University of Southampton – summary

The tuberculosis (TB) research group at the University of Southampton conducts cross-disciplinary research into the pathogenesis of human disease to identify new diagnostic and treatment approaches. Our group includes clinicians, basic scientists, engineers, systems biologists, chemists, mathematicians and structural biologists. Since being established in 2012, key outputs include:

1. The development of a bioengineered cell culture model to study the host-pathogen interaction in TB (*Advanced Functional Materials, eLife, mBio, JID*)
2. The demonstration that mycolic acids from *Mycobacterium tuberculosis* (Mtb) have different immunogenicity (*PNAS*)
3. The identification of matrix degradation products as novel diagnostic markers (*JID, CID*)
4. Observations on human TB, leading to the hypothesis that Mtb drives an autoimmune process to transmit (*Lancet Inf Dis, Trends Immunol, AJRCCM*)
5. Proof of potential of doxycycline as a host-directed therapy (*AJRCCM, CID*)
6. Identification of entirely novel plasma biomarkers of TB using non-depletion based proteomic methodology (*unpublished*)

Clinical service and population screening: We have a very dynamic community screening programme, having tested over 1,000 individuals from high incidence countries over the last 2 years. Over 15% have been exposed to Mtb and have been offered chemoprophylaxis. We anticipate this programme will significantly reduce the incidence of TB in the city if sustained for the coming years.

Selected publications

- A Chancellor, AS Tocheva, C Cave-Ayland, LB Tezera, A White, JR Al.Dulayymi, JS Bridgman, I Tews, S Wilson, NM Lissin, M Tebruegge, BG Marshall, SA Sharpe, T Elliott, C Skylaris, JW Essex , MS Baird, SD Gadola, PT Elkington, S Mansour CD1b-restricted GEM T cell responses are modulated by *Mycobacterium tuberculosis* mycolic acid meromycolate chains *PNAS* 2017 *ePub* 114: E10964
- NF Walker, KA Wilkinson, G Meintjes, L Tezera, R Goliath, JM Peyper, R Tadokera, AK Coussens, RJ Wilkinson, JS Friedland, PT Elkington. Matrix degradation in HIV-1-associated tuberculosis and tuberculosis immune reconstitution inflammatory syndrome: a prospective, observational study *Clin Infect Dis* 2017 65: 121-132
- MK Bielecka, LB Tezera, R Zmijan, F Drobniewski, X Zhang, S Jayasinghe, PT Elkington. A Bioengineered 3-Dimensional Cell Culture Platform Integrated With Microfluidics to Address Antimicrobial Resistance in Tuberculosis *mBio* 2017 8: e02073
- L Tezera, MK Bielecka, A Chancellor, MT Reichmann, B Al Shammari, P Brace, A Batty, A Tocheva, S Jogai, BG Marshall, M Tebruegge, SN Jayasinghe, S Mansour, PT Elkington. Dissection of the host-pathogen interaction in human tuberculosis using a bioengineered 3-dimensional model *eLife* 2017 6: e21283
- P Brace, L Tezera, MK Bielecka, T Mellows, D Garay, S Tian, L Rand, J Green, S Jogai, A Steele, TM Millar, T Sanchez-Elsner, JS Friedland, C Proud, PT Elkington. Mycobacterium tuberculosis subverts negative regulatory pathways in human macrophages to drive immunopathology *PLOS Pathogens* 2017 13: e1006367
- K Clayton, ME Polak, CH Woelk, PT Elkington. Gene expression signatures in tuberculosis have greater overlap with autoimmune than infectious diseases AJRCCM 2017 196: 655
- PT Elkington, M Tebruegge, S Mansour. Tuberculosis: an infection-initiated autoimmune disease? *Trends in Immunology* 2016 37: 815 - 818
- B Al Shammari, T Shiomi, L Tezera, MK Bielecka, V Workman, T Sathyamoorthy, F Mauri, SN Jayasinghe, BD Robertson, J D'Armiento, Jon S Friedland, PT Elkington. The extracellular matrix regulates granuloma necrosis in tuberculosis *J Infect Dis* 2015 212: 463-73
- PT Elkington, JS Friedland. Permutations of time and place in tuberculosis *Lancet Inf Dis* 2015 15: 1357-60
- J Seddon, V Kasprowicz, NF Walker, HM Yuen, H Sunpath, L Tezera, G Meintjes, RJ Wilkinson, WR Bishai, JS Friedland, PT Elkington. Procollagen III N-terminal propeptide and desmosine are released by matrix destruction in pulmonary tuberculosis *J Inf Dis* 2013 208: 1571-9