

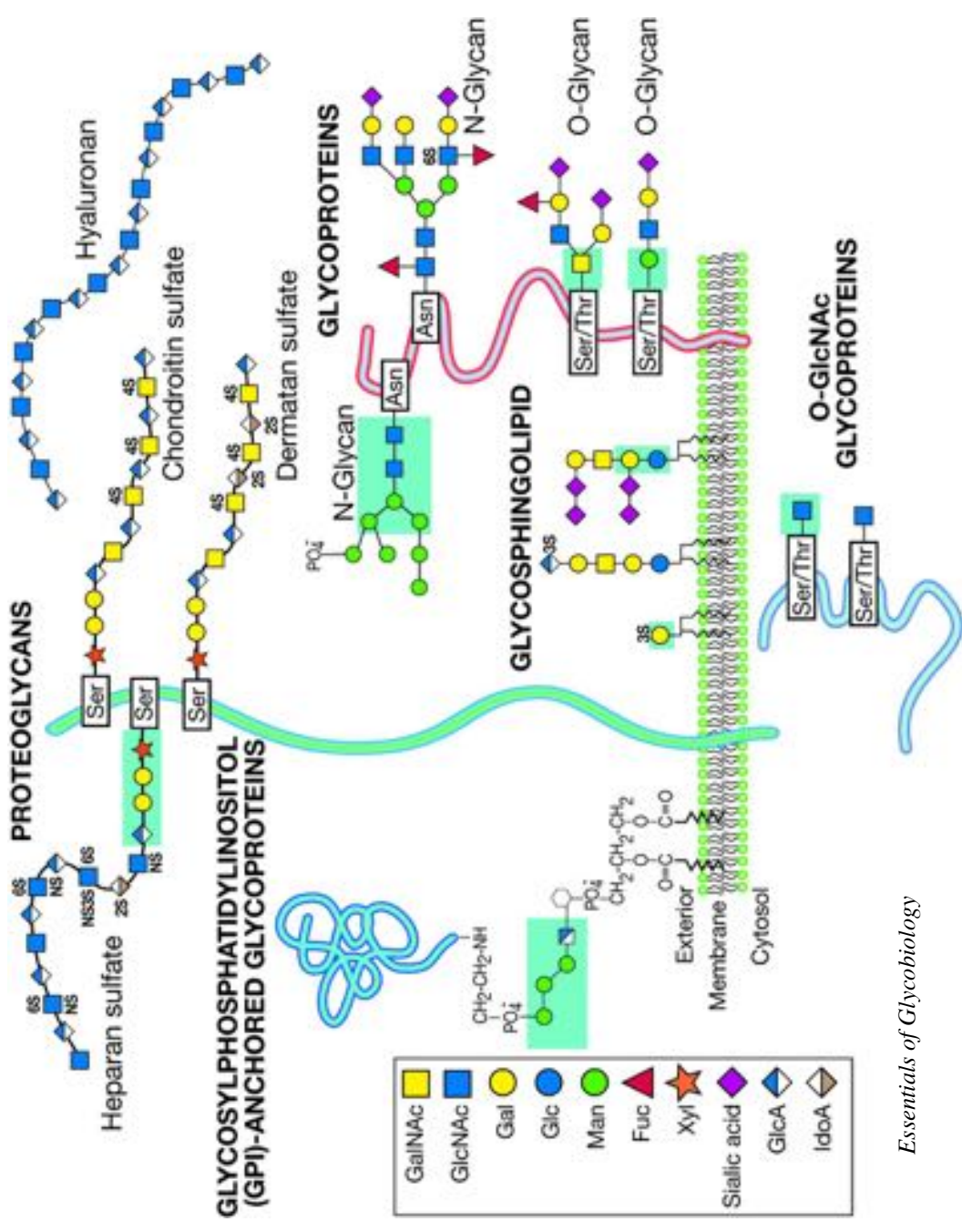
Glycosciences Laboratory

Division of Reproductive and Developmental Biology

**Dr Yan Liu
Lecturer of Glycosciences**

**Department of MDR Away Day
7th October 2019**

Glycans are prominently displayed on cells and tissues and are enormously diverse



Essentials of Glycobiology



Glycosylation is the most complex form of posttranslational modification

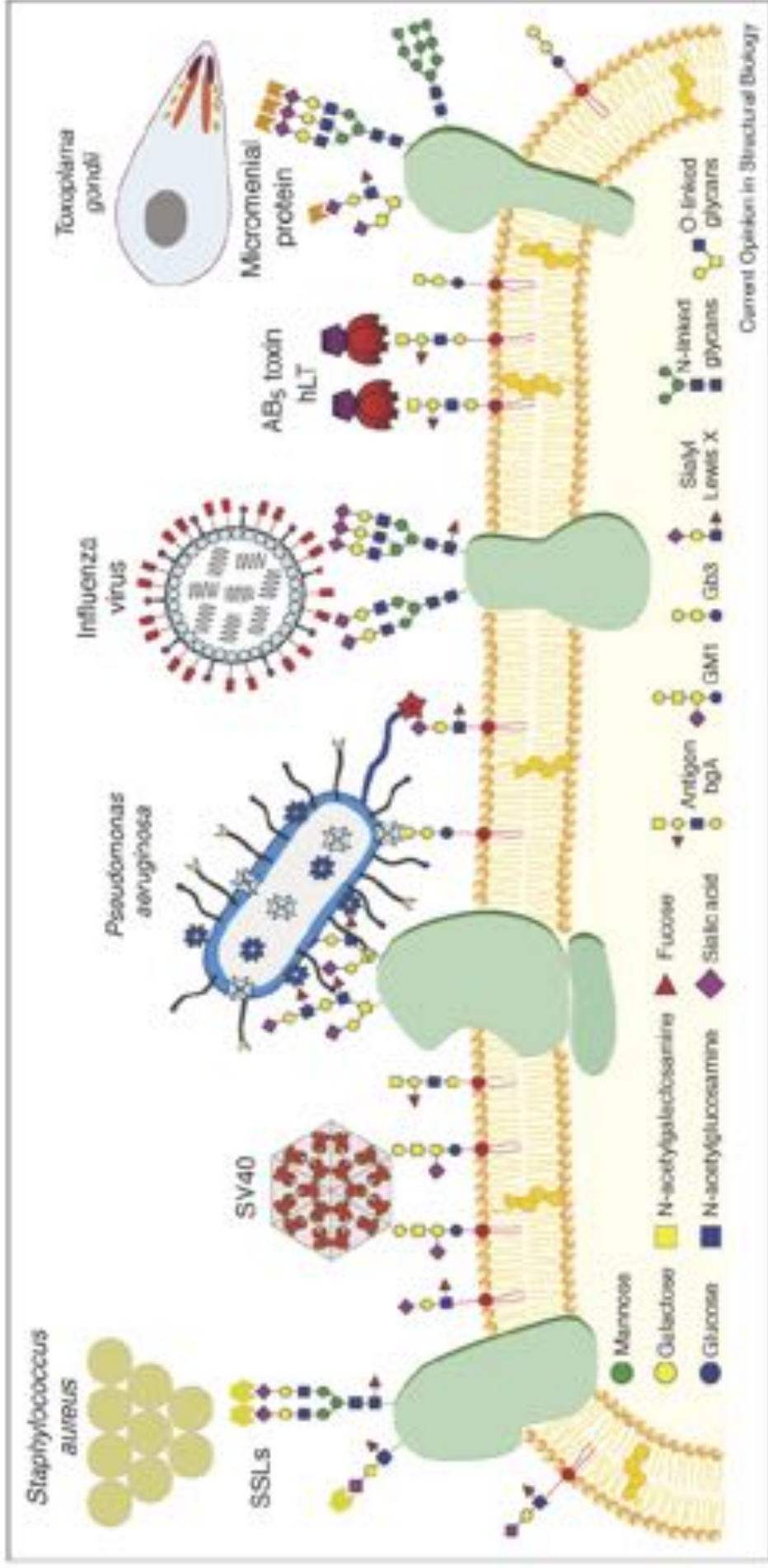
Glycans play roles in many biological processes and are involved in almost every major disease

specific glycan-protein interactions



Cover Page of Book 'Lectins', by Nathan Sharon

Glycan Recognition in Pathogen-Host Interactions



Schematic representation of some of the strategies used by pathogens for host glycoconjugates recognition and adhesion.

Who are we

A team of biologists, synthetic & analytical chemists, and bioinformatician with special expertise in the biological roles of glycans.



**MRC Biomedical
NMR Centre**

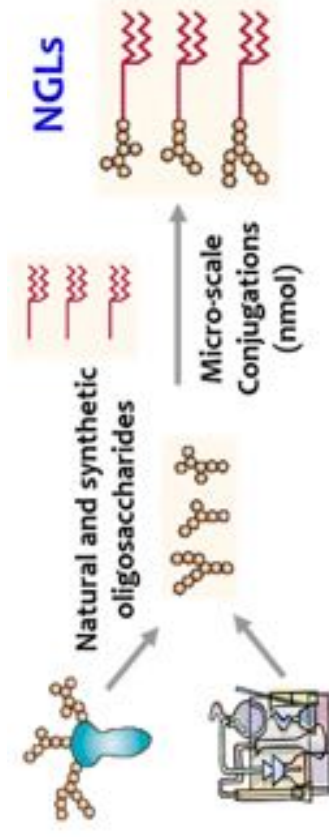


What we do

Dating from work pioneered by Ten Feizi, our speciality is the discovery of **glycan ligands** for proteins involved in **innate and acquired immunity** and **pathogen-host interactions**, also the characterization of **developmentally-regulated and cancer associated antigens**.

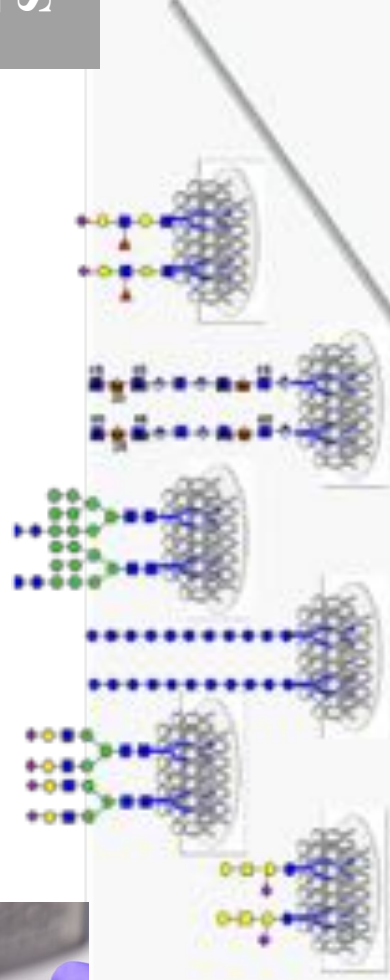
At the heart of our research are ***Glycan Microarrays***

Neoglycolipid (NGL) technology for probing glycan recognition



Professor Ten Feizi

Foundation of the first microarray system for sequence-defined glycans



Endogenous glycan-binding proteins
Neutralizing and cancer-specific Abs
Pathogens (adhesins, viruses, VLPs)
Serum samples

N, Nat. Rev. Mol. Cell Biol. (2004)
et al, Chem Biol (2007)
et al. Biol. Chem. (2009)

Methods in Molecular Biology (2012)

Palma A, Feizi T, Chai W, Liu Y. Curr Opin Chem Biol (2014)

Robotically printed in a liposomal formulation
at low femtomole levels

The Carbohydrate Microarray Facility

a biomedical resource supported by Wellcome Trust since 2012
for the broad international scientific community

<http://www.imperial.ac.uk/glycosciences>



**~1000 Lipid-linked saccharide probes derived from
natural sources or chemically synthesized
the largest glycan library in Europe**

Assignments we have made >70 recognition systems (published) since the establishment of the glycan microarray system

Ligands for endogenous carbohydrate-binding proteins

Siglecs (*Chem Biol* 2007, *JBC* 2011) Dectin-1 (*MCP* 2015)
 Malectin (*Mol. Biol. Cell.* 2008) DC-SIGN (*Glycobiology*
 2016)
 CLEC5A (*JBC* 2011) Notum (*Nature* 2015)
 Selectins (*JBC* 2014) ~~2011~~ H1N1-melanin (*Nature* 2018)
 ZG16p (*JBC* 2014; *ChemBiochem* 2011)

Epitopes of neutralizing and cancer-specific antibodies

Anti-fungal b-glucan antibodies
 (*PLoS ONE* 2009, *Plant Biotech. J.* 2011, *MCP* 2015)
 Broadly neutralizing anti-HIV antibodies
 (*Science* 2011; *J Exp Med* 2012; *PNAS* 2012;
Nat Struct Mol Biol 2013; *Immunity* 2014)
 Anti-epithelial cancer
 AE3 (*BBRC* 2011)
 F77 (*JBC* 2014)
 Anti-O-Mannosyl antibody (*PLoS ONE* 2016)
 Human stem cell glycan markers (*MCP* 2019)

Ligands for bacterial CBMs

Streptococcus pneumoniae hyaluronate lyase CBM (*JBC* 2014)
 Glucan binding CBMs (*MCP* 2015)

Ligands for recombinant bioactive plant lectins

ArtinM (*Data Brief* 2015, *Int J Biol Macromol.* 2016)

'Receptors' for cell-adhesion proteins of pathogens

Toxoplasma gondii and other Apicomplexan micronemal (MIC)
 proteins
 - *T. gondii* MIC1 (*Protein Sci.* 2009; *ChemBioChem* 2009)
 - *T. gondii* MIC13 (*JBC* 2010)
 - *Neospora caninum* MIC1 (*JBC* 2010)
 - *Eimeria tenella* MIC3 (*PLoS Pathog* 2011)
 - *T. gondii* MIC4 (*JBC* 2012)

Influenza viruses

- Pandemic 2009 H1N1 viruses (*Nat. Biotechnol.* 2009)
 - Pandemic 2009 H1N1 from fatal cases (*J Virol.* 2010)
 - H5N1 influenza viruses isolated from humans (*Virology* 2013)
 - Recent H3N2 vaccine viruses (*J Gen Virol.* 2016)

Polyomaviruses

- Human BK polyomavirus (BKPyV) (*PLoS Pathog.* 2013)
 - B-Lymphotropic Polyomavirus (LPyV) (*PLoS Pathog.* 2013)
 - Human Polyomavirus 9 (HPyV9) (*J Virol.* 2014)

Human Serotype 1 Reovirus (*PLoS Pathog* 2012)

Human papillomavirus subtype-16 (2013)

Rotaviruses

- P[10] and P[19] (*J Virol.* 2016, *MCP* 2018)

Human adenoviruses

- Human Ad52 (*PLoS Pathog.* 2015, *PNAS* 2018)
 - Human Ad37 (*Viruses* 2019)

NGL-based microarray system

**Provision for generating ‘Beam Search Arrays’
from ligand-bearing glycomes
to identify novel ligands of biological relevance**

Research

Glycan Markers of Human Stem Cells Assigned with Beam Search Arrays

Authors

Nian Wu, Lisete M. Silva, Yan Liu, Yibing Zhang, Chao Gao, Fuming Zhang, Li Fu, Yanfei Peng,
Robert Linhardt, Toshisuke Kawasaki, Barbara Mulloy, Wengang Chai, and Ten Feizi

Wu et al Mol Cell proteomics
2019

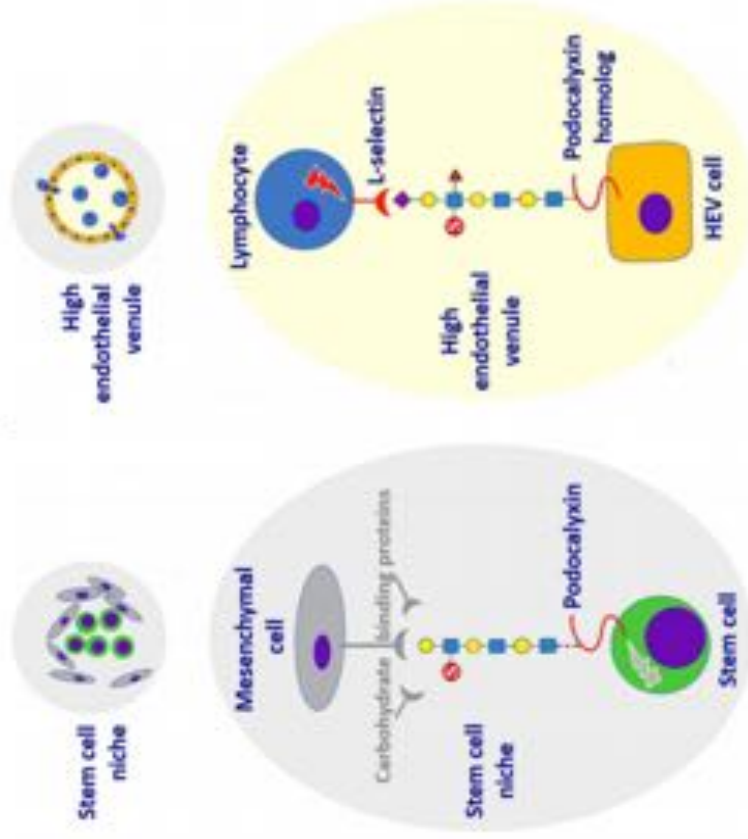
We assigned a **mono-sulfated glycan (R10G)** on the signalling molecule **podocalyxin** as a **marker of human induced pluripotent stem cells**.

By analogy with the ligand of **L-selectin**, which, upon ligand-binding, **activates lymphocyte migration** into lymph nodes,

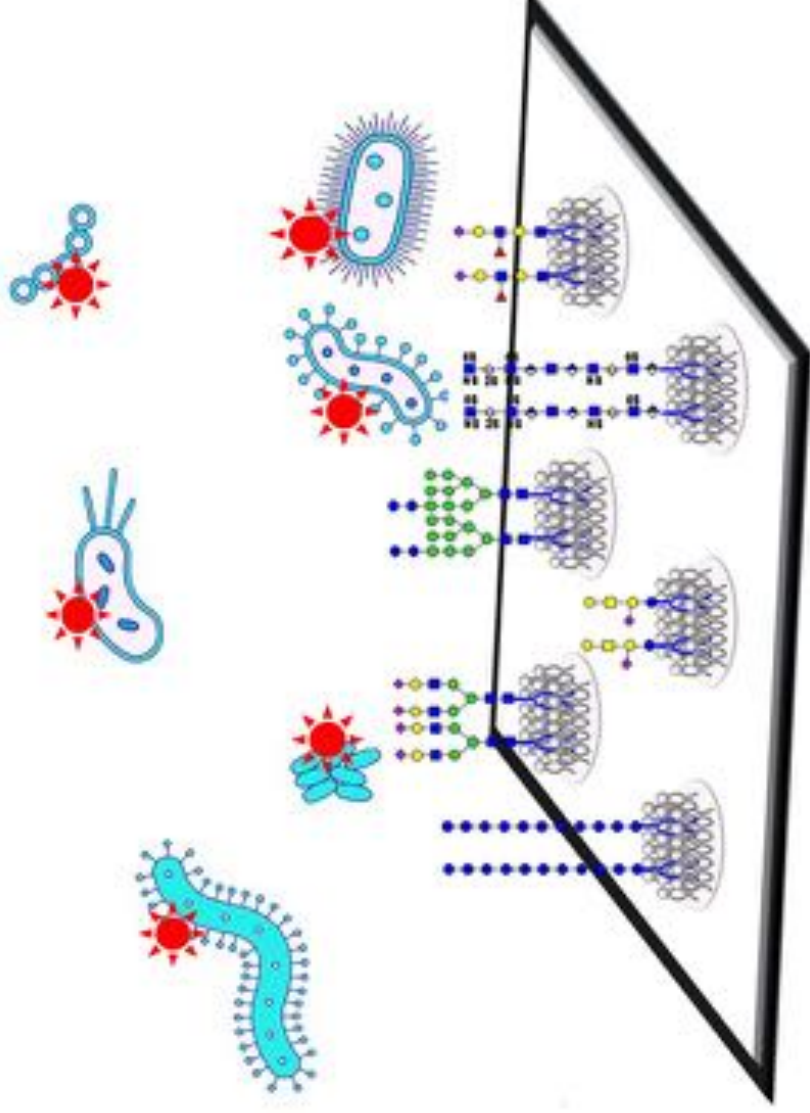
we propose that **interactions of R10G with carbohydrate-binding proteins** (e.g. lectins, growth factors and cytokines), in stem cell niche, are among cues for **stem cell survival, maintenance, self-renewal or differentiation**.



WWW.MCPONLINE.ORG | OCTOBER 2019



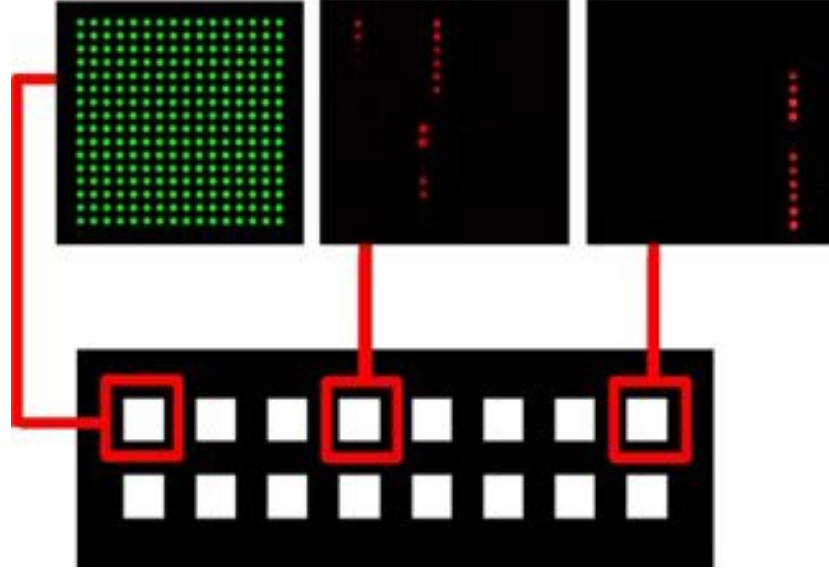
We are applying our technologies
to investigate **microbiome – host interactions**
using whole bacteria



Imperial College - March of Dimes European Prematurity Research Centre



A new centre investigating the causes of premature birth and finding new ways to prevent it.



Prof Phillip Bennett



David MacIntyre



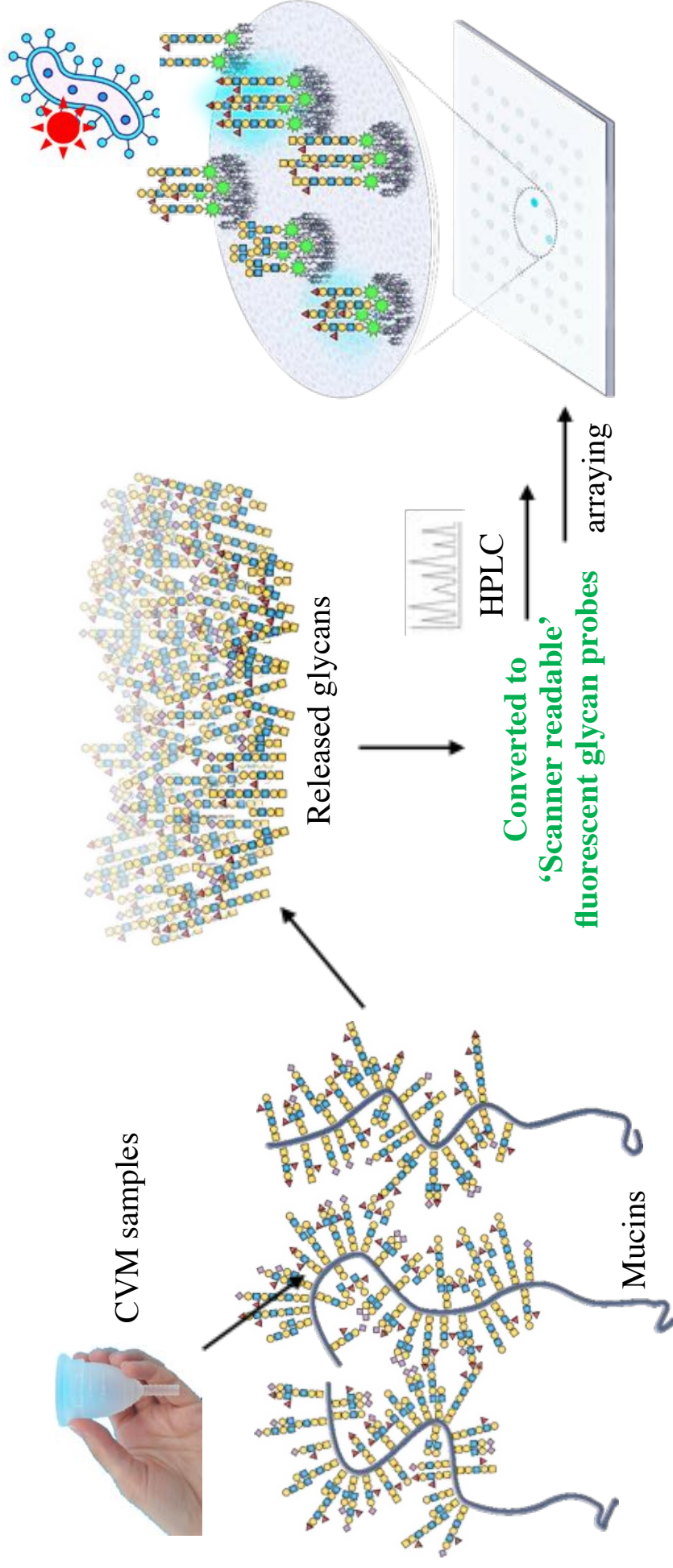
Lynne Sykes



Julian Marchesi

To determine the structures of the glycan ligands
for **pathogenic and commensal microbiota in
the lower reproductive tract**

Miniaturized glycome arrays of cervicovaginal mucosa (CVMs)



- To reveal 'glyco-binding signatures' for patient-derived microbiota and **establish correlation with blood group and sector status** as well as the immuno- and metabolic phenotyping

Imperial College - March of Dimes
European Prematurity Research Centre



Translational prospects

- Novel **'receptor typing kits'** for microbiota, for routine use
- Future designs of **anti-adhesion agents** for pathogenic bacteria
- Personalized applications

A potential future direction – Gut Microbiome

- o Understanding **the molecular basis of gut microbial tropism**
e.g. genetics related to blood groups and secretor status
- o Therapeutic designs, e.g. for intestinal microbiota modulation by
microbiome transplantation which we learnt about last week

“Carbohydrate Microarray Facility for the New Era of Glycomics”



Wellcome Trust Biomedical Resource Grant
(Nov 2019 – Nov 2023)
£1.34 M



Prof Ten Feizi



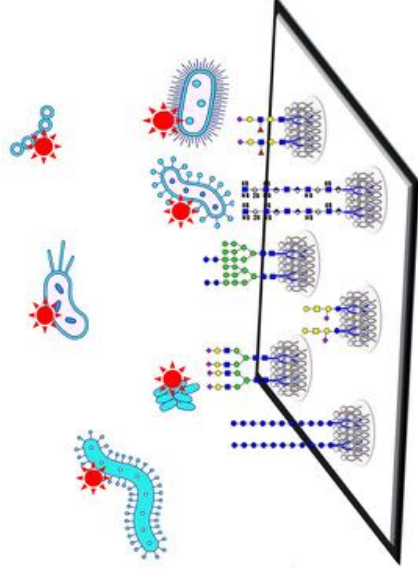
Dr Wengang Chai



Dr Ben Schumann
(Department of Chemistry)



Prof Phillip Bennett



Dr Virginia
Tajadura-
Ortega



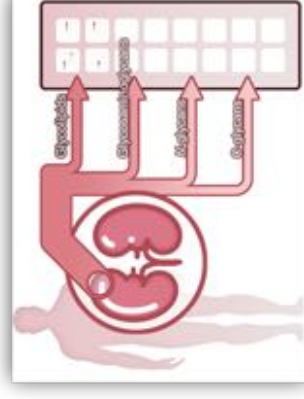
Dr Wengang Chai



Dr Yukie Akune



Carbohydrate Microarray Facility



Dr Jin Yu



Dr Antonio Di Maio



We invite new collaborations !

Where are we



**Burlington Danes Building (Level 5)
Hammersmith Campus**