despite their immense potential, both PfWsp and PbWsp immunization approaches face important TRANSVERSAL CHALLENGES, including 1) the absolute requirement of mosquitoes in order to obtain the spz required for immunization, 2) the dramatic loss of spz viability due to currently sub-optimal cryopreservation protocols, and 3) the limited potency of Wsp vaccines, which demand high numbers of immunizing spz and compromise the durability of the immune response. In this context, the ULTIMATE GOAL of the current project is to deliver adequate solutions to those limitations, towards unleashing the full potential of Wsp malaria vaccination.

The PbWsp model displays a SET OF UNIQUE FEATURES that make it most appropriate to address the critical issues faced by the Wsp field. Among these, its non-pathogenicity to humans and its ability to infect various liver cell and animal models make it ideally suited for laboratory evaluation of in vitro methods of spz production and for the development of effective spz cryopreservation strategies. Additionally, its amenability to genetic manipulation and its immunogenicity make PbWsp the ideal model to develop strategies aimed at improving Wsp vaccination efficacy. Crucially, the achievements enabled by this model are not only of immediate application to PbWsp vaccines but also constitute the ideal basis for the development of strategies that are readily employable by the PfWsp field. Thus, at the core of our INNOVATIVE METHODOLOGICAL APPROACH lies the systematic and sequential use of the PbWsp and PfWsp models to generate knowledge, tools and vaccine candidates that are directly relevant to both areas of Wsp vaccination.

To achieve our goals, we will synergize the complementary scientific and technological expertise of the host lab and world-renowned collaborators, placing our findings on a clear path to SCIENTIFIC INNOVATION and TRANSLATIONAL APPLICABILITY.