UNIVERSITY OF ABERDEEN

Biologics Drug Discovery

Developing alternative therapeutics and novel diagnostics for bacterial and fungal infections

Dr Soumya Palliyil
Head of the Scottish Biologics Facility

Scottish Biologics Facility
Antibodies for research & commercialisation

Celebrating

10 years

Research in translational biology 2009-2019

The Scottish Biologics Facility

- Biologic drug discovery centre : Academic institutions & Companies
- Antibodies and peptides against a range of targets
  - Proteins, Peptides and Haptens
- Reagent tools, diagnostics, therapeutics
  - Anti-infectives, Neurodegeneration, Inflammatory Liver Disease
- Technology platform – Phage display & Binding site reformatting

Bacterial resistance: Small molecule monotherapy is inadequate

Biologic compounds as antimicrobial agents

- 5 biologics drugs approved so far

Pathogen type	Drug type	No of drugs in clinical trails
Gram negative bacteria	**Human/Humanised mAb**	**4**
Gram positive bacteria	**Human/Humanised mAb**	**6**

Novel drug discovery approaches

- Targeting proteins essential for viability during infection ✓
- Targeting bacterial virulence pathway ✓
- Narrow spectrum disease specific drugs ✓

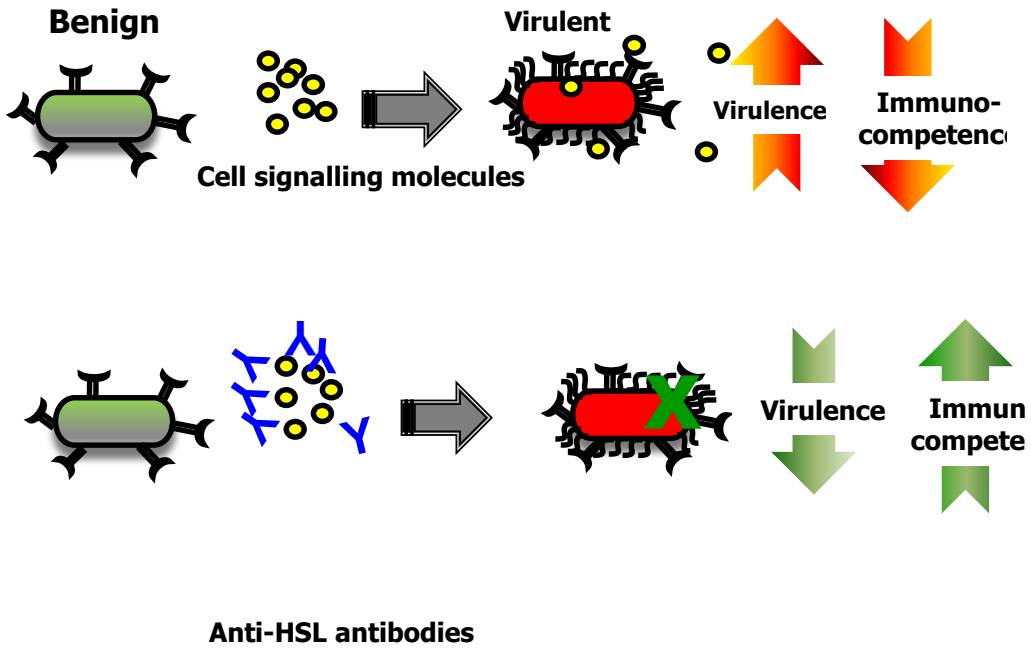
Improved Diagnostics

- Rapid point-of-care diagnostics ✓
- Narrow spectrum diagnostics for targeted therapy ✓
- Personalised medicine ✓

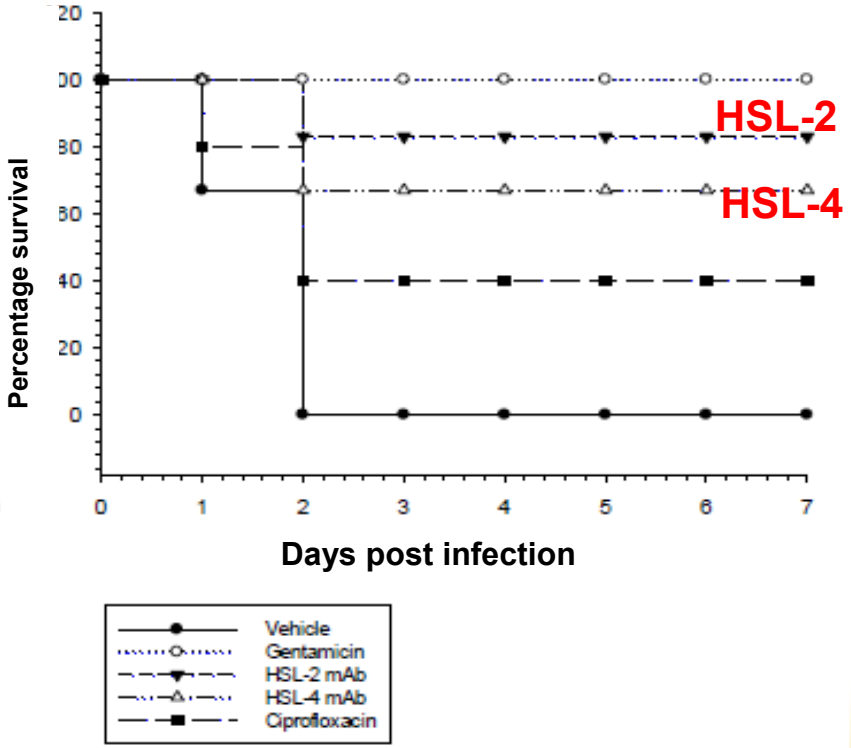
Targeting bacterial cell-cell communication

Monoclonal antibody treating life threatening *Pseudomonas* infections

- Antibodies bind to autoinducers outside the cell and disrupt cell-cell communication
- Reduces expression of virulence factors
- Enhanced clearance by the immune system
- Less chance of resistance development



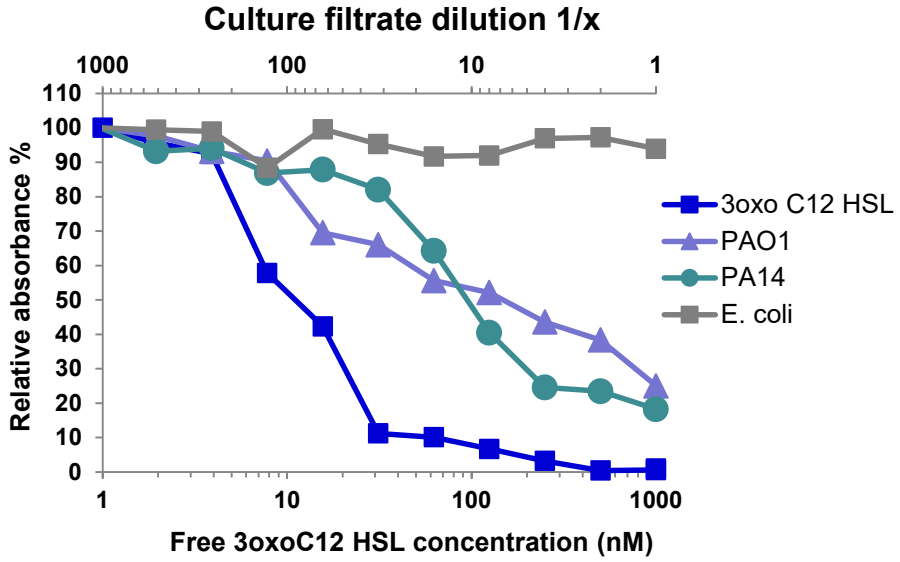
Non-neutropenic lung infection model



- HSL mAbs increased mice survival in a lung infection model

Anti-HSL antibodies as diagnostics

Immunoassay based diagnostic system

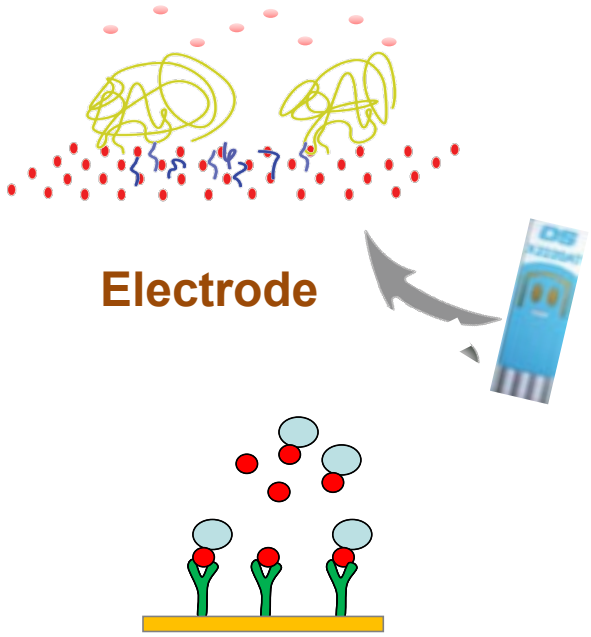


	Detection limit (IC20)
HSL-2 mAb in PBS	**1.5 nM**
HSL-2 mAb in urine	**5 nM**

Palliyil *et al*., Appl Environ Microbiol.

Electrochemical Impedance Spectroscopy

Label free detection of antigen –antibody interaction



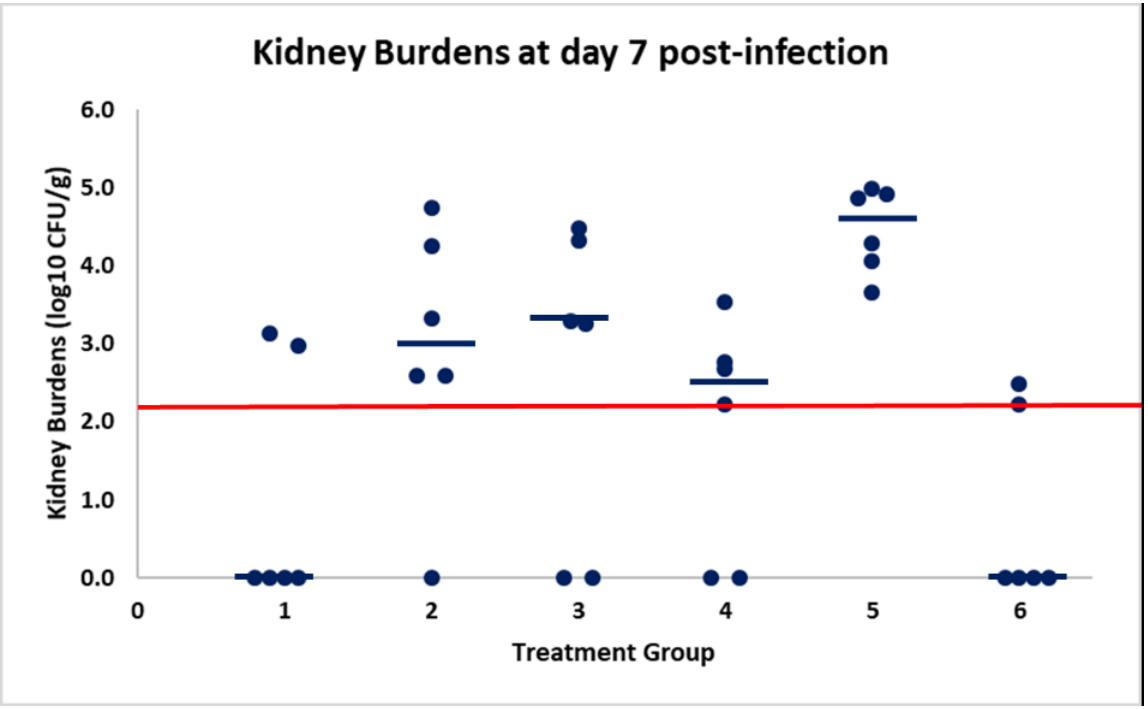
LOD for HSL 0.5 ng/mL (1.7 pmol/mL)

In collaboration with Prof Till Bachmann

THE UNIVERSITY of EDINBURGH

Generation of antifungal diagnostics and therapeutics

- Invasive fungal infections affect over 2 million immunocompromised patients
  - death rate up to 50%
- Novel antifungal therapeutics pipeline is sparse
- Emergence of drug resistant species
  - *Candida auris*



- Anti-Candida antibodies targeting cell wall proteins
- Lead antibodies were able to reduce fungal burden in kidneys in mice model of infection

1. **mAb1 pre & post infection**
2. **mAb1 post infection**
3. **mAb2 pre & post infection**
4. **mAb2 post infection**
5. **Saline control**
6. **Caspofungin**

What we can provide

- Strong expertise in developing recombinant antibodies with high affinity and epitope specificity
- Generate single chain antibodies and fully human mAbs
- Co- develop prescreening experiments using non-mammalian *in vivo* models such as *Galleria mellonella and Caenorhabditis elegans*
- ***Develop biologics as therapeutics, in vivo diagnostics and PoC diagnostics***
- ***Expertise to take biologics to IND through commercialization of assets***

Our Challenges

- Limited resources to identify novel antimicrobial targets
- Medium through-put bioassays for more rapid identification of functional biologic binders
- Access to a greater panel of appropriate animal models of infection

We are looking to develop networks

- Developing alternative therapies using the benefits of biologics
- Expertise in bacterial and fungal pathogenicity to identify druggable bacterial/fungal targets
- Design proof -of-concept experiments to more rapidly evaluate our binders

Acknowledgments

Scottish Biologics Facility
Prof Andy Porter – Director
Lily Fogg
Christina Downham

Aberdeen Fungal Group
Prof Carol Munro
Dr Donna McCallum
Dr Louise Walker

Dr Keith Charlton
Dr Ian Broadbent

Dr Tyng Tan
Mark Mawer
Emily Candlish

Prof Till Bachmann
Dr Holger Schulze
Division of Infection & Pathway Medicine
University of Edinburgh

SULSA Scottish Universities Life Sciences Alliance
Knowledge Transfer Partnerships
Innovate UK Technology Strategy Board
MRC Medical Research Council
euprotec
Knowledge Transfer Grant
1495 UNIVERSITY OF ABERDEEN
Pfizer