

Lipids to detect tuberculosis?



PRIFYSGOL
BANGOR
UNIVERSITY

Chris Gwenin

c.d.gwenin@bangor.ac.uk

Stop TB Partnership

New Diagnostics Working Group

Mycolic acids

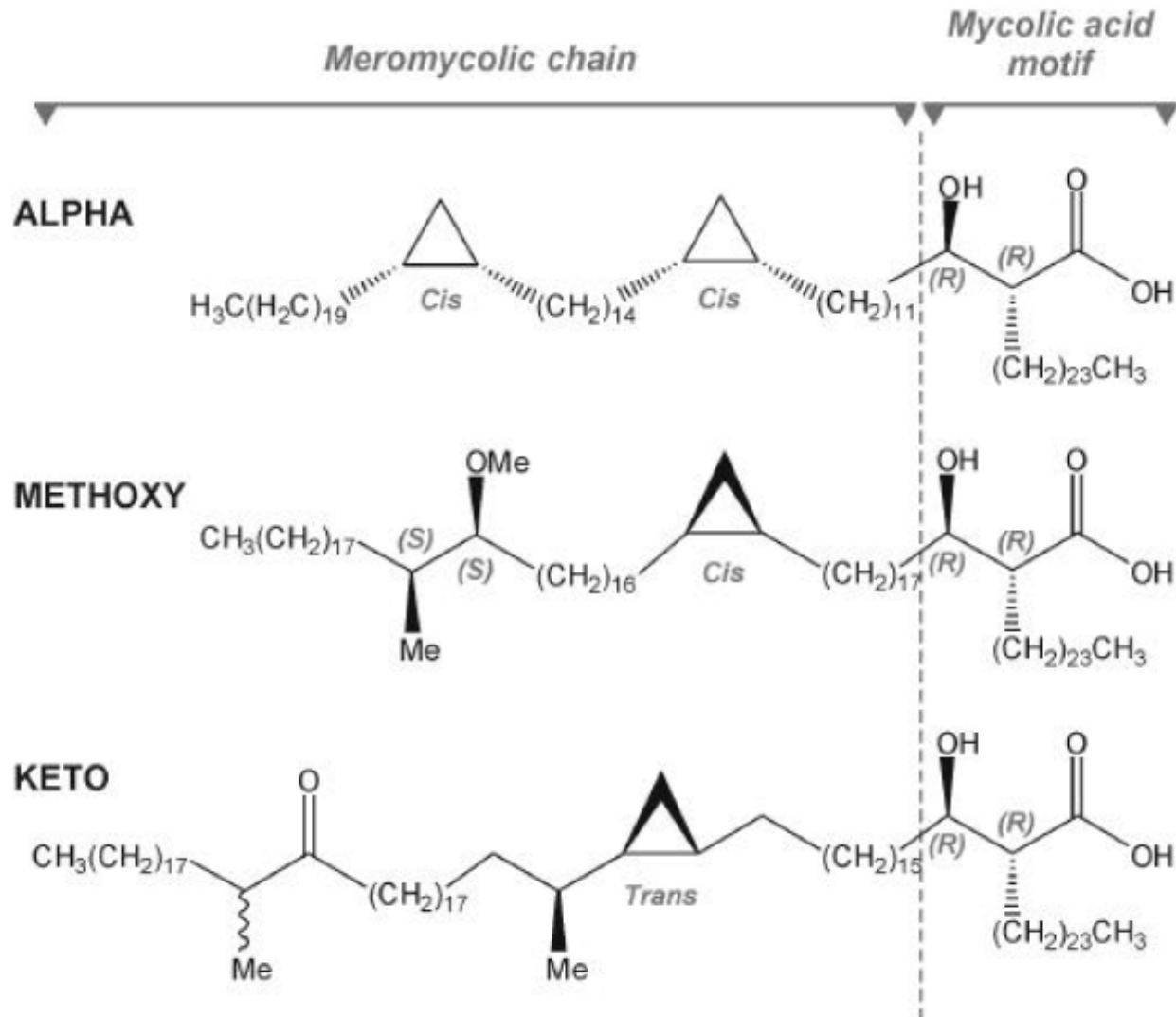


Prof. M. Baird
m.baird@bangor.ac.uk

Different Mycobacteria have their own unique Mycolic Acid (MA) compositions

Mycolic acids

Three main classes of MA for *M. Tuberculosis*

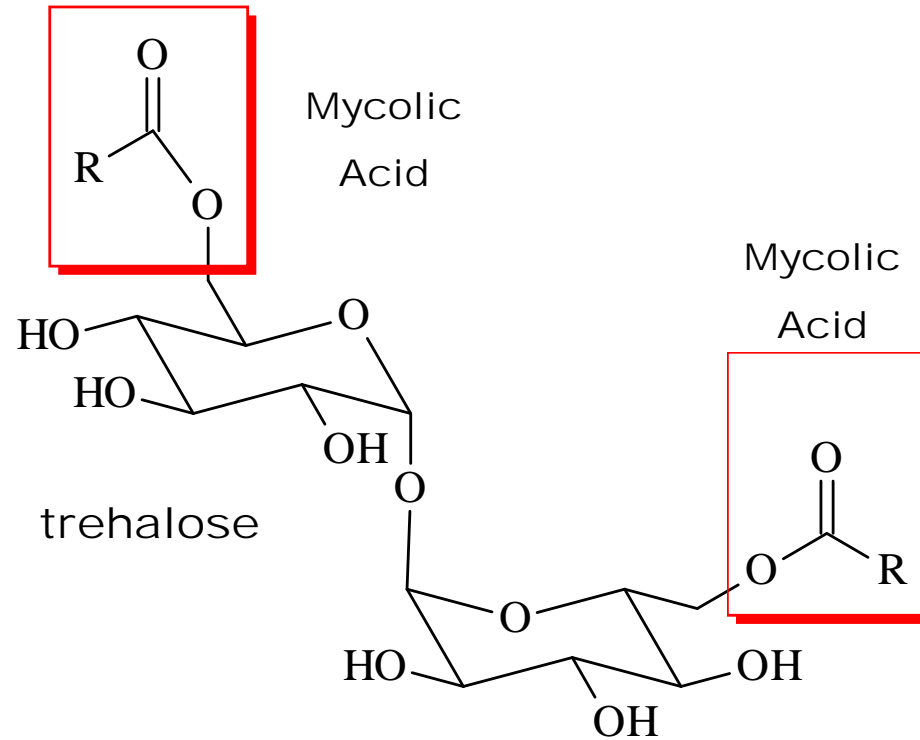


Cord Factors (sugar esters)

(trehalose dimycolate, TDM)



Dr. Pritchard



Dr. Dulayymi

We now have > 60 individual isomers to test!

Encouraging literature

Complex natural mixtures of cord factors can be used as an antigen for TB

(Yano *et al* 1991)

Isolated MA sub-classes are recognised by IgG antibodies

(Pan *et al* 1999)

Natural MA can be used as an antigen for TB in the presence of HIV-AIDS

(Verschoor *et al* 2002)

Can we improve on this with synthetic single isomers?



Special Program for Research and Training in Tropical Diseases



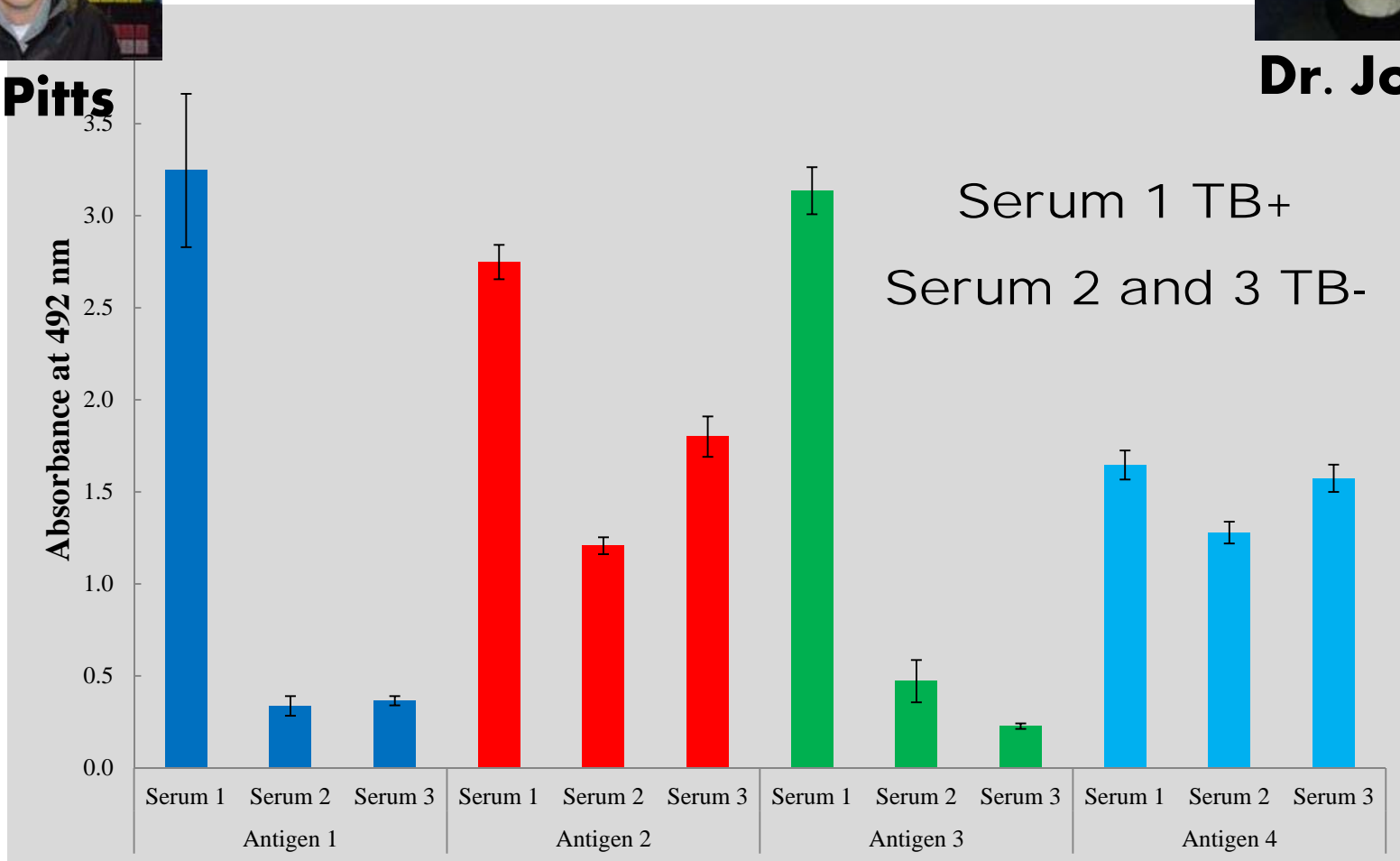
Different antigens give selective responses



Dr. Pitts

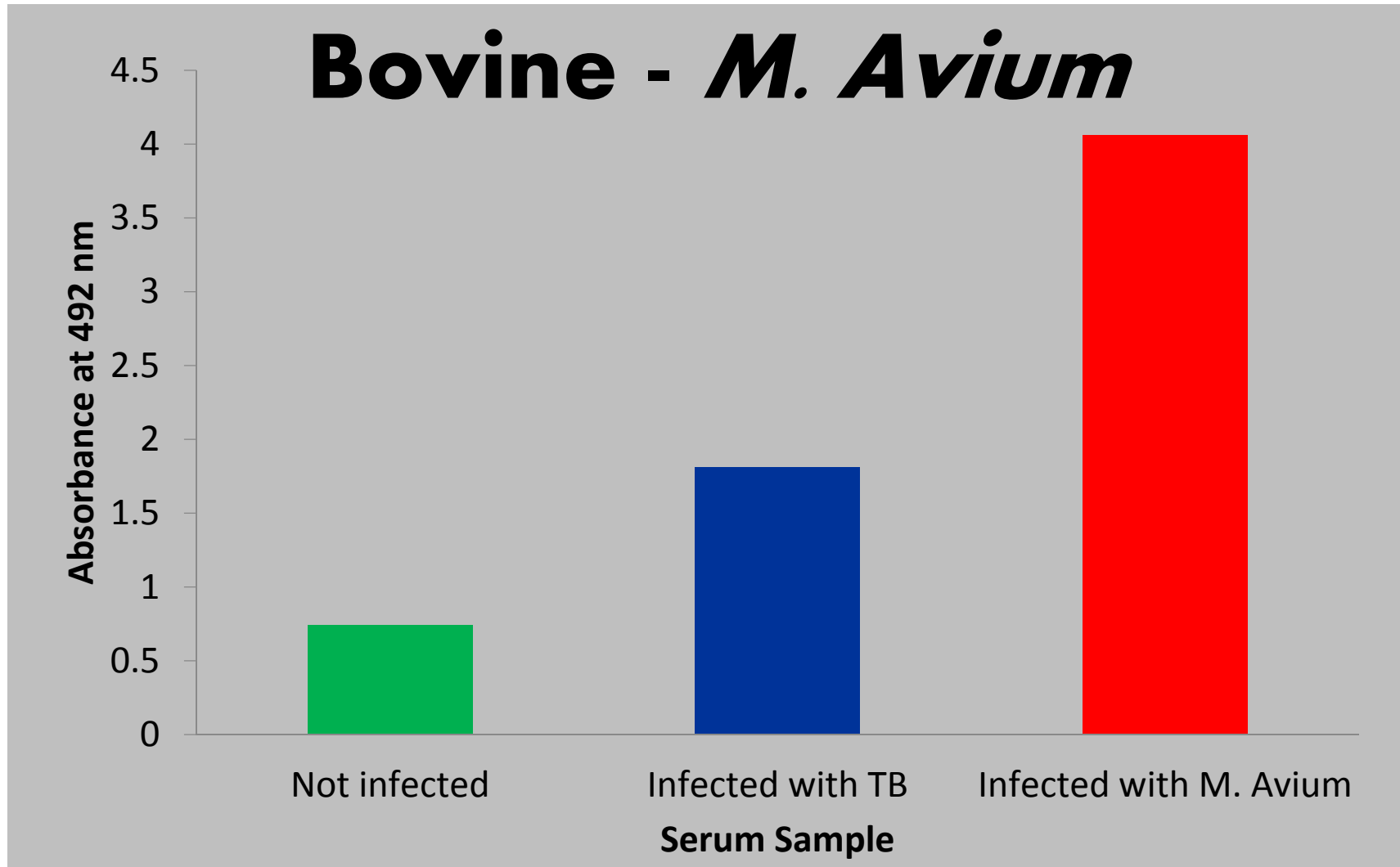


Dr. Jones



Patent No. WO 2012/153111 A1

Other microbial infections



ELISA results from a blind study of 350 WHO TB indigenous samples

Vaccination does not interfere

Different single synthetic MA and their
derivatives give differential responses

Our best antigen gave
85% Sensitivity and 85% Specificity

UK negatives are much cleaner

Country variations!

By using two antigens with a set of Gambia samples we used a 'traffic light' system that gave

100 % Sensitivity

91 % Specificity

From a clinical setting to the field

We have taken 4 additional approaches

1. Evanesce

On 350 blind samples

73 % Sensitivity - 81 % Specificity

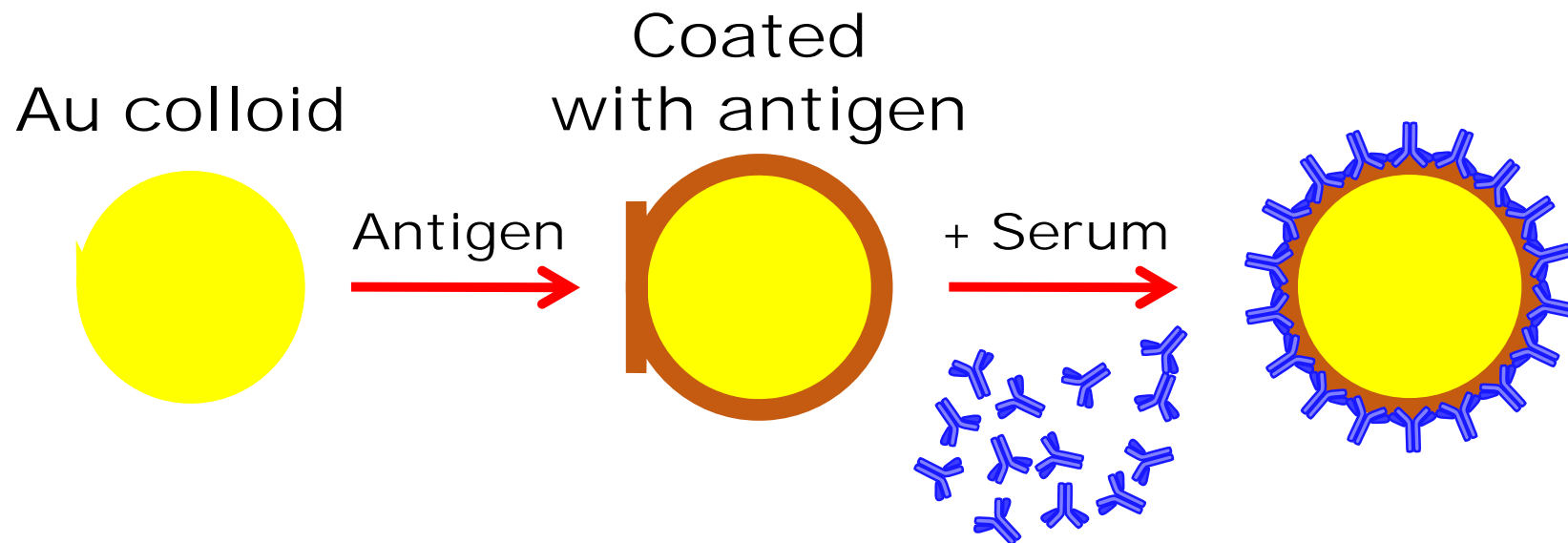
2. Impedance

Plus two PoC systems

Assay development

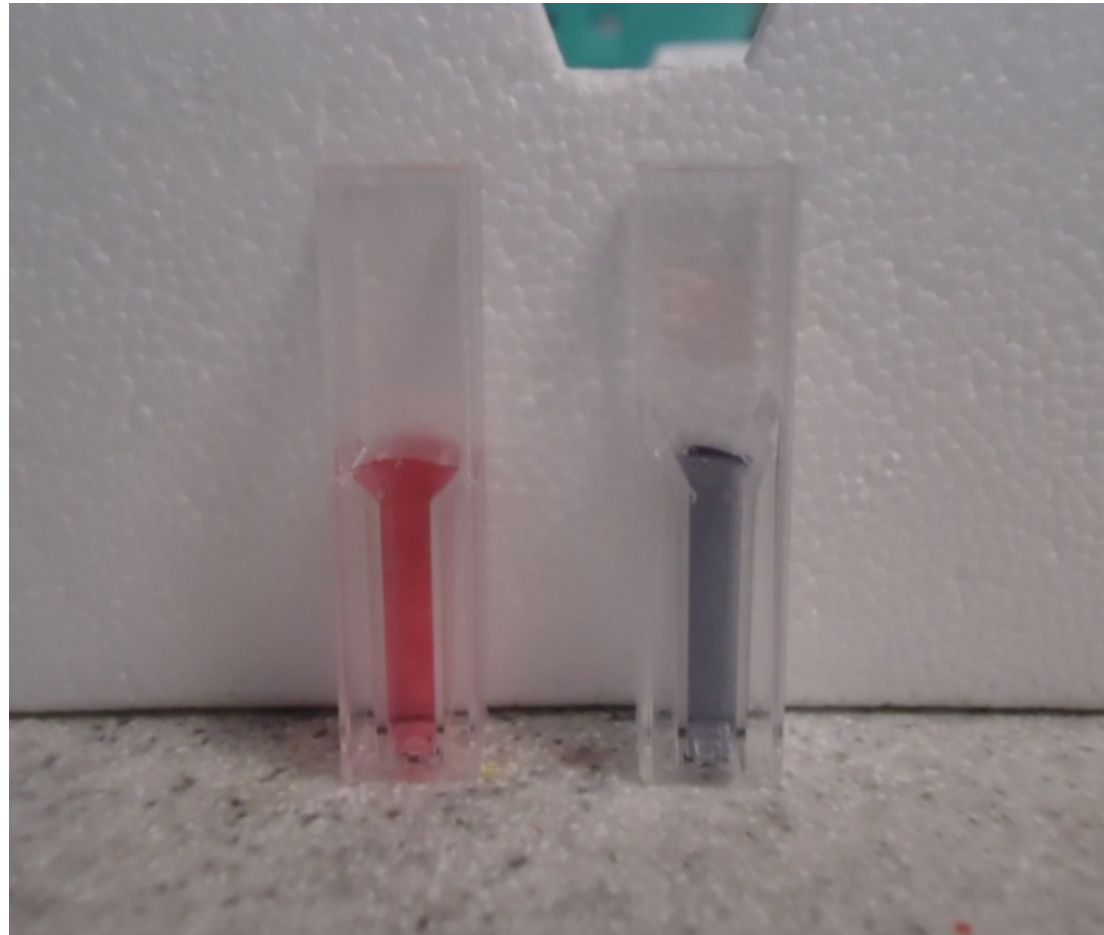


Dr. Pitts



Look for a change in the absorbance

Colour response within minutes



Positive

Negative

Sensor development

On 350 blind samples
89 % Sensitivity - 62 % Specificity

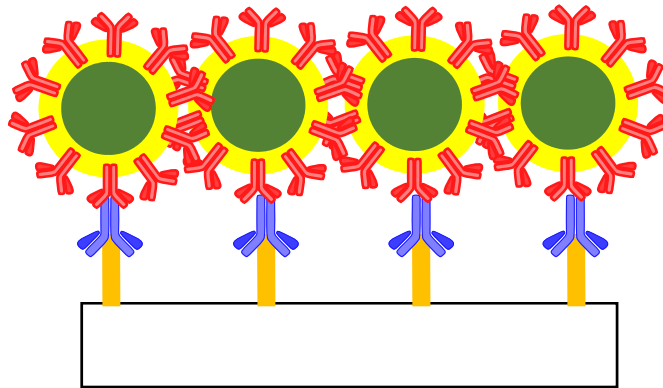


Paper based device



Particle
secondary
antibody
conjugate

Lipid Antigens



Sera containing
the antibodies
of interest are
added

Paper based device

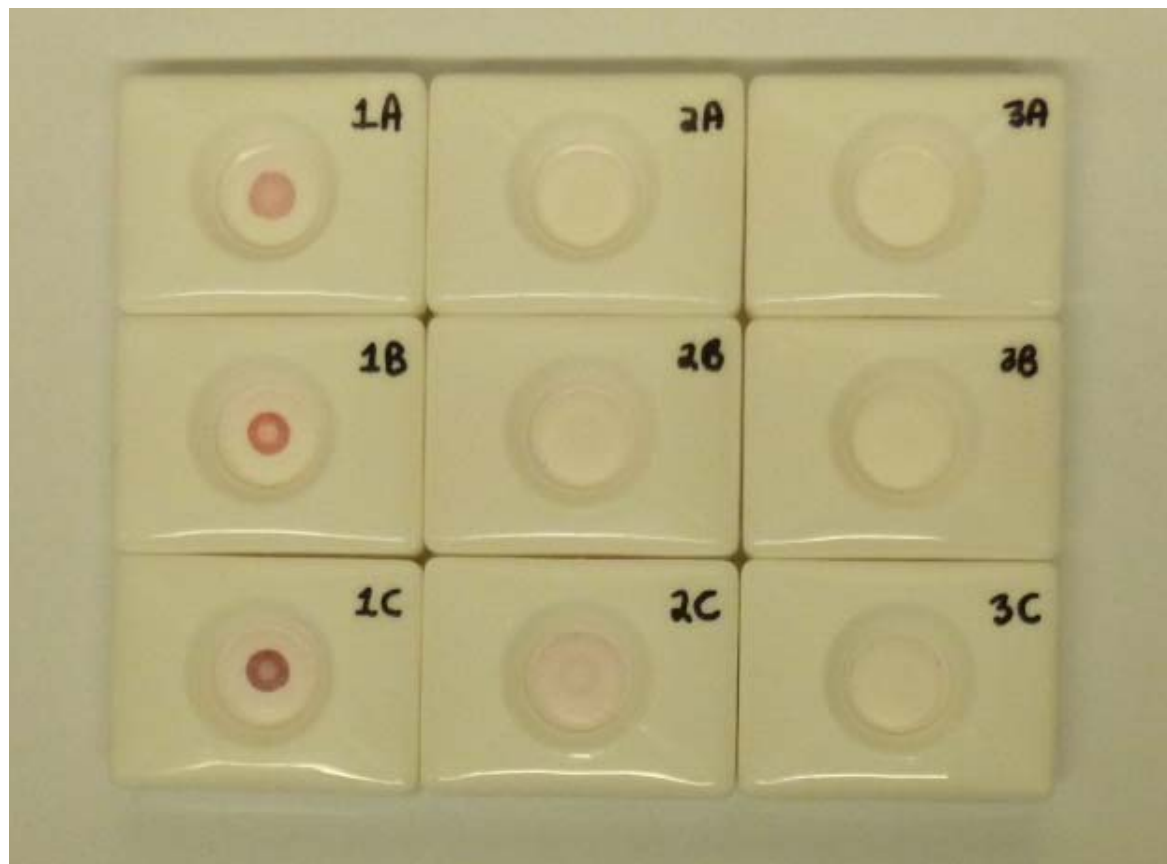


Paper based device

TB positive
serum

TB negative
serum

Control
(no serum)



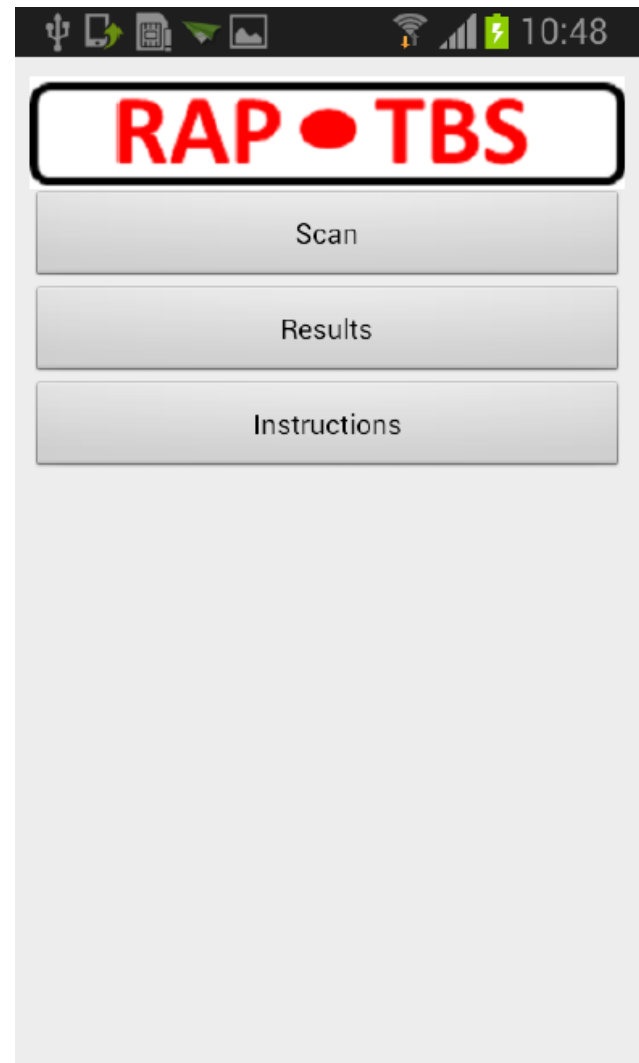
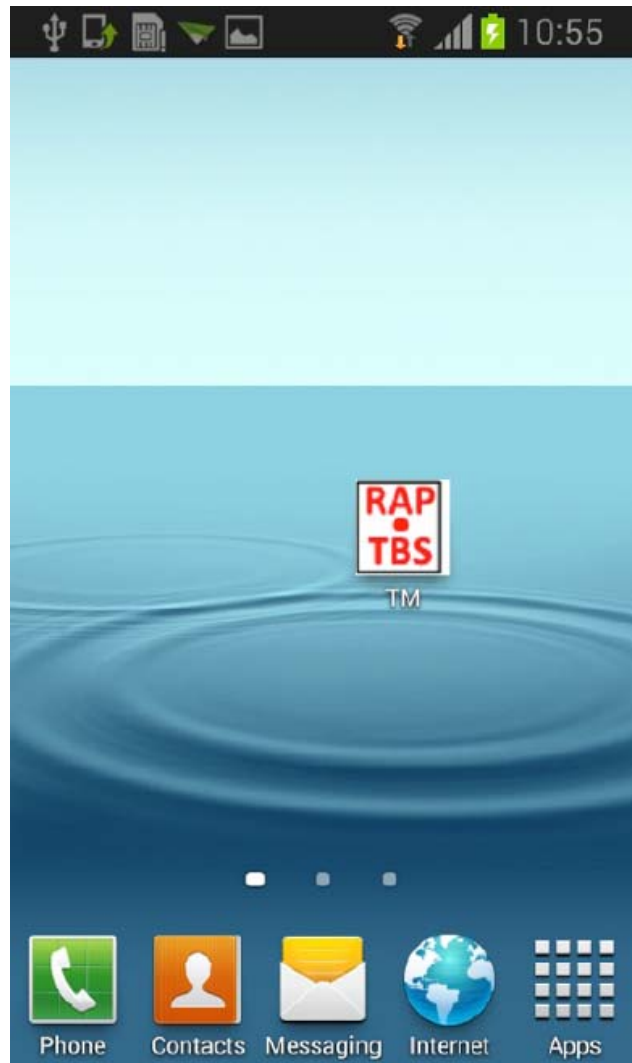
Paper based device

TB positive
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TB negative
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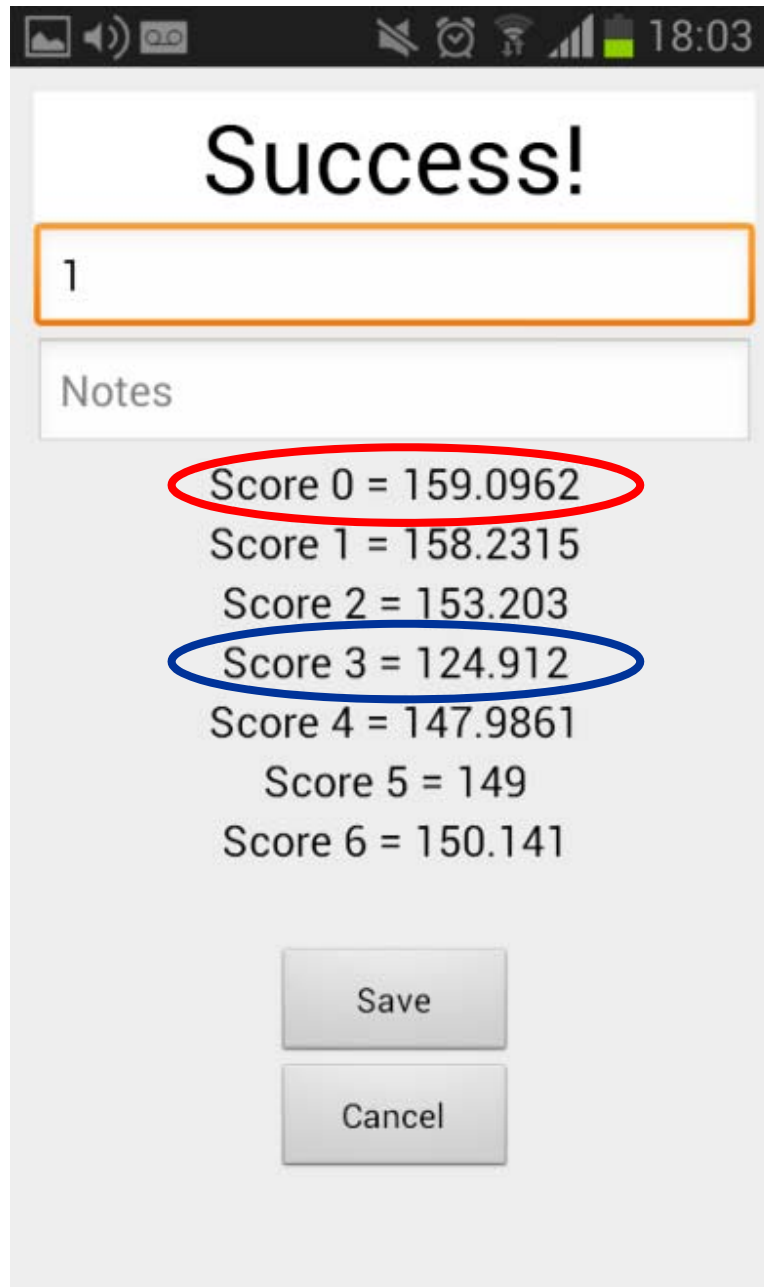
Control
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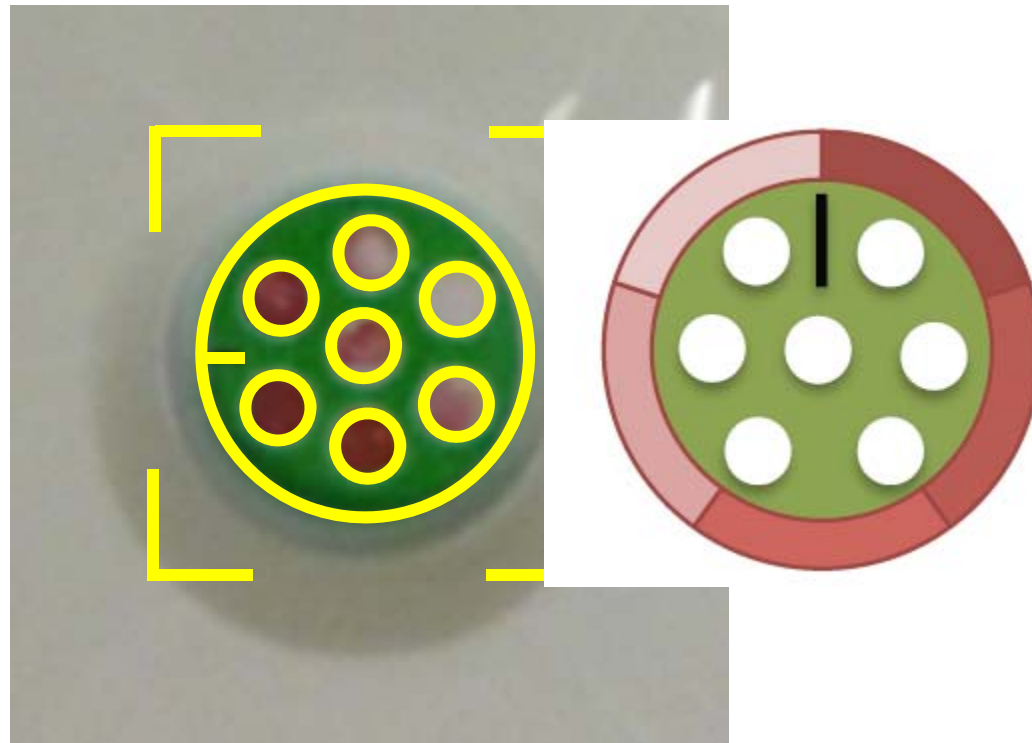


Paper based device





Paper based device



The second stage of the development will have extra controls built into the application to take account of variations in lighting

Imminent work

The flow through device needs optimizing in conjunction with the phone application

We will then test the known 350 WHO serum samples

Most likely re-optimize

Then test 200 of FINDs blind serum samples

Conclusions

Lipid antigens do detect TB antibodies
We get different responses for different mycobacterial infections

The response is dependant on which lipid antigens are used

We can get a result in under 10 mins, which is readable by eye and/or by phone for under 10\$

Needs no external power supply

The response is not affected by BCG and does not appear to give a signal from latent TB

Thanks you for your attention



Chris Gwenin
(c.d.gwenin@bangor.ac.uk)

<http://gwenin.com/>