Primum non nocere
Vooral geen schade berokkenen

Clinical vaccine research at UGent/UZGent
The impact of vaccines on global health cannot be overestimated

• Safe water and sanitation
• Vaccines
• Antibiotics
• ...
## Impact of vaccination in the US

Disease and death, before and after introduction of vaccines

<table>
<thead>
<tr>
<th>Disease</th>
<th>Before vaccination</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cases</td>
<td>deaths</td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>472</td>
<td></td>
</tr>
<tr>
<td>Diphteria</td>
<td>21053</td>
<td>1822</td>
<td></td>
</tr>
<tr>
<td>Pertussis</td>
<td>200752</td>
<td>4034</td>
<td></td>
</tr>
<tr>
<td>Paralytic polio</td>
<td>16316</td>
<td>1879</td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>530217</td>
<td>440</td>
<td></td>
</tr>
<tr>
<td>Mumps</td>
<td>162344</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Congenital rubella</td>
<td>152</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

Roush et al. JAMA. 2007;298(18):2155-2163
Impact of vaccination
Estimated deaths averted with vaccines in low-income countries

2011-2020
Estimated deaths averted with vaccines in low-income countries

NO. OF DEATHS AVERTED

4.8m
2.9m
0.3m
0.8m
1.5m
1.4m

Measles vaccine
Diseases with new or underutilized vaccines

Total estimated number of deaths averted, 2011-2020
23.3 million

Source: Vaccine 2013; 18;31 (Suppl 2): B61-72
Figure: 5
25 diseases are currently preventable by vaccination

Center for Vaccinology - CEVAC Mission

Contribute to the development of new, safe and efficacious vaccines and the improvement (safety, immunogenicity) of existing vaccines for the prevention or treatment of infectious diseases.

via

- Evaluation of candidate vaccines => Clinical Trials
- Monitoring immune response = innate, humoral, cellular
- Development or improvement of assays to monitor these immune responses
CEVAC Clinical team

Cathy Maes
Martine Cornette
Lieve Van Crombrugge
Fien De Boever
Annelies Aerssens

Not on the picture

- Katrien Demaegd
- Lien Lievens
- Corinne Vanbruwaene
- Marleen Vandeputte
- Caroline Vanden Bulcke

Marleen Aps
Rebecca Lawaise
Hermien Sergeant
Anniek De Simpel
Conducted more than 200 vaccine trials since 1986.

Has **vast experience** in supporting ALL aspects of clinical vaccine evaluation ‘from protocol development to study report’.

Applies Good Clinical Practice (GCP) guidelines and quality standards.

**Fast recruitment of large numbers of participants**

- DATABASE with **11,000 adult volunteers** (≥18 years).
- Participants included in CEVAC trials varied from 20 to 700.

**CEVAXIS**: software system for participant management

- Smart recruitment, exporting logs, custom workflow per study, dashboard, document generation, label printing, ..
CEVAC Core Lab team

Sibyl Couvent
Peter Vander Linden
Leen Van Kerckhove
Annelies Coussaert
Geert Leroux

Sibyl Leen
Peter Annelies
Leen Geert
Annelies Coussaert
Geert Leroux

Sabrina Verlee
Sofie Librecht
Yvonne Gijbels
Caroline Buysschaert
Gwenn Waerlop
Anja Coen
Frédéric Clement
Core Lab services

Pre-analytical procedures

- **PBMC processing**
  - Up to 100 samples/day (50ml of whole blood)
  - Samples cryopreserved within 6 h post sampling
  - Viability of > 98%
  - Monitored storage capacity (in liquid nitrogen) of > 80 000 vials

- **Serum and Plasma collection following sponsors’ guidelines**
  - Serum and/or plasma are frozen within 1h post sampling
  - Full Chain of Custody

- **Mucosal samples**
  - Saliva, throat swabs, vaginal and rectal fluid
  - Validated sample preparation procedures
Core Lab services

Immuno-Monitoring
- Commercially available assays
- Assays developed and validated in-house (CBER, EMA)
- Assays transfer from sponsor lab → CEVAC lab

Humoral Immunity
- Antibody
  - ELISA
  - Functional-Assays
- B-cell
  - Ex-Vivo Antibody Secreting Cells
  - Memory B-cell
Core Lab services

Cellular Immunity

Soluble factors:
Cytokine/chemokine ELISA
Cytometric Bead Array

Cell based Assays
Thymidine incorporation proliferation
CFSE proliferation

Intracellular Cytokines Staining Assay
BD- LSRII
BD- LSR Fortessa X20
CEVAC scientific output

192 A1 papers on vaccines and host-pathogen interactions

- HBV – 59
- HAV, Twinrix – 6
- HCV – 50
- Adjuvants – 34
- Animal models/Methods/Assays – 8
- HIV – 11, TB – 2, Malaria – 6
- Influenza – 22
- Mumps – 5
- Pneumo (3), Hib (2), Meningo (1)
- HSV (3) – Zoster (1) – HPV (1) – Polio (2),

Challenges and responses in human vaccine development

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develop vaccines against <strong>HIV, malaria, TB</strong></td>
<td>Define correlates of protection</td>
</tr>
<tr>
<td></td>
<td>Target discovery</td>
</tr>
<tr>
<td>Accelerate vaccine development and production (emergencies: pandemic flu,</td>
<td>Target discovery</td>
</tr>
<tr>
<td>Ebola, Zika, ..)</td>
<td>- Genomics and proteomics</td>
</tr>
<tr>
<td></td>
<td>- Structural biology</td>
</tr>
<tr>
<td>Improve immunogenicity and persistence</td>
<td>Adjuvants and immune potentiators</td>
</tr>
<tr>
<td>Improve vaccine safety</td>
<td>Predictive bio-signatures of vaccine safety</td>
</tr>
<tr>
<td>Improve vaccine production methods</td>
<td>Novel technologies</td>
</tr>
<tr>
<td>Improve vaccine stability</td>
<td>New stabilizers (polyphosphazenes, silk, ..)</td>
</tr>
<tr>
<td>Improve vaccine delivery</td>
<td>New devices, needle-free technologies</td>
</tr>
</tbody>
</table>
## CEVAC contributions to challenges and responses

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Responses</th>
<th>CEVAC contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV, TB, malaria</td>
<td>Correlate of protection</td>
<td>Mouse models for HIV, malaria</td>
</tr>
<tr>
<td></td>
<td>Target discovery</td>
<td>Numerous candidate vaccine trials</td>
</tr>
<tr>
<td></td>
<td>Adjuvants</td>
<td>Clinical evaluation of adjuvant effects</td>
</tr>
<tr>
<td>Influenza</td>
<td>Correlate of protection</td>
<td>FLUCOP – IMI project</td>
</tr>
<tr>
<td>Improve immunogenicity and persistence</td>
<td>Adjuvants and immune potentiators</td>
<td>Selection of adjuvant for TB, HIV, malaria vax</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Effect of adjuvant on pandemic vaccine candidates (H5N1, H1N1)</td>
</tr>
<tr>
<td>Improve vaccine safety</td>
<td>Predictive biosignatures of vaccine safety</td>
<td>BIOVACSAFE – IMI project</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biosignatures of vaccine safety (systems biology, innate and adaptive responses)</td>
</tr>
<tr>
<td>Improve vaccine delivery</td>
<td>Needle-free technologies</td>
<td>Clinical trials of new devices (microneedles, patches)</td>
</tr>
</tbody>
</table>
CEVAC teams enjoy the comfort and pleasure of excellent facilities.