

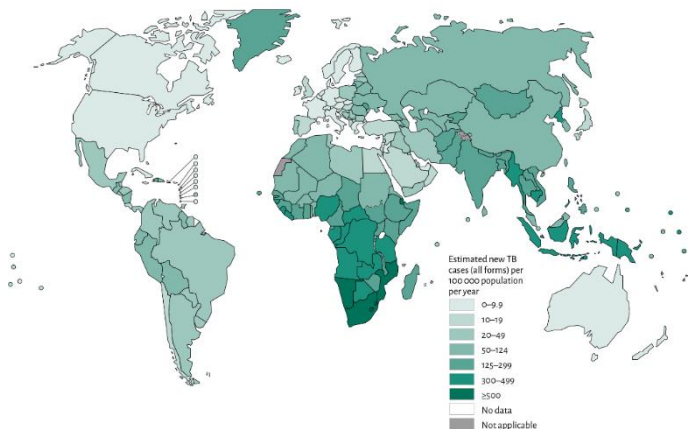


Southampton Centre for
Biomedical Research

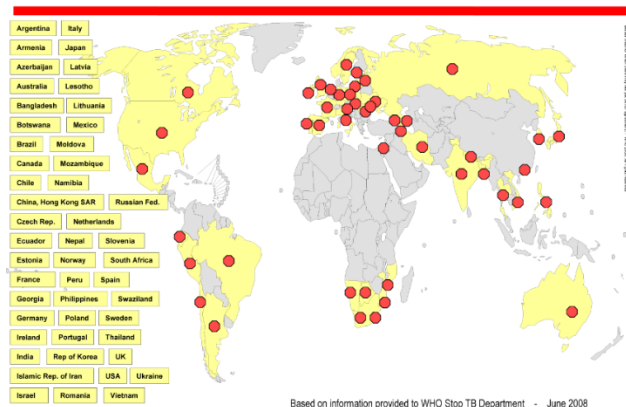
Developing novel approaches to control multi-drug resistant tuberculosis through interdisciplinary research

Paul Elkington
Faculty of Medicine

TB drug resistance is progressing

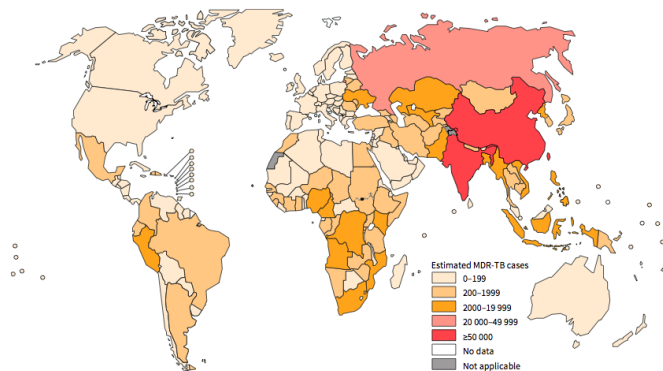


Overall TB incidence



Extensively-drug resistant TB: 2005

Number of MDR-TB cases estimated to occur among notified pulmonary TB cases, 2013



Multi-drug resistant TB: 1990's

NATURE | NEWS

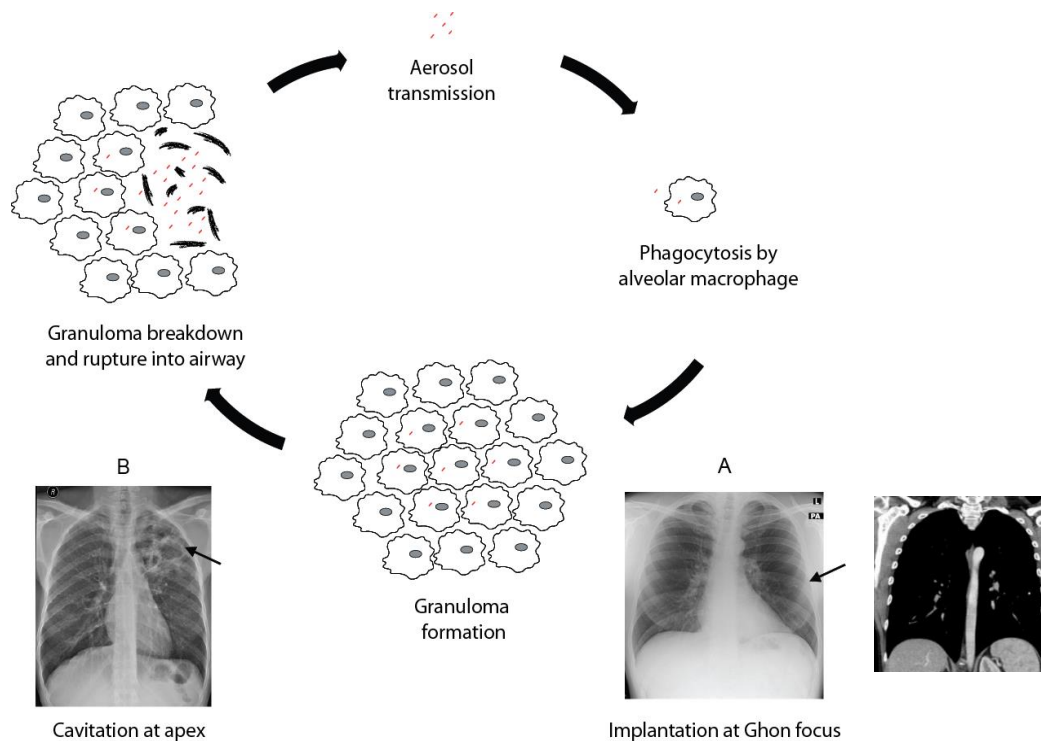
Totally drug-resistant TB emerges in India

Discovery of a deadly form of TB highlights crisis of 'mismanagement'.



Totally-drug resistant TB: 2012

Better understanding of the TB life cycle is required



Established dogma:

Science 2010 328: 852

Nature 2013 502: S2

Nat Immunol 2014 16: 57

Cell 2014: 159: 1497

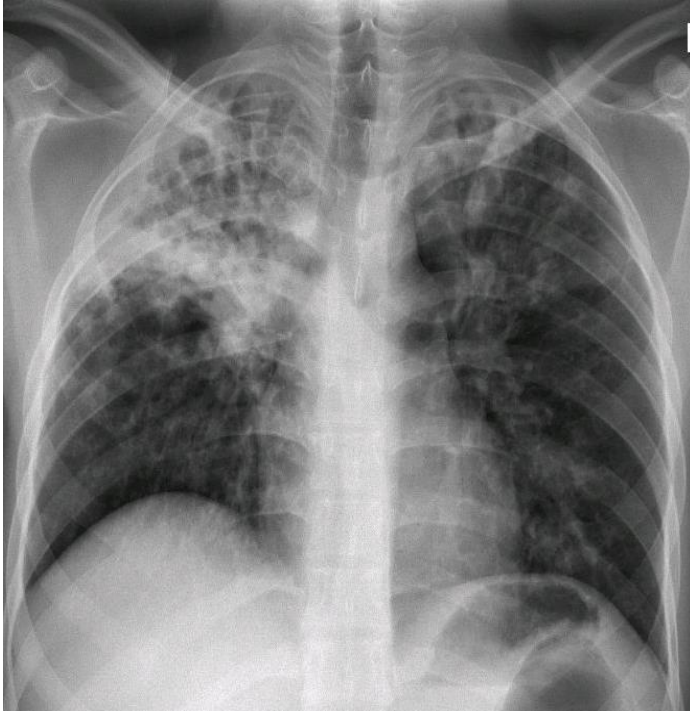
Southampton paradigm:

Science Trans Med 2011 71: ps6

J Infection 2013 66: 299

Lancet Inf Dis 2015 15: 1357

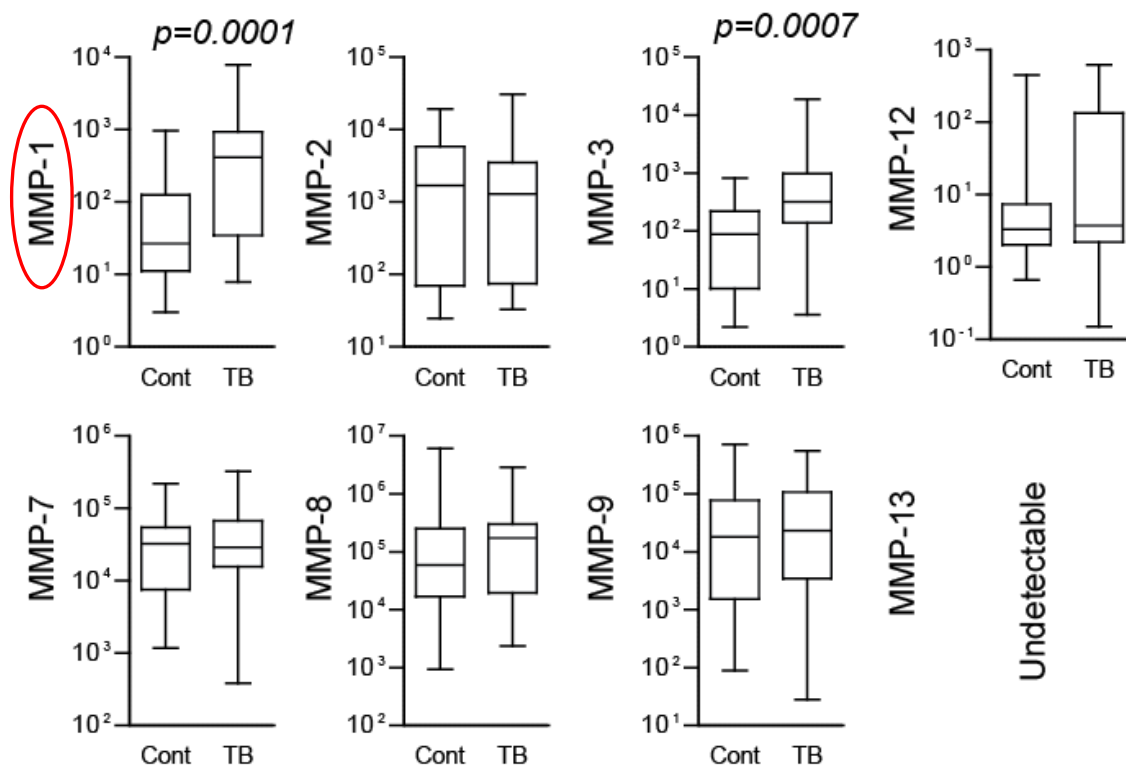
Lung destruction is key to the success of TB



6/6 sputum samples positive for bacilli

- Drives transmission
- Causes morbidity and mortality
- Suggests matrix metalloproteinase enzymes are key mediators

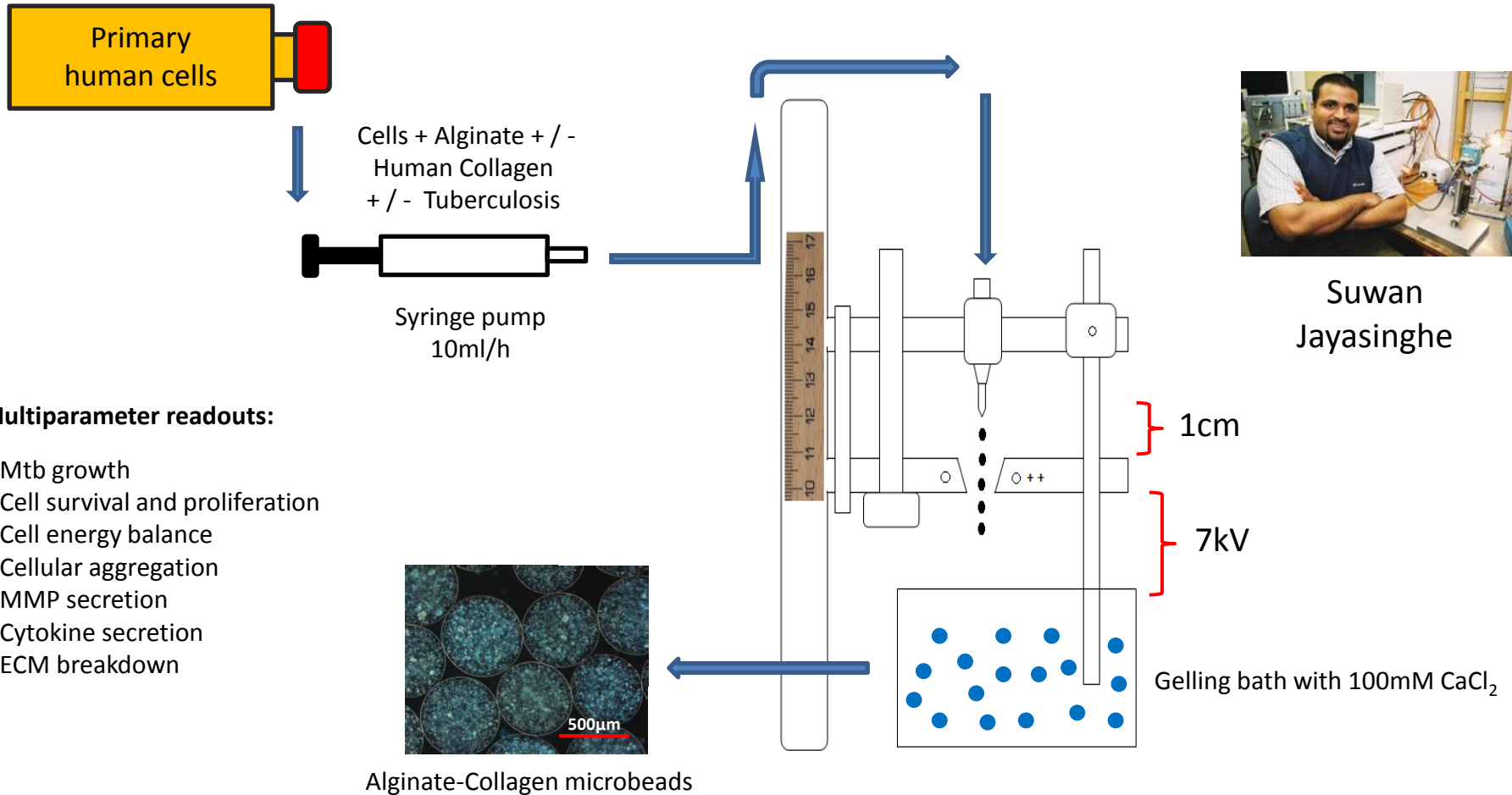
Matrix metalloproteinase-1 is the dominant collagenase causing lung destruction in TB



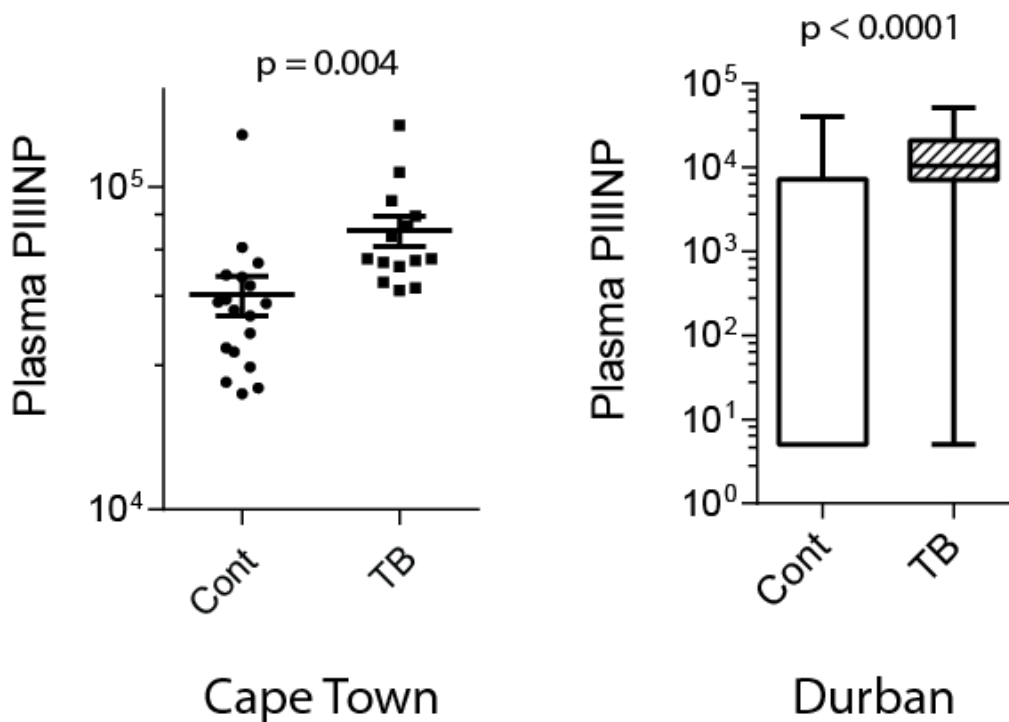
Elkington et al *J Clin Invest* 2011 121: 1827

Walker et al *AJRCCM* 2012 185: 989

Developing a 3-D model to address cell-matrix regulation of immune response to TB



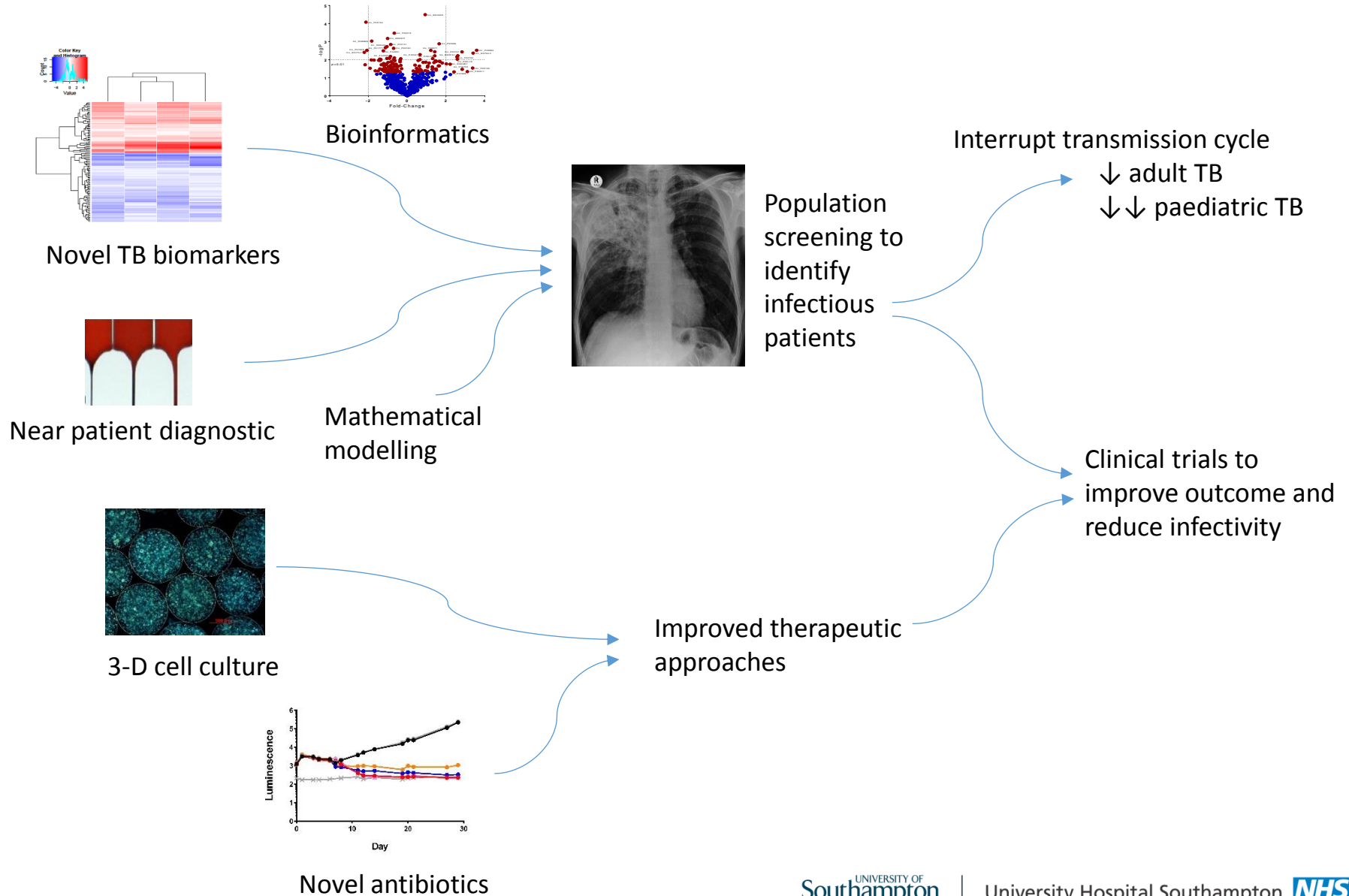
Matrix breakdown releases collagen fragments that are novel TB diagnostic markers



Seddon et al *J Infect Dis* 2013 208: 1571

Sathyamoorthy et al *PLOS One* 2015 e0117605

Southampton TB research



Acknowledgements



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**All the patients who
have taken part**

