

“BCG Moreau RDJ basic and clinical research”

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BCG Moreau RDJ

- History
- Oral and Id vaccines
- Adverse effects
- Genomics and proteomics
- Clinical trials
- WHO strain & vaccine
- Future



First BCG immunization



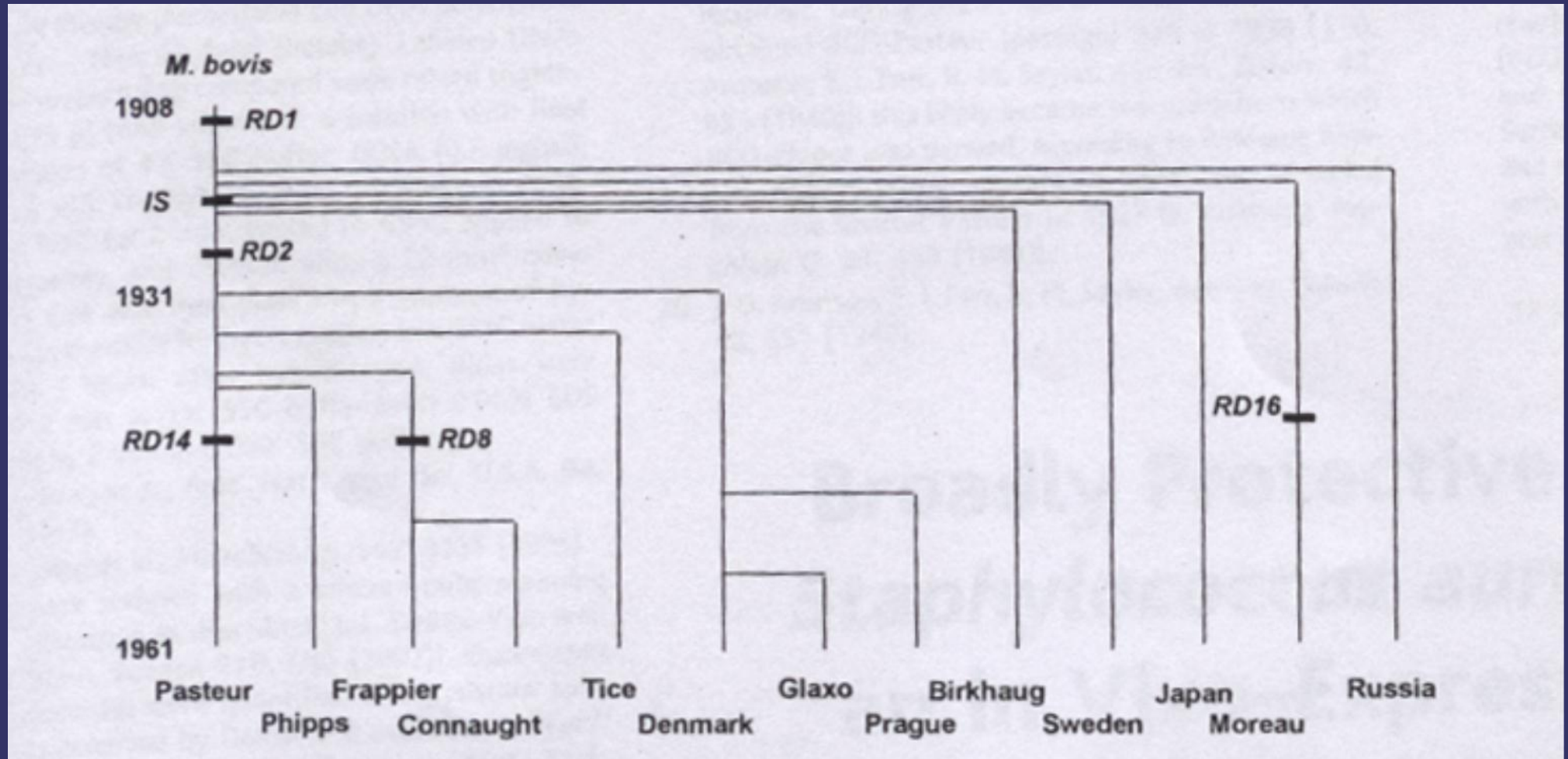
BCG as an oral vaccine

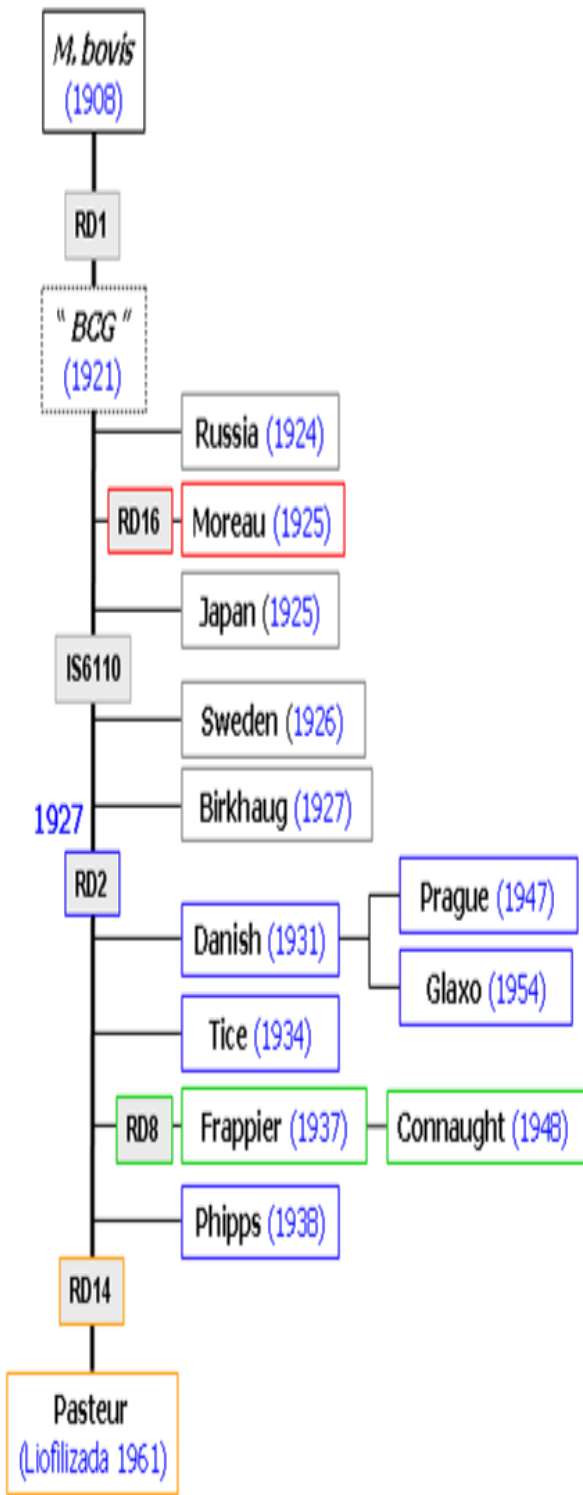
- BCG originally was an oral vaccine
- Used worldwide as an oral vaccine till the Lubeck accident
- . Mantoux tests were negative in the majority of immunized subjects
- . Correlated Mantoux test and immunogenicity.
- Strain was developed in Brazil from the thirties
- . No cervical adenitis
- Used in the National Programme until 1974



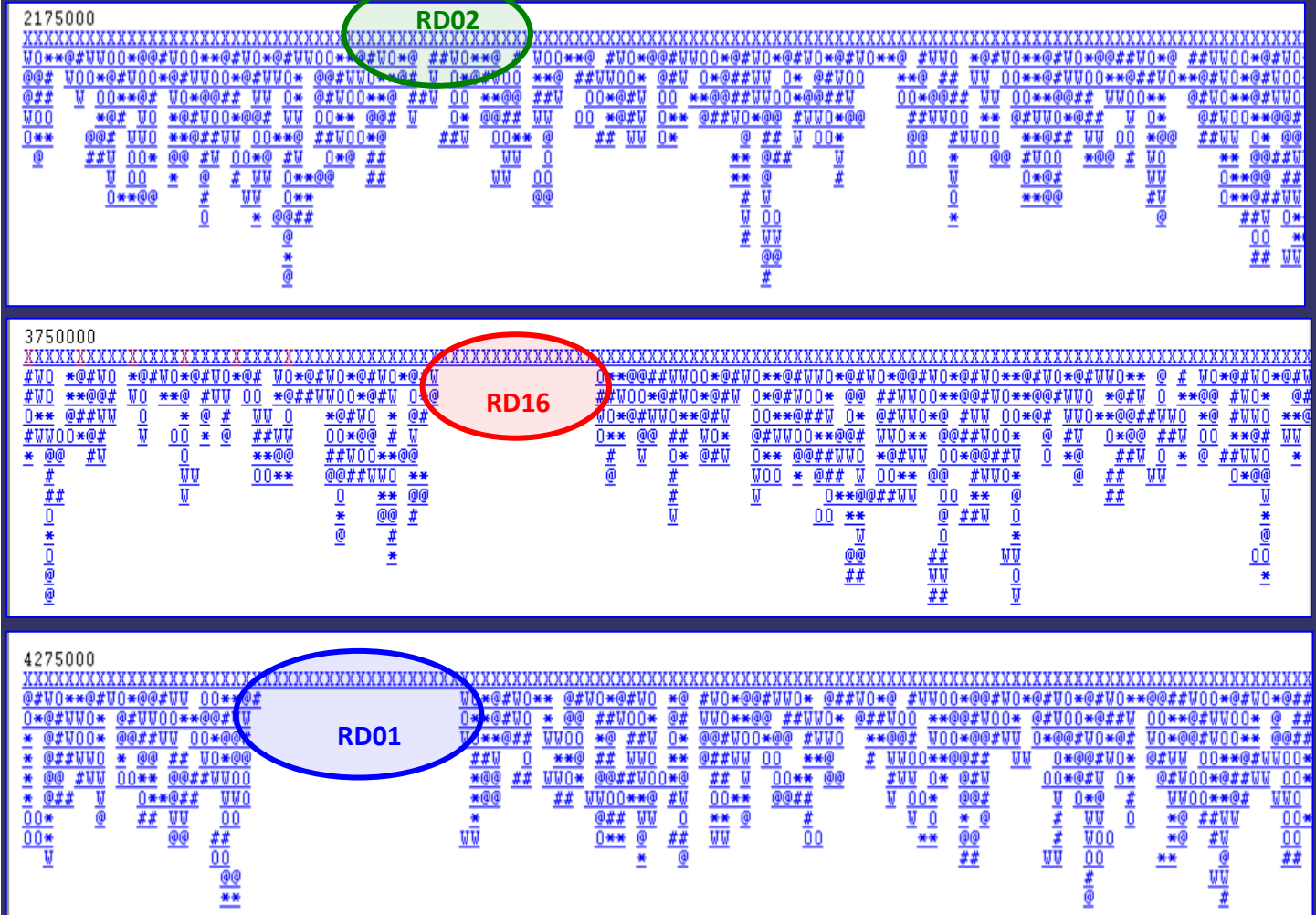
BCG Genealogy

Distinct sub strains of BCG developed worldwide





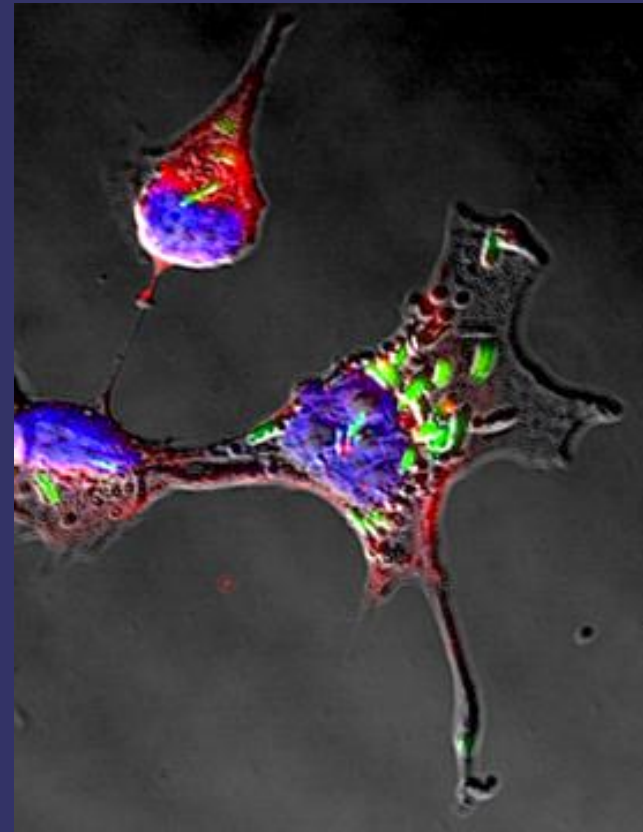
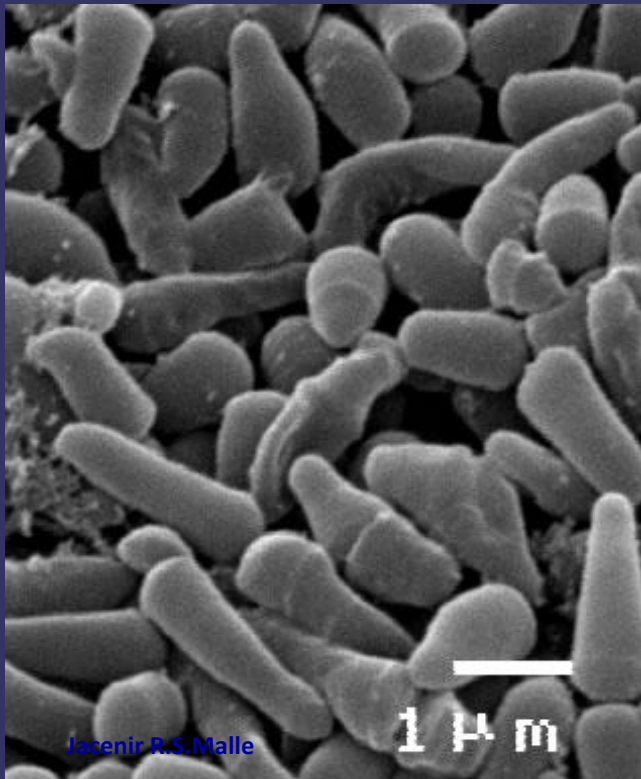
Genomics BCG Moreau RDJ



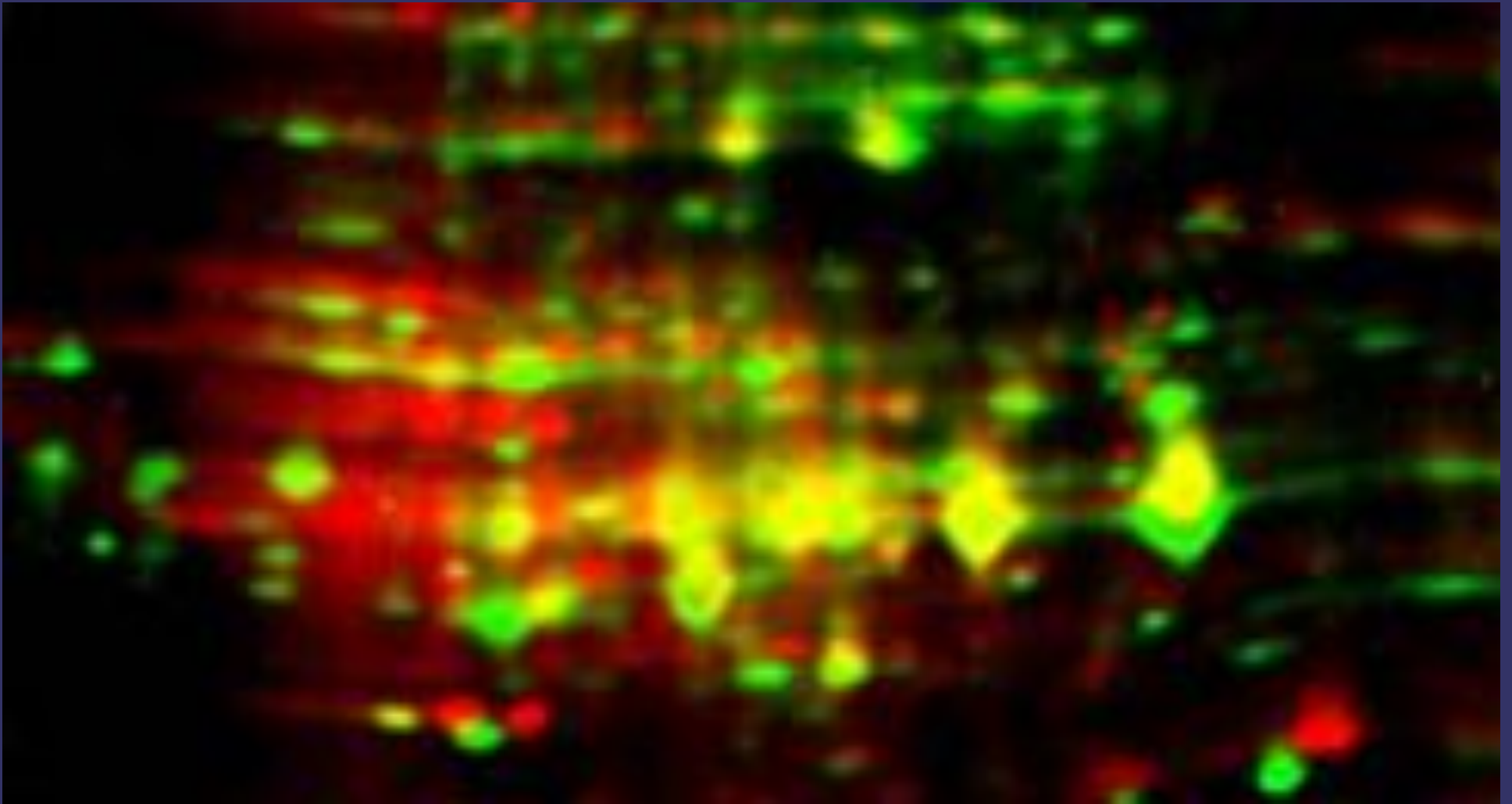
Genomics

Size: 4.340.000 pb

% G+C = 65.64



Proteomics BCG Moreau RDJ



Proteomics

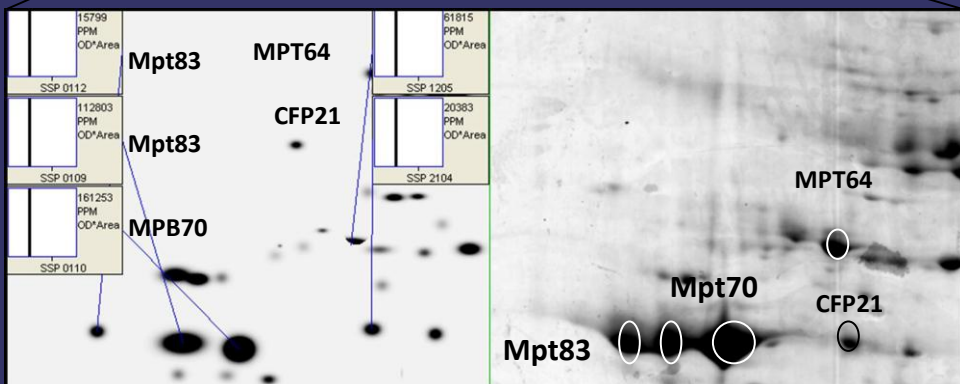
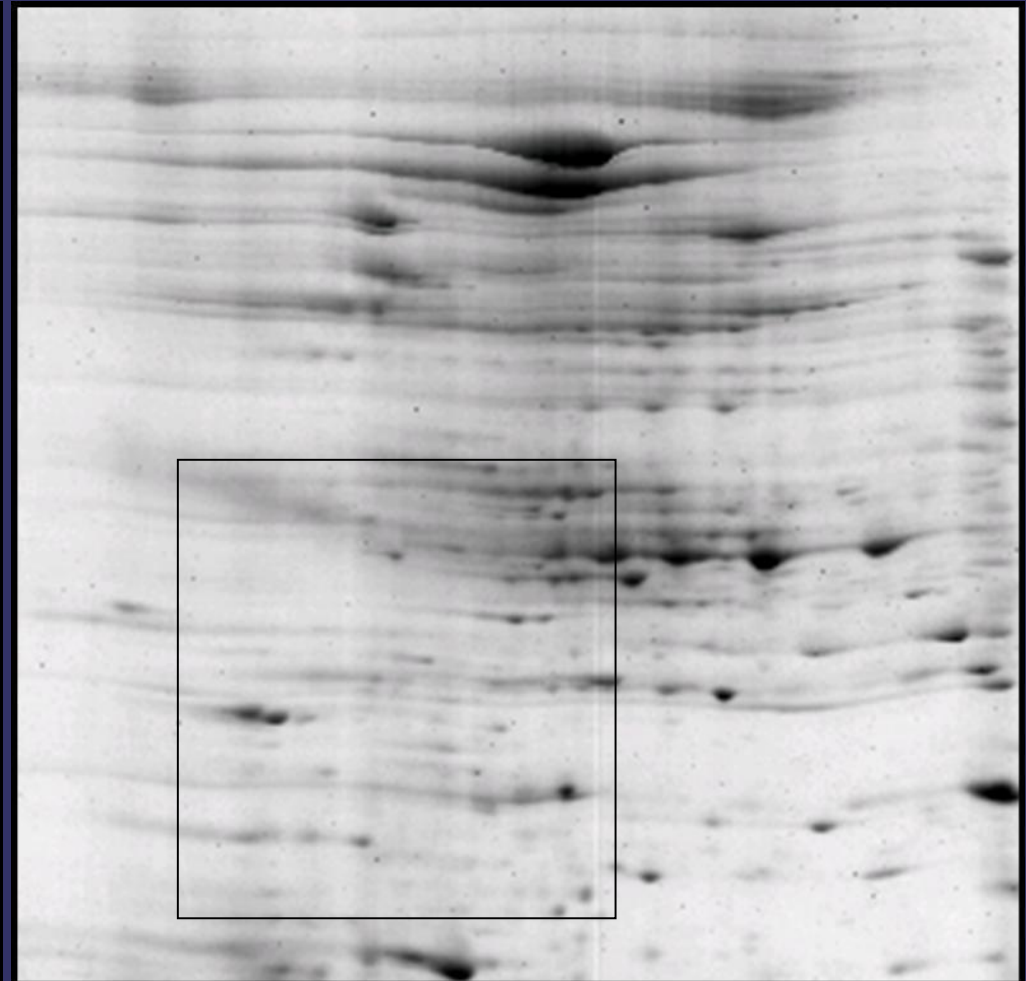
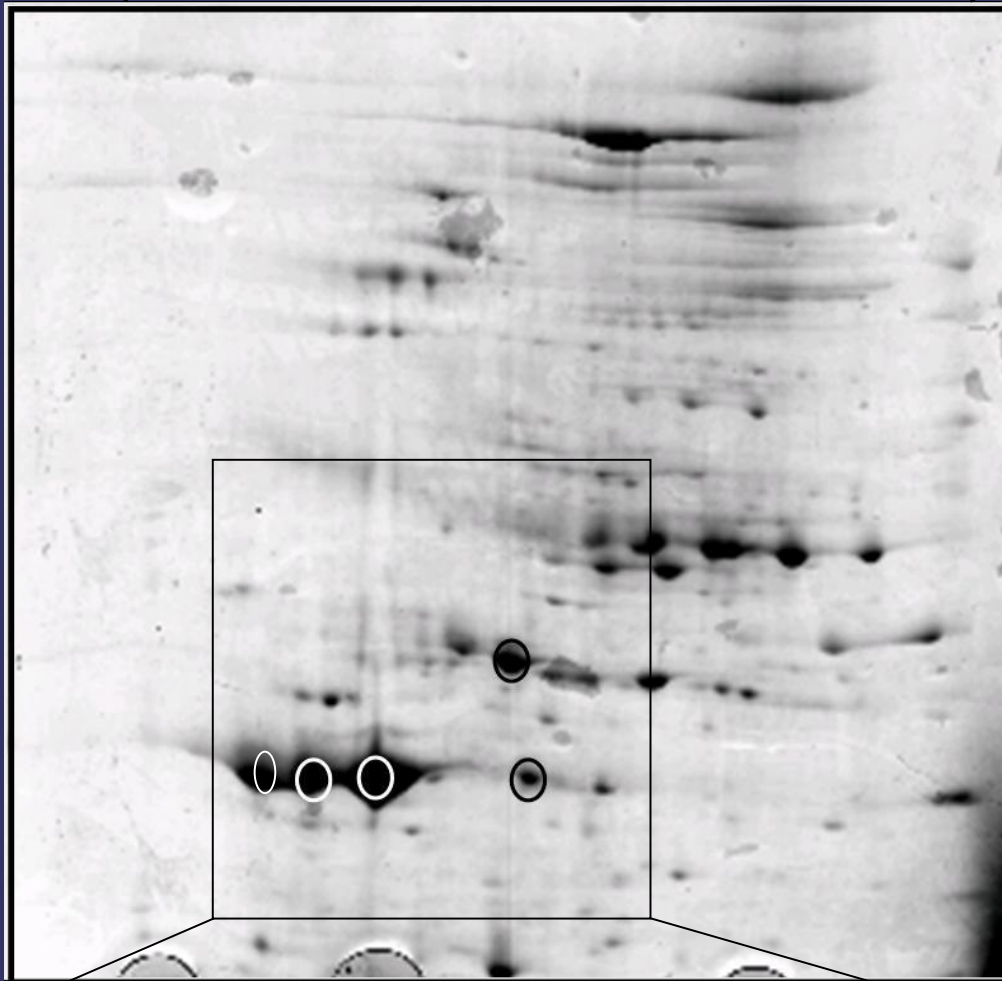
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BCG-Moreau

6 3

BCG-Pasteur

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Genomics BCG Moreau RDJ (FAP/FIOCRUZ)

New tools for:

- Quality control
- Production control
- Traceability
- Development of new vaccines



Antibiotic sensitivity of BCG Moreau RDJ

PHLS laboratory in Greenwich, UK

Amikacin SENSITIVE SENSITIVE
Capreomycin SENSITIVE SENSITIVE
Ciprofloxacin SENSITIVE SENSITIVE
Clarithromycin SENSITIVE SENSITIVE
Ethambutol SENSITIVE SENSITIVE
Isoniazid SENSITIVE SENSITIVE
PAS SENSITIVE SENSITIVE
Pyrazinamide RESISTANT RESISTANT *
Rifampicin SENSITIVE SENSITIVE
Streptomycin SENSITIVE SENSITIVE

*This resistance pattern is in keeping with the natural resistance of M.bovis to pyrazinamide.

Therefore the Moreau RDJ strain falls well below the acceptable MICs for the oral agents tested. It was determined that chemoprophylaxis could employ isoniazid +/- rifampicin. Three-drug regimes could add ofloxacin/ciprofloxacin



Clinical Trials

- Largest trial of Id BCG in the world (Barreto et al.)
- Adverse effects were minimal (Dourado et al.)
- BCG Moreau RJ is the only BCG used in babies born to HIV+ mothers
- Phase IV BCG for bladder cancer



Id BCG Moreau RDJ - Adverse effects

71,347 Children 7-14 years old

BCG Moreau RJ from FAP – 100,000 viable bacilli per 0.1 ml.

11,981 (16.8%) no scar

59,360 (83.2%) one scar

25 adverse reactions – no death, permanent injuries or disseminated infections.

2 in no scar students (1 in 5,990, 95% CI 1/1485-1/34,482)

23 in one scar students (1 in 2580, 95%CI 1/1692-1/3984)

“In conclusion, the rate of adverse reactions associated with a second dose of BCG vaccination was found to be roughly twice the rate associated with a first dose but this difference was not statistically significant. As a result, we conclude that adverse reactions to a second dose of BCG are rare, and that these adverse reactions do not represent an important hindrance to the policy of vaccination”.



BCG Moreau RDJ in HIV vertical transmission

Brazil is the only country that BCG immunizes babies born to HIV + mothers.

There is no case of disseminated BCG disease amongst HIV-infected children immunised with BCG Moreau RJ.



WHO strain & vaccine

➤ BCG Moreau Rio de Janeiro - Strain certified (RDJ)

Report

WHO Consultation on the characterization of BCG vaccines

**WHO, Geneva, Switzerland
8-9 December 2004**



WHO strain & vaccine

➤ Vaccine certified by WHO

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION
Geneva, 15 to 19 October 2012

**International collaborative study to evaluate and establish the 1st WHO
Reference Reagent of BCG vaccine of Moreau-RJ sub-strain**

Belinda Dagg, *Peter Rigsby, *Jason Hockley and ⁺Mei M. Ho

*Bacteriology Division and *BioStatistics Group, National Institute for Biological Standards
and Control, South Mimms, Potters Bar, Hertfordshire, EN6 3QG, UK.*



WHO Reference Reagent
The 1st WHO Reference Reagent for BCG vaccine of Moreau-RJ
sub-strain
NIBSC code: 10/272
Instructions for use
(Version 2.0, Dated 22/04/2013)



Quality Control – New Methods

➤ PCR – Seed lots

➤ Bioluminescence – Production (+UFCs)



FAP New Plant





Thank you

