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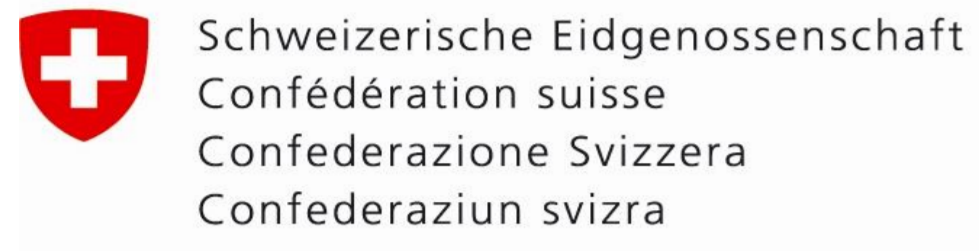
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AIM: to increase understanding of immune protection in the lung in *M. tuberculosis* (*Mtb*) infection and develop mucosal vaccination strategies for translation towards clinical evaluation. TBAC-HORIZON (2023-2027) links 19 institutions building on >25 years of EU-funded collaborations.

Project funded by:



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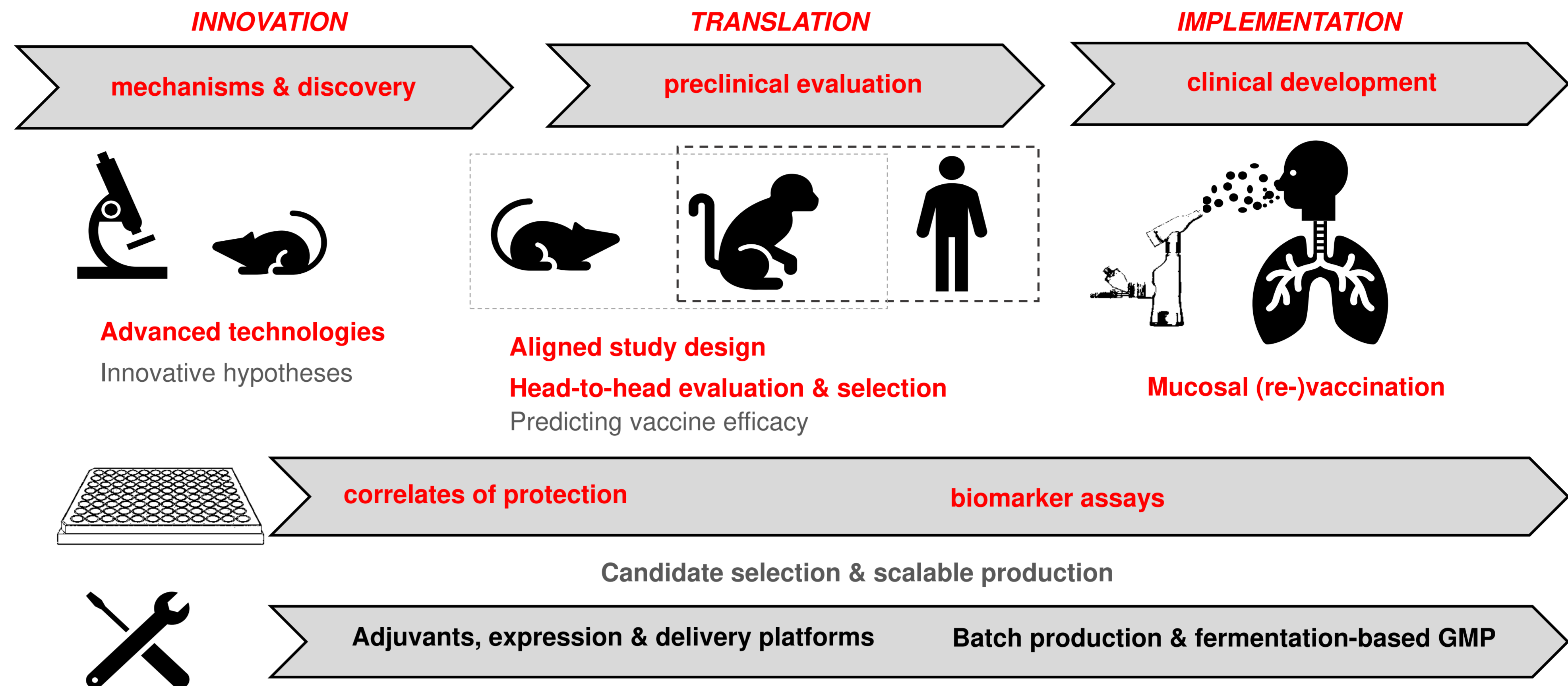
Schweizerische Eidgenossenschaft
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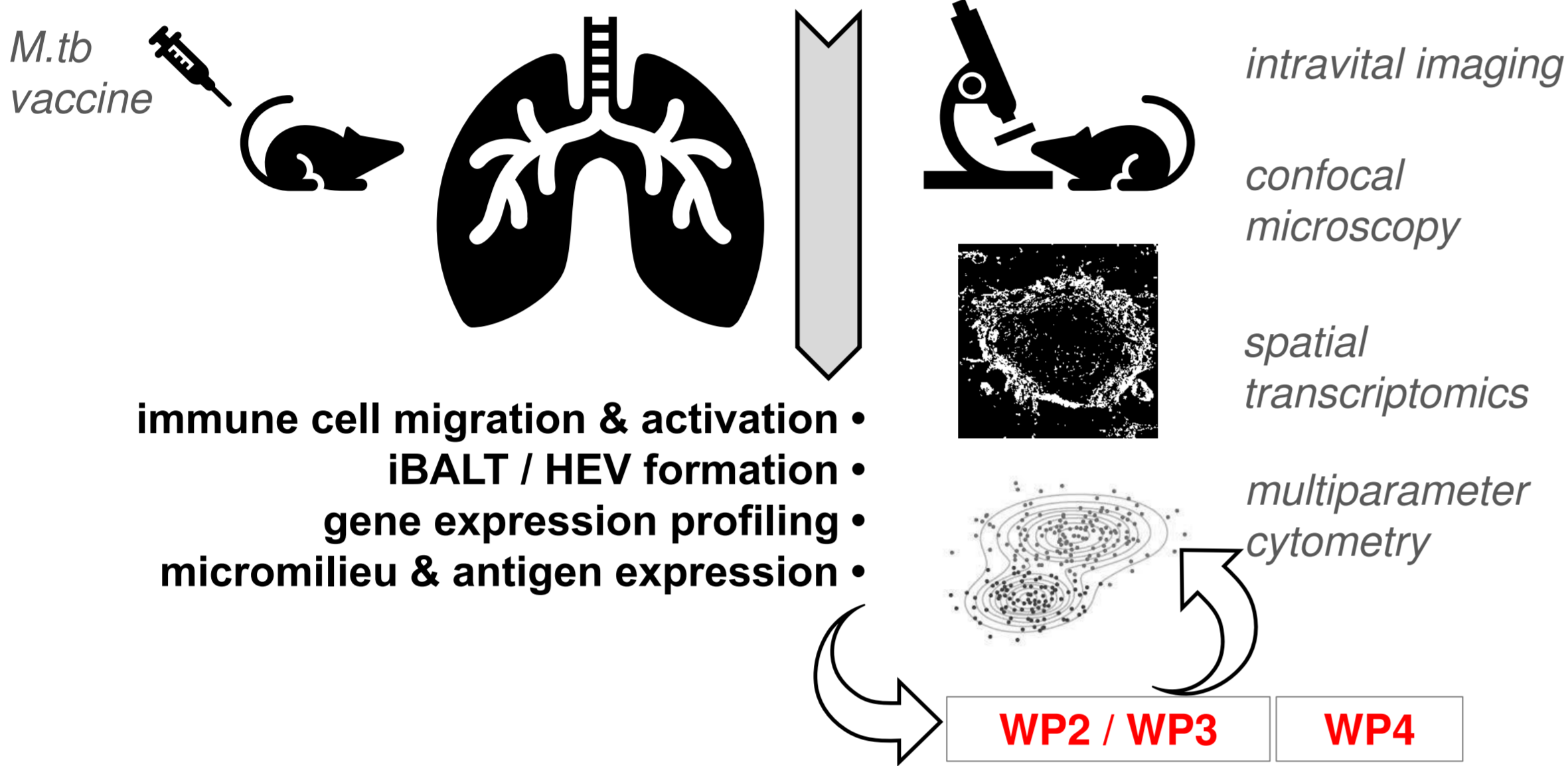
Federal Department of Economic Affairs,
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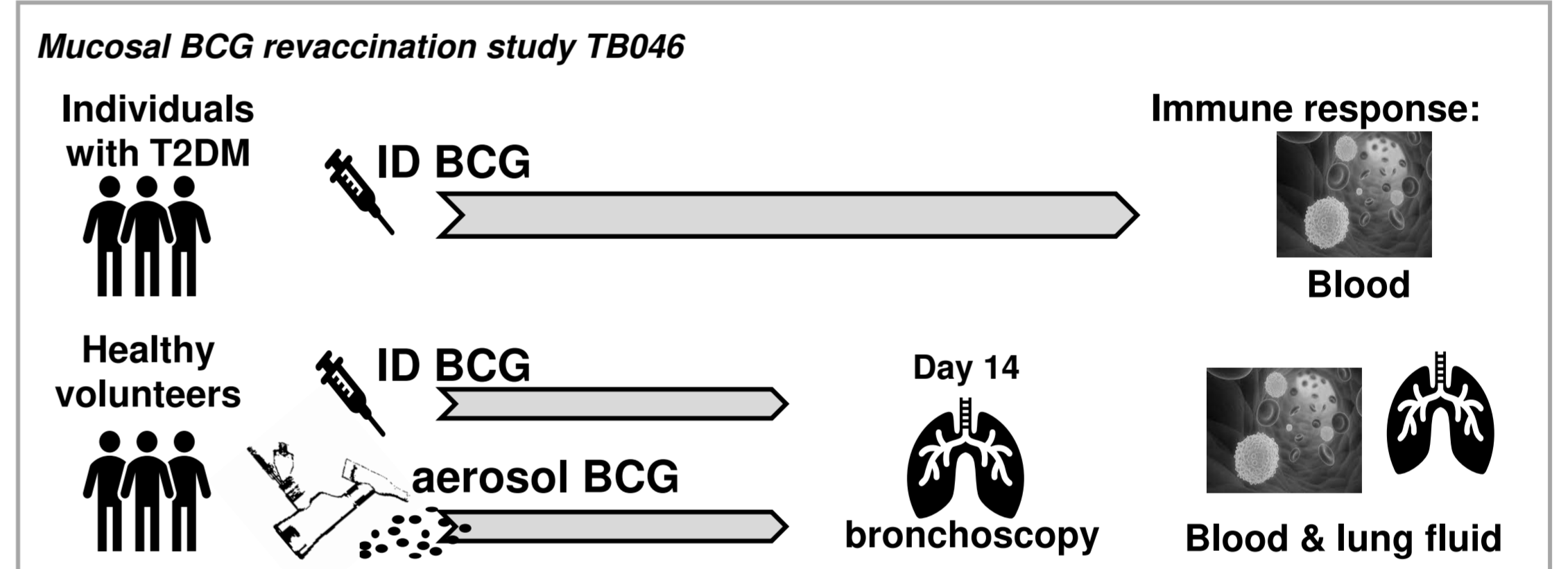
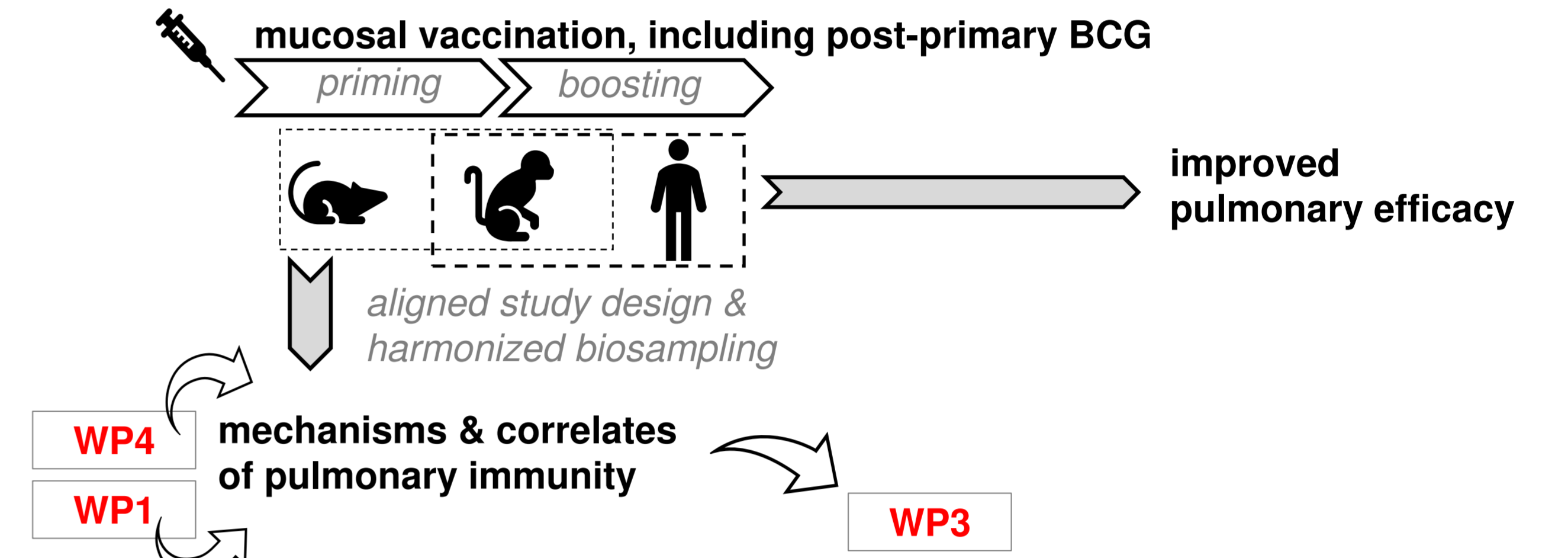


Objective 1 | WP1 - Basic Research into Local Immunity understanding mechanisms towards new biomarkers & better vaccines



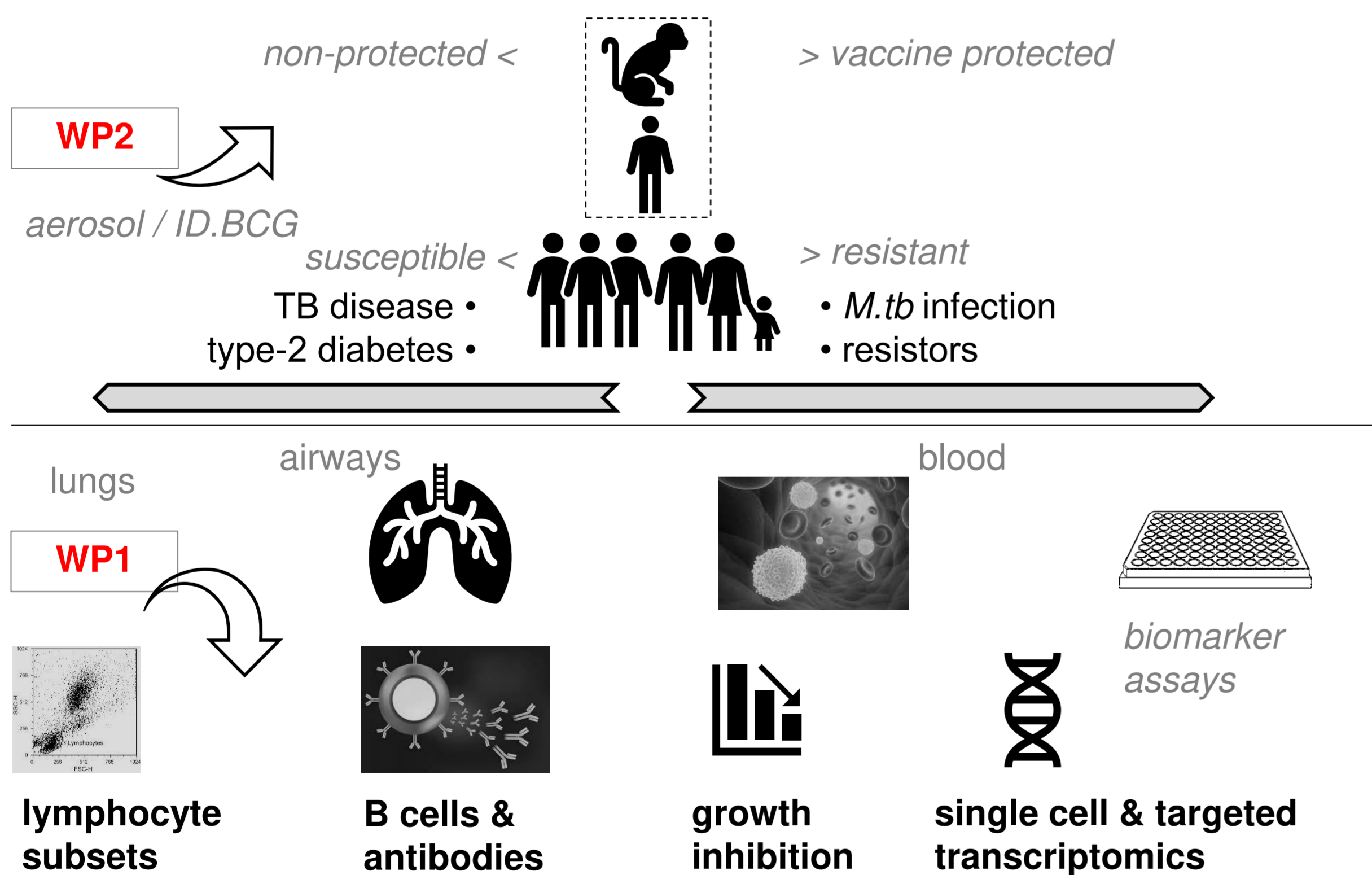
- Two *Mtb*-specific immunoglobulin knock-in mouse lines generated and characterized
- Procedure for analyzing lipid epitopes associated with CD1b in cell environments developed
- Transcriptional differences between vaccines of varying TCR strength analyzed, showing significant pathway differences
- Accelerated formation and maturation of High endothelial venule (HEV) in *Mtb*-infected lungs due to H107e/CAF® vaccination
- HEVs identified as a homing portal to granulomatous lesions in mice, potentially an unknown mechanism of T cell homing and vaccine protection
- Significantly higher pulmonary T cell numbers and greater diversity in SP140-competent mice, with robust cytokine-producing effector and memory T cells
- Analysis pipeline for spatial data established to identify and compare immune cells and their spatial niches in the lung

Objective 2 | WP2 - Translational Vaccine Research towards improving pulmonary protection by mucosal vaccine delivery



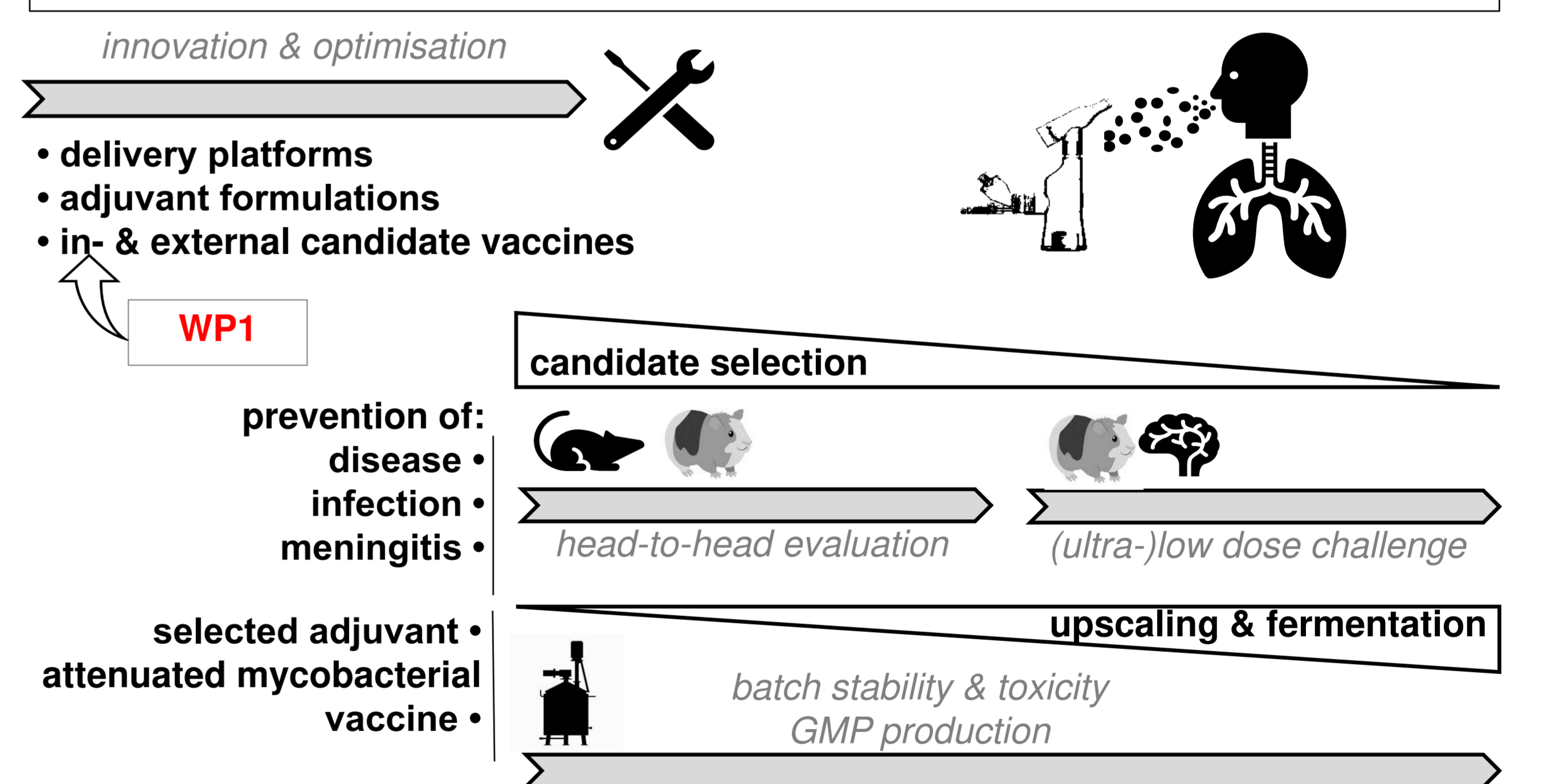
- Clinical trial underway (clinicaltrials.gov NCT06246851), 50% enrolment reached with 6 participants in each arm enrolled
- Immunological analysis underway

Objective 3 | WP3 - Identifying Biomarker Assays from identifying correlates to predicting vaccine-induced protection



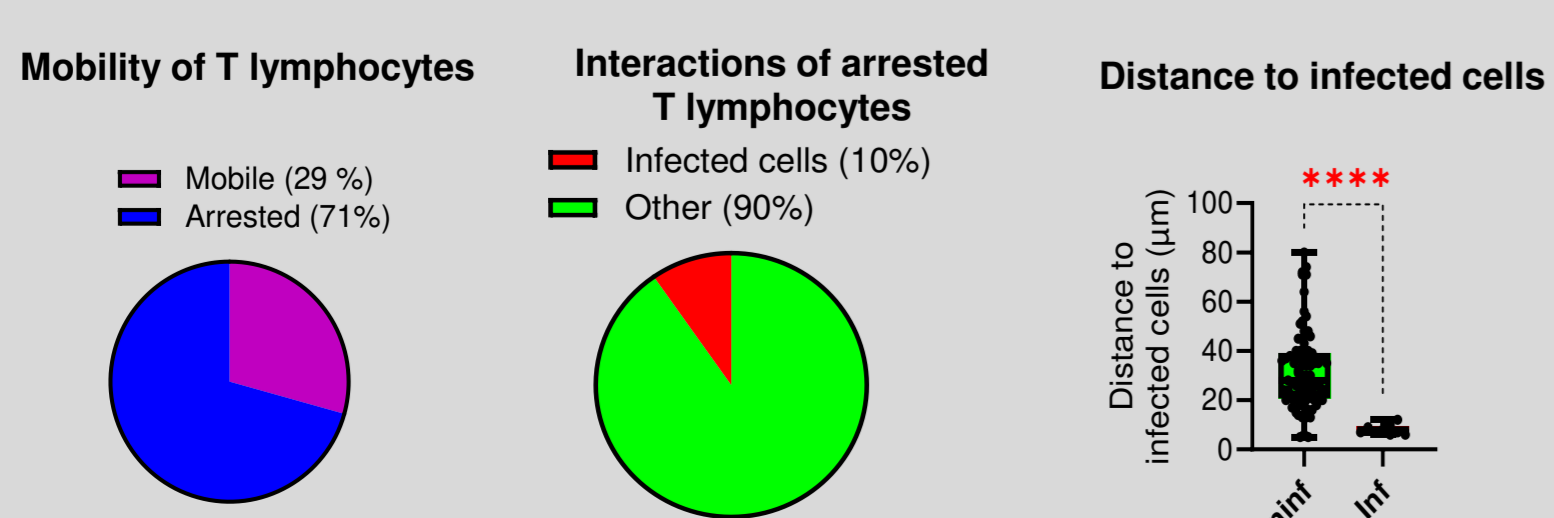
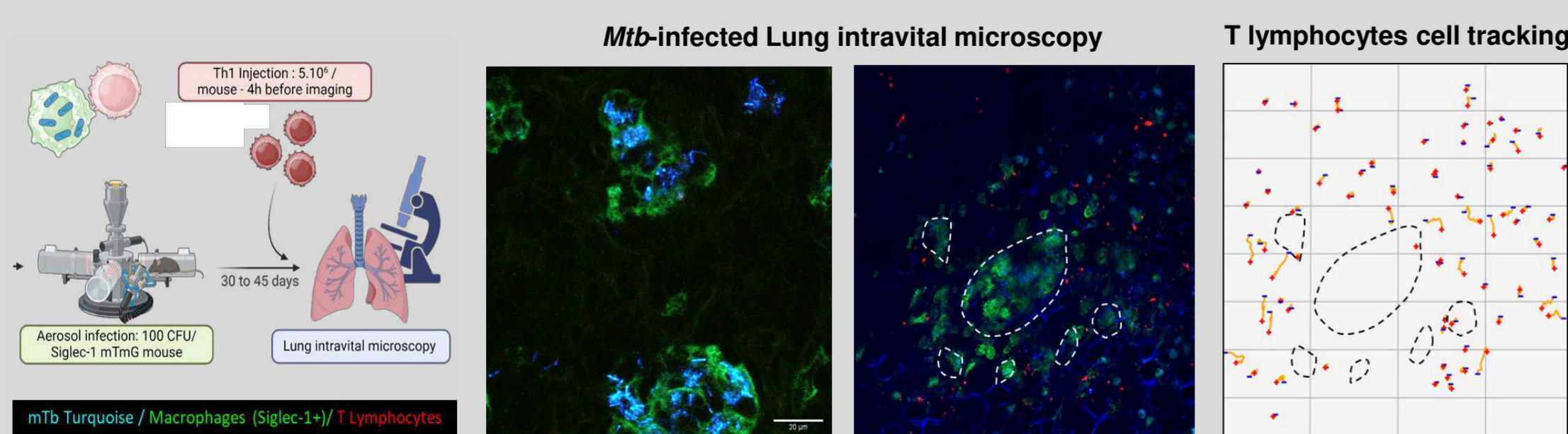
- Harmonisation of assay protocols in non-human primates and human studies
- Optimisation of protocols for handling bronchoalveolar lavage cells
- Selection of core markers for cell subset identification
- Collection of samples from WP2 for local and central analysis
- Panel of BAITs developed for antigen specific B cell enumeration

Objective 4 | WP4 - Vaccine Production & Selection Tools towards the clinical development of next generation vaccines



- Several TB antigens successfully expressed and secreted by live attenuated *Bordetella pertussis* platforms
- Extracellular vesicles from different mycobacterial backgrounds successfully isolated and characterization underway
- Various TB antigens successfully formulated with VFI Open Access adjuvants
- Three vaccine candidates selected by the portfolio advisory committee for the first experiment in the standard aerosol mouse model
- Successful construction of a marker-free version of rBCG::ESX-1^{mmar}
- GMP submerged fermentation process for rBCG::ESX-1 Mmar successfully developed

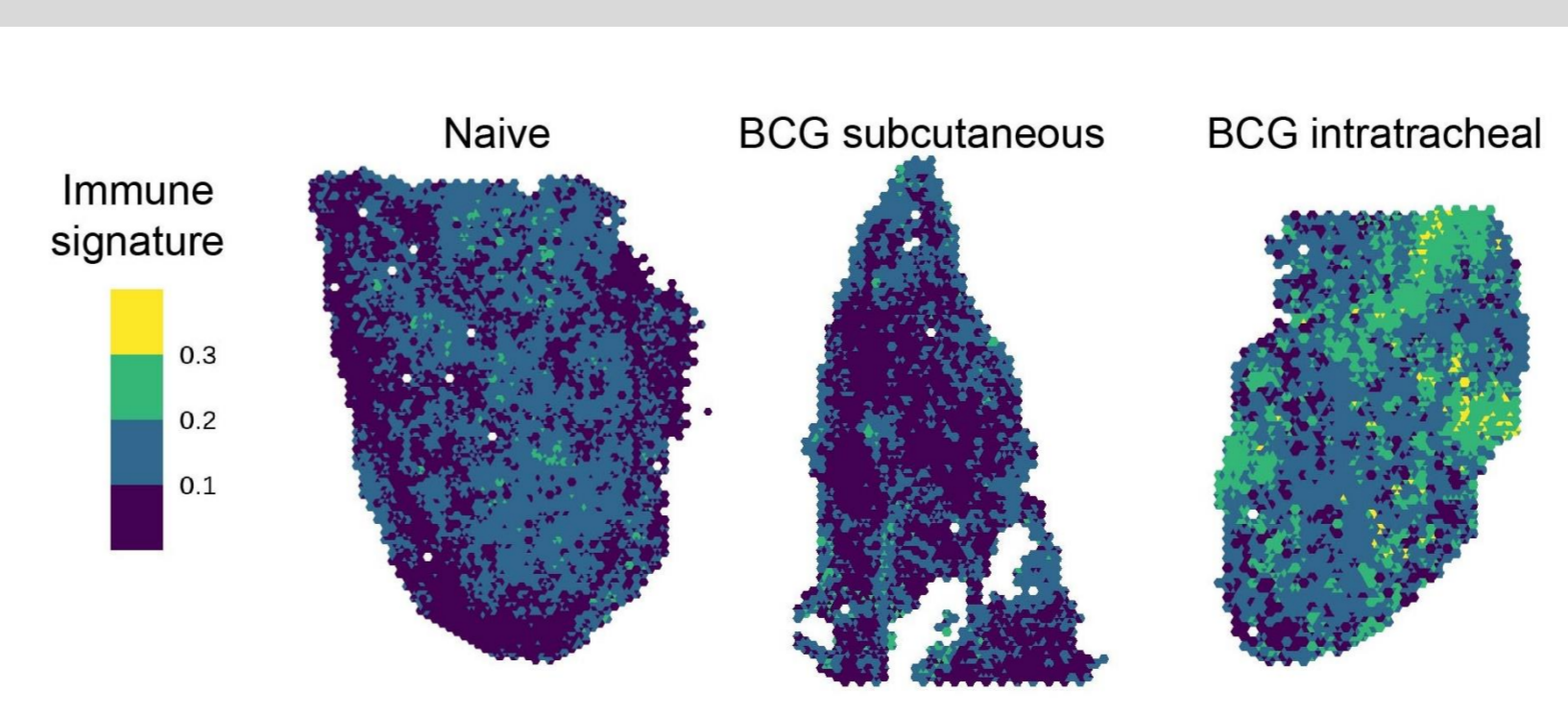
Live imaging of immunity to *Mtb*



- *Mtb* is detected in macrophages in the lungs of live mice
- T Lymphocytes localization, migration and interaction are analysed *in vivo*
- CD4 T cells are rarely located near *Mtb* infected cells
- Most extravascular CD4 T cells are arrested (70%)
 - Majority are not in interaction with infected cells (90%)
 - Arrested 20-40 μ m away from infected cells

→ Access to infected cells impaired by non infected macrophage cluster surrounded by collagen ?

In situ spatial technology



- ... comprehensive view of all cell types present at and around the site of infection
- ... analysis of cellular neighbourhoods around cell types of interest
- ... evidence of receptor-ligand interactions