TBVI, TuBerculosis Vaccine Initiative:
To facilitate the global development of new TB vaccines.

Foundation to facilitate European efforts towards the global development of new TB vaccines

www.tbvi.eu
TuBerculosis Vaccine Initiative (TBVI)

- Integrated European effort to develop effective, safe, globally accessible & affordable TB vaccines
  - Over 40 of world’s best universities, research institutes, and industries in TB vaccine development
  - Responsibility and ownership for each candidate left with partner

- TBVI TB vaccine pipeline
  - Priming vaccine
  - Boosting vaccine

- TBVI builds on the success of EU TB vaccine research programs
  - 4 new priming and boosting vaccines in clinical phase I to II stages
  - 4 new priming and boosting vaccines in preclinical and non clinical stages
  - 3 new adjuvants, one of which in clinical phase I studies
  - 15 new biomarkers with potential to be used in monitoring of clinical trials
TBVI’s partners

**Argentinia**
- Veterinary and Agriculture Research Centre
- National Institute for Agricultural Technology

**Belgium**
- Université Libre de Bruxelles
- Institut Scientifique de Sante Publique
- GSK-Biologicals
- European Commission

**Denmark**
- Statens Serum Institute
- European Malaria Vaccine Initiative (EMVI)

**Ethiopia**
- Armauer Hansen Research Institute

**Finland**
- FIT Biotech

**France**
- Centre National de la Recherche Scientifique
- Institute National de la Santé et de la Recherche Médicale
- Institute Pasteur Paris
- Institute Pasteur Lille
- Institut Merieux
- PX’ therapeutics

**Germany**
- University of Lübeck

**Italy**
- National Institute for Infectious Diseases “Lazzaro Spallanzani”
- University of Palermo
- Istituto Superiore Di Sanita
- University of Padua

**Netherlands**
- Central Veterinary Institute of Wageningen UR
- Biomedical Primate Research Centre
- BioMedical Research of Wageningen UR
- Leiden University Medical Center
- Netherlands Vaccine Institute
- European Developing Countries Clinical Trials Partnership

**Senegal**
- Hospital Le Dantec

**South Africa**
- University of Cape Town

**South Korea**
- Institut Pasteur Korea
- Educational Foundation Yonsei University
- International Vaccine institute

**Portugal**
- Gulbankian foundation

**Spain**
- Universidad de Zaragoza Facultad de Medicina
- Fundacio Institut De Investigado de Ciencies De La Salut Germans Trias I Pujol
- CZ Veterinaria/BIOFABRI

**Switzerland**
- Institute for Research in Biomedicine
- University of Geneva
- University Hospital of Basel
- University of Zürich
- Centre Hospitalier Universitaire Vaudois
- STOP TB Partnership

**United Kingdom**
- University of Birmingham
- Aston University
- Manchester University Medical School,
- Imperial College of Science Technology and Medicine
- National Institute for Biological Standards
- University of Oxford
- London School of Hygiene and Tropical Medicine
- Health Protection Agency Porton Down
- Veterinary Laboratory Agencies
- University College London

**USA**
- Aeras Global TB vaccine Foundation
- Bill and Melinda Gates Foundation.
European R and D Effort for New TB Vaccines, in the R and D Frame Work Programs

  B. GICQUEL, Institute Pasteur, Paris, France

  J. THOLE, ID-Lelystad, The Netherlands
  (P.H. LAMBERT, University of Geneva, Steering Committee Chair)

- FWP7: 2010–2013: NEWTBVAC, Collaborative Project
  J. THOLE, TBVI, Lelystad, The Netherlands
  (S.H.E KAUFMANN, MPII, Berlin, Steering Committee Chair)
PRODUCT DEVELOPMENT TEAM: PDT

Composition

The Product Development Team (PDT) is a neutral group, composed of experts in vaccine development:

- Mei MEI HO
- Micha ROUMIANTZEFF
- Georges THIRY (Chair)
- Barry WALKER
- + additional experts, as needed
How PDT operates

- Expert advisory group with recommendations to Developers and (TBVI) SC.
- Link / advisor to consultants or groups (CMO, CRO)
- Final decisions are from Developer.

- Annual review meeting called by developer or PDT.
- Additional meetings, at relevant points in the development pathway, called by Developer or recommended by PDT.
- Regular informal contacts with developers.
PDT responsibilities

In Research,
- Transit from Research to Development
- Identify vaccine candidate to enter into pre-clinical development;
- Assist developers in preparation for Phase 1.

In Development,
- Continue to advise development of products in Phase 1.
- Build on knowhow on products, and relationship with developers.
- Ensures continuum in the development of the products.
- Close collaboration with the Clinical Development Team.
The Clinical Development Team: CDT Composition

The Clinical Development Team (CDT) is a neutral group, composed of clinician experts in vaccine development:

- Juhani ESKOLA, Finland (Chair)
- Francois SPERTINI, Switzerland
- Roland DOBBELAER (Belgium)
- + additional experts, as needed
CDT operations

- CDT will operate similarly to the PDT
- PI or developer has the ownership of the product, and has ultimate power in development decisions
- plan is to have one annual review meeting for each project in appropriate phase (often jointly with PDT)
- recommendations of CDT will be communicated to NEWTBVAC SC
CDT responsibilities

(1) project management
(2) development of CD strategy
(3) planning and preparation of clinical studies
(4) product specifications from CD point of view
(5) selection of CRO
(6) regulatory policies and requirements
(7) guidance during Phase 1 and Phase 2 studies
(8) facilitate access to informal pathways for expert advice
## New Vaccines in the Pipeline

### BCG Replacing Vaccines

**Improve BCG**
- Adding TB specific antigens (eg. ESAT6)
- Overexpression of antigens (Ag85)
- Adding Latency and resuscitation Ag (DosR, Rv3407)
- Engineering phagosome escape (Hly, Pfo)

**Attenuate M. Tuberculosis**
- Deleting essential genes (eg. PhoP, auxotrophic mutants)

### Boosting Vaccines

**(Viral) vector based**
- MVA, Adenovirus (Ag85, ESAT6, etc.)

**Subunit antigens combined with adjuvants**
- Secreted antigens (Ag85, ESAT6, TB10.4)
- Strong T cell immunogens (Rv1196, Rv0125)
- Latency antigens (hsp16, DosR etc)
- Adjuvants (IC31, AS02/1B, DDA/TDB)
TBVI Vaccine Strategy

Two Pillar Strategy

Develop priming vaccine
- Given to newborns,
- Protective in latently infected persons
- Safe in persons w/HIV

Develop boosting vaccine
- Used in infants, adolescents & young adults
- Protective in non-infected as well as latently infected
## Products Supported In Clinic

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Manufacturer</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVA85A</td>
<td>Oxford (UK)</td>
<td>Recombinant Vaccinia expressing Ag85A, to boost BCG</td>
</tr>
<tr>
<td>M72 in AS01B</td>
<td>GSKBio (Belgium)</td>
<td>Subunit fusion protein of Rv1196 and Rv0125 in AS01B adjuvant, to boost BCG</td>
</tr>
<tr>
<td>85B-ESAT6 in IC31 (Hyb1)</td>
<td>SSI (Denmark)</td>
<td>Subunit fusion protein of Ag85B and ESAT6 in IC31 adjuvant, to boost BCG</td>
</tr>
<tr>
<td>rBCGΔUreA::Hly</td>
<td>VPM (Germany)</td>
<td>Recombinant BCG expressing Lysteriolysin, to replace BCG</td>
</tr>
</tbody>
</table>
## Products Supported: Preclinical

<table>
<thead>
<tr>
<th>Product</th>
<th>Institution</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SO2 (PhoP)</td>
<td>Un. Zaragoza (Spain)</td>
<td>Recombinant M. tuberculosis attenuated MTB, to replace BCG</td>
</tr>
<tr>
<td>HBHA</td>
<td>Institut Pasteur de Lille (France)</td>
<td>Protein extract, in adjuvant, to replace / boost BCG</td>
</tr>
<tr>
<td>Ac2SGL</td>
<td>CNRS, Toulouse (France)</td>
<td>Glycolipid extract, in adjuvant, to replace / boost BCG</td>
</tr>
</tbody>
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TBVI CONTRIBUTION for NEW LIVE TB VACCINES

2 MEETINGS "Geneva 1" and "Geneva 2"
Organized at WHO by TBVAC / TBVI
with Co-Sponsorship of AERAS and WHO

Geneva 1  3-4 November 2004
"New live mycobacterial vaccines: the Geneva consensus on essential steps towards clinical development"

A.T. KAMATH et al  Vaccine 23 (2005) 3753-3761

Geneva 2  6-7 April 2009
"The second Geneva Consensus: Recommandations for novel live TB vaccines"

K.B. WALKER et al  Vaccine 28 (2010) 2259-2270
Steven REED, IDRI, Seattle – Targeting innate immunity with traditional, live attenuated and adjuvanted subunit vaccines.

Ennio de GREGORIO, NOVARTIS, Siena – The mode of action of oil-in-water emulsion adjuvants

Peter L. ANDERSEN, SSI, Copenhagen – Directing and maintaining the immune response by cationic liposomes

Nathalie GARÇON, GSK Biologicals, Rixensart – TLR4 agonists

Paul-Henri LAMBERT, University of Geneva – Which target disease vaccine may require an adjuvant?

Claire-Anne SIEGRIST, University of Geneva – Which challenges for early life vaccine adjuvants?

Stefan KAUFMANN, Max Plank Institute, Berlin – Adjuvants for tuberculosis vaccines
THANKS to:

Partners of TB Vaccine Cluster, TBVAC, NEWTBVAC
European Commission, TBVI, WHO, AERAS

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