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# **TBVI, TuBerculosis Vaccine Initiative:**

**To facilitate the global  
development of new TB vaccines.**



**TBVI**

TuBerculosis Vaccine Initiative



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

[www.tbvi.eu](http://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

## Argentina

- 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
- Institut National de la Santé et de la Recherche Médicale
- Institut Pasteur Paris
- Institut Pasteur Lille
- Institut Merieux
- PX' therapeutics

## The Gambia

- MRC The Gambia

## Germany

- University of Lübeck

- Technical University of Munich
- Max-Planck Institute for Infection Biology
- University of Tübingen
- University of Ulm
- University of Erlangen-Nürnberg
- Vakzine Projekt Management

## 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 Ciencias 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.

# Our Partners



# European R and D Effort for New TB Vaccines, in the R and D Frame Work Programs

- FWP5: 2000–2003: TB Vaccine Cluster  
B. GICQUEL, Institute Pasteur, Paris, France
- FWP6: 2004–2009: TBVAC, Integrated Project  
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

<b>MVA85A</b>	Oxford (UK)	Recombinant Vaccinia expressing Ag85A, to boost BCG
<b>M72 in AS01B</b>	GSKBio (Belgium)	Subunit fusion protein of Rv1196 and Rv0125 in AS01B adjuvant, to boost BCG
<b>85B-ESAT6 in IC31 (Hyb1)</b>	SSI (Denmark)	Subunit fusion protein of Ag85B and ESAT6 in IC31 adjuvant, to boost BCG
<b>rBCGΔUreA::Hly</b>	VPM (Germany)	Recombinant BCG expressing Lysteriolysin, to replace BCG



# Products Supported: Preclinical

<b>SO2 (PhoP)</b>	Un. Zaragoza (Spain)	Recombinant M. tuberculosis attenuated MTB,  to replace BCG
<b>HBHA</b>	Institut Pasteur de Lille (France)	Protein extract, in adjuvant,  to replace / boost BCG
 <b>Ac2SGL</b>	CNRS, Toulouse (France)	Glycolipid extract, in adjuvant,  to replace / boost BCG

# 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

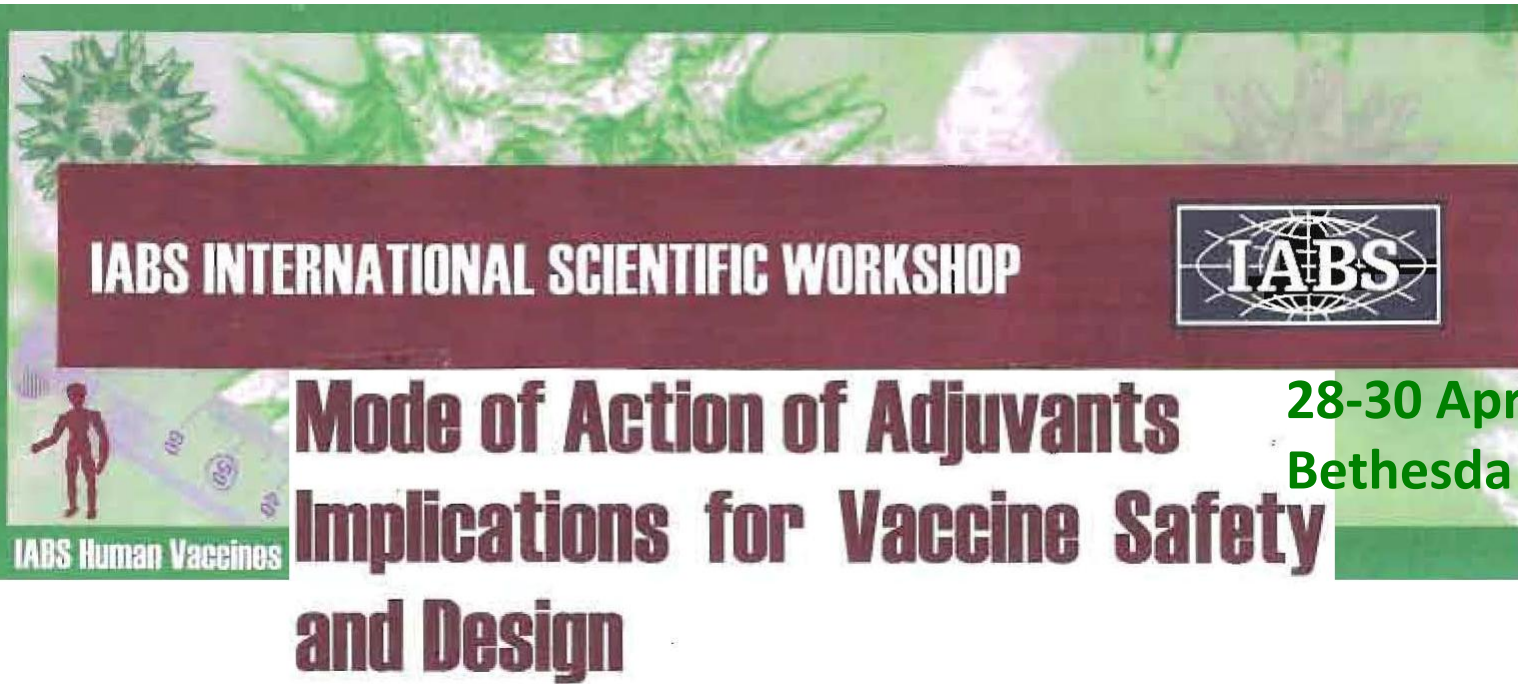
"The second Geneva Consensus: Recommendations for novel live TB vaccines"

K.B. WALKER et al Vaccine 28 (2010) 2259-2270





# TBVI CONTRIBUTION for ADJUVANTED TB VACCINES



28-30 April 2010  
Bethesda Maryland, USA

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

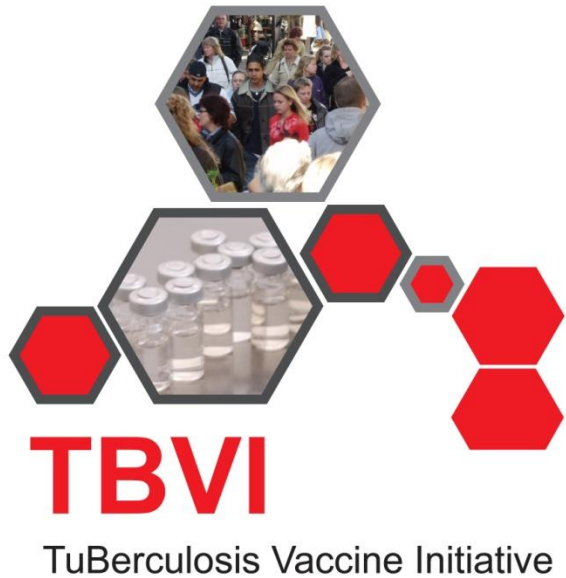
Peter L. ANDERSEN, SSI, Copenhagen – Directing and maintaining the immune response by cationic liposomes

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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