An oily start towards a medical biotechnology institute

Jan Verschoor

Department of Biochemistry
Lecture layout

- Start
  Department history 1976 – 2009

- Medical
  Current research momentum

- Biotech
  In the UP environment

- Oil
  Case study: mycolic acids in TB

- Institute
  The need and vision for

* A facilitator between bench and bedside
Medical: Current momentum of the department

Gene technology

Computational biology

Protein biochemistry

Plant medicines

Mammalian cell culture

AIDS

Malaria

TB

Animal vaccines

D Meyer

L Birkholtz

J Verschoor

A Gaspar

Recombinant monoclonal antibodies

M Beukes
Biotech: in the UP environment

Malaria

Drug target analysis
Oil: Case study of mycolic acids in TB

- 8-10 million infections per year
- 1.6 million deaths annually
- 33% HIV+ patients co-infected with TB
- Challenges: Treatment and diagnosis

3000 bacilli hanging in the air
For 5 hours
**Oil:** The mycolic acid wax-layer of the mycobacterial envelope
**Oil: Mycolic acids (MA) = Mycobacterial identikit**

- Unique MA composition each for 60 different species of *Mycobacterium*!
- Mycobacterial MA molecules larger than from other species, eg *Nocardia* and *Corynebacterium*
- Three main classes of MA for *M. tuberculosis*:
Breakthrough, Harvard, USA: A lipid (MA) presenting role described for the CD1 protein on antigen presenting cells:

- Stimulation of T cell immunity (and antibodies?) without needing the CD4 T helper cell\(^1\).
- A possibility to bolster immunity in HIV infected patients with MA\(^2\).

Oil: Three research questions on MA:

- Can antibodies to MA be used as highly specific and sensitive surrogate markers for active TB, even in HIV burdened individuals/communities?

- Are MAs good immune stimulants to assist the body against immune related diseases such as arthritis and asthma?

- What is the role of MA in the establishment of TB?
Oil: First to purify natural MA on large scale with simple method

- Countercurrent distribution ideal for MA separation from a crude mycobacterial extract – The MA fraction forms different emulsion pattern visible by eye.
- HPLC confirmed purity and yield
- Stimulation of primary cultures of human PBL confirmed biological activity

Oil: First to report anti-MA antibodies in HIV infected patients with low CD4 counts

**Oil:** First with an anti-MA antibody TB biosensor test for TB with >80% accuracy

Oil: How MARTI Works

Rapid reliable Diagnostic Technique
Oil: First to show MA /cholesterol similarities

- Cross-reactivity in immunoassays
- MA attracts cholesterol
- Both recognised by Amphotericin B

Benadie et al. (2008) Chemistry and Physics of Lipids 152: 95-103
Oil: MA as immune stimulant: with Prof Johan Grooten

- PhD students Dr Anton Stoltz, Dr Hannelie Korf (2005): MA = PAMP = induces foamy macrophage with cholesterol accumulation in mice.
- Dr Hannelie Korf (2006): Reprogramming of macrophages by MA to make mice tolerant to asthma allergen challenge.
First to achieve stereocontrolled chemical synthesis of all three major subclasses of MA from *Mtb*.

- **Methoxy-MA**: Al-Dulayymi *et al.* (2007) Tetrahedron 63:2571*
  *First involvement of UP PhD student: Madrey Deysel
Oil: Conclusions:

- Antibodies to MA can be highly specific, sensitive surrogate markers for active TB in HIV burdened individuals/communities when performed as an inhibition test in real-time using a biosensor.

- MAs are highly specific pronounced inducers of innate immunity in mice leading to allergen tolerance

- MA induces foam cells typical of granulomas in the lungs of mice and attracts cholesterol - the main carbon diet of persistent TB bacilli.
Oil: Envisioned commercial products from mycolic acids

- A faster and more accurate test for TB diagnosis by 2012
- Adjuvants for vaccines by 2013
- Targeting of nano-encapsulated anti-TB drugs by 2014
- An asthma cure by 2015?
An oily, early, slippery start for a UP medical biotech institute that strives to be a facilitator between bench and bedside.
Institute: Why a medical biotechnology institute?

- The conversion of scientific discoveries into practical applications for the improvement of health and the standard of living

- To comply with the new South African act on: *Intellectual property rights from publicly financed research and development*, January 2009

- To facilitate between academia and industry

*A facilitator between bench and bedside*
Institute: Who mediated between the bald and the beautiful?

Mycolic acids purified: Patent, thesis and paper

Countercurrent technology

University of Pretoria, Prof Jan Verschoor

Facilitator, Dr Ela Johannsen

Adcock Ingram, Rina van der Merwe
Medical Institute: world examples

- Yeda Research and Development Company
- Hadassit Technology Transfer Company
- University of Rochester Medical Center
Medical Biotechnology Institute: Task-list

- Enterprising medical technologies for Faculties of Natural/Agricultural, Health and Veterinary Sciences
- National and international networking: Advisory Board
- Business incubation for SMME spin-out companies
- Acquisition of technology – even through spin-in
- Liaison with NIPMO umbrella organisation

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Medical Biotechnology Institute: Task-list (2)

- Marketing of UP technologies to companies.
- Presenting confidential information to interested companies (under secrecy agreements)
- Funding of research by companies and Ministries of Trade and Industry/Science and Technology
- Patent disclosures written and submitted
- License and option agreements negotiated

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Institute: Existing building blocks

- F ABI – ready for NIPMO patent demand?
- U P Research Support – long term vision?
- S AMI – emphasis on entrepreneurship?
- E nterprise @ UP - good at logistics!
- D r Ela Johannsen - needs to be cloned!

FUSED: An ideal Medical Biotech Institute!

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