Southampton





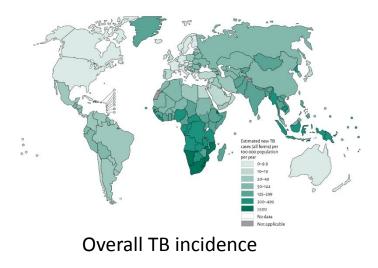
Southampton Centre for Biomedical Research

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

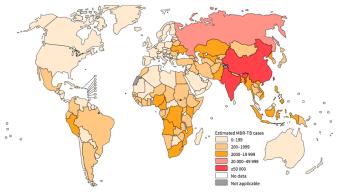
Paul Elkington Faculty of Medicine

The Southampton Respiratory Biomedical Research Unit is funded by the National Institute for Health Research (NIHR) and is a partnership between University Hospital Southampton Foundation Trust and the University of Southampton.

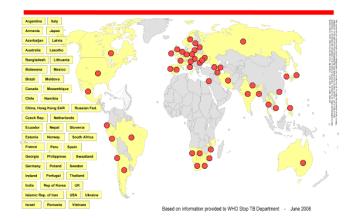
TB drug resistance is progressing



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



Multi-drug resistant TB: 1990's



Extensively-drug resistant TB: 2005

NATURE | NEWS

Totally drug-resistant TB emerges in India

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

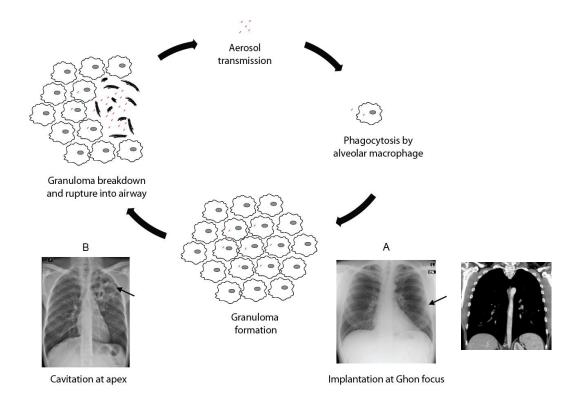


Totally-drug resistant TB: 2012

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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

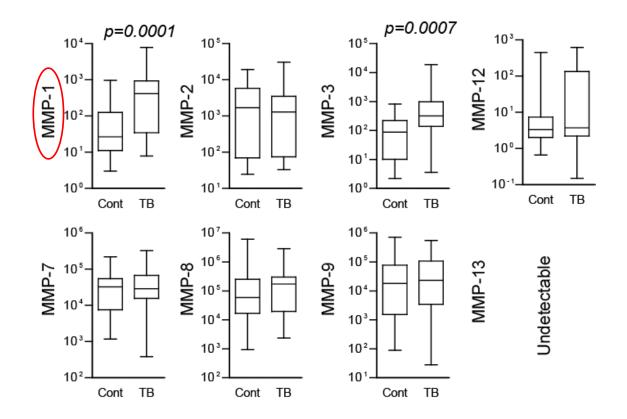


6/6 sputum samples positive for bacilli

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



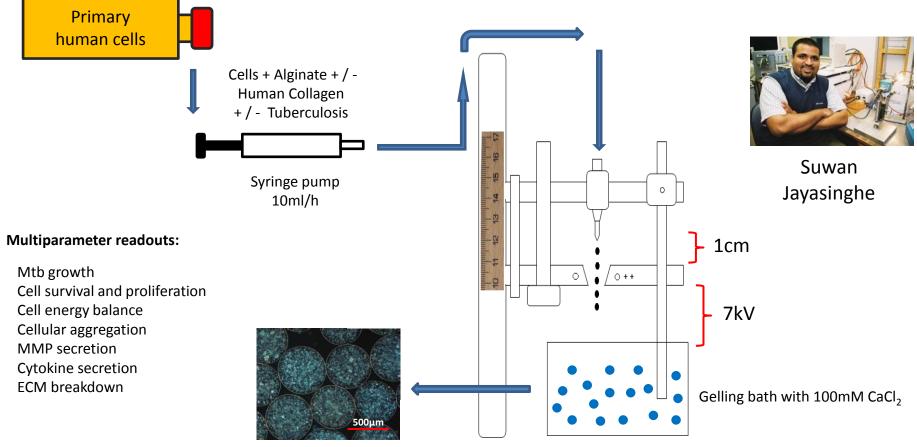
Matrix metalloproteinase-1 is the dominant collagenase causing lung destruction in TB



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



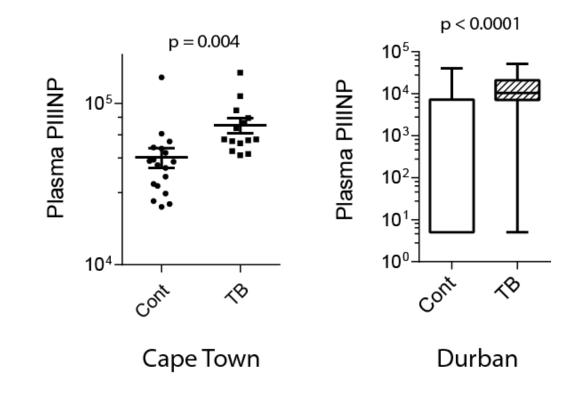
Alginate-Collagen microbeads

Workman et al Advanced Functional Materials 2014 24:2648



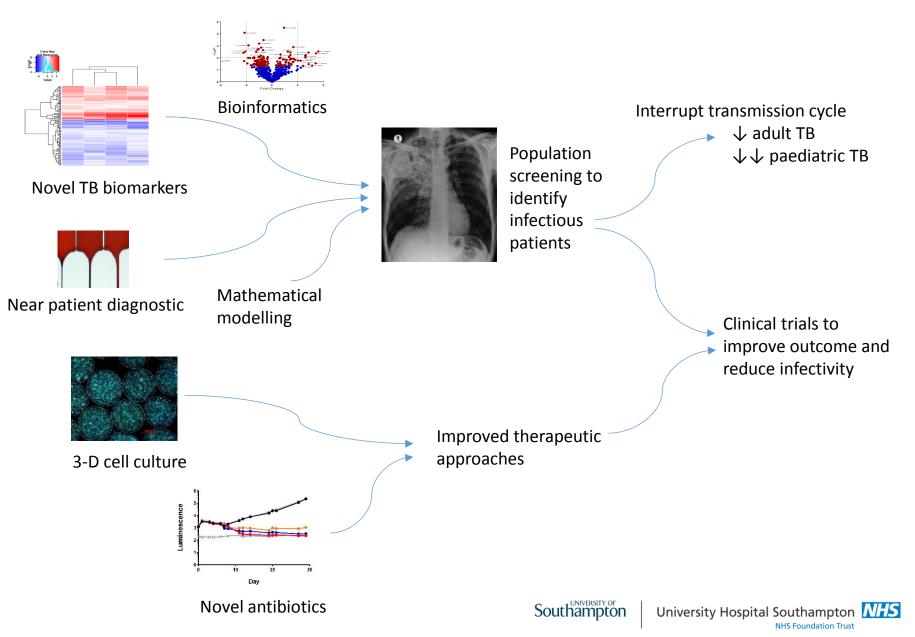


Matrix breakdown releases collagen fragments that are novel TB diagnostic markers



Seddon et al *J Infect Dis* 2013 208: 1571 Sathyamoorthy et al *PLOS One 2015* e0117605

Southampton TB research



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All the patients who have taken part

NHS National Institute for Health Research



NIH National Institute of Allergy and Infectious Diseases Leading research to understand, treat, and prevent infectious, immunologic, and atlergic diseases.



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The Wellcome Trust



National Centre for the Replacement Refinement & Reduction of Animals in Research

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