



AGRC

Alimentary Glycoscience Research Cluster

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NOTE FROM THE DIRECTOR

Welcome to the first newsletter of the Alimentary Glycosciences Research Cluster (AGRC). In the recent years, Glycoscience has become an integral and established part of Irish science. The SFI-funded AGRC is the flagship Glycoscience research consortium, bringing Irish researchers from multiple disciplines together and promoting Irish Glycoscience research activities internationally. In the past 18 months since it was established, the AGRC has created a cohesive network of researchers, exploring the effect of microbial colonization on glycosylation of the gastrointestinal tract and developing different natural and synthetic agents to manipulate the host-microbial interactions. In the era when both glycoscience and the study of human microbiome are becoming increasingly popular, AGRC's objective to bring these two areas together has led to a unique research cluster with tremendous opportunities to develop novel technologies, biomarkers, therapeutics and nutraceuticals. Working with our partners in Teagasc, the Irish Agriculture and Food Development Authority, and our industry collaborators - Alimentary Health, Agilent Technologies, Biomining, and Bristol-Myers Squibb, we expect that the AGRC will be the springboard (or catalyst) from which other collaborations and networks will emerge to enhance Irish science in academia, the clinic and industry.



The AGRC Team members at a recent meeting in NUI Galway

AGRC INVOLVED IN CURATION OF SUGARBIND DATABASE

The SugarBind database is a repository of all publically available sugar-binding data and a very useful resource for Glycobiologists. SugarBind was established in 2003 by the MITRE Corporation, a not-for-profit US national technology resource engaged in scientific and technical activities for various government organizations. SugarBind has recently been installed and made publically available on the ExPASy portal by members of the Proteome Informatics Group of the Swiss Institute of Bioinformatics (SIB) in Geneva, Switzerland.

The AGRC have received an open source license for the SugarBind database from MITRE Corporation and will contribute to its continued development in collaboration with Elaine Mullen of MITRE and members of the BioMolecular Frontiers Research Centre (BFRC) of MacQuarie University New South Wales Australia. Improvements will include addition of newly curated material, the expansion of data fields and the cross-linking to other databases maintained at SIB.
Website: <http://sugarbind.expasy.org/sugarbind/>

TEDX PRESENTATION

AGRC Director, Prof. Lokesh Joshi, took part in NUI Galway's first TEDx event organised by CELT, the Centre for Excellence in Learning and Teaching, at NUI Galway. TEDx are independently organised events which like the original TED events provide a platform for spreading new ideas. Prof. Joshi spoke on the topic: Glycoscience the sweet and sticky language of biology. <http://www.tedxgalway.ie/speakers/speakers.html>



3RD ANNUAL MEETING OF GLYCOSCIENCE IRELAND



The 3rd Annual Meeting of GlycoScience Ireland was held in University College Dublin at the start of September. GlycoScience Ireland is an academic organization led by Prof. Lokesh Joshi and Prof. Pauline

Rudd, which aims to build support for and promote Glycosciences research in Ireland and to provide visibility and collaborative opportunities for Irish glycoscientists with international academic and industrial communities. Attendees included representatives from Irish academic institutions, Irish and multinational Biopharmaceutical and Biotechnology industries, the major Irish funding agencies, and a distinguished panel of speakers from the US and Europe. Web-site: www.glycoscienceireland.ie

CHICKEN MUCIN ATTENUATES PATHOGENICITY OF CAMPYLOBACTER JEJUNI

Campylobacter jejuni is the leading cause of bacterial gastroenteritis in humans worldwide. Poultry, in particular, are an important source of human infection. Interestingly, *C. jejuni* is a commensal in avian hosts and colonises them asymptotically.

AGRC researchers, Prof. Billy Bourke and Dr. Marguerite Clyne of UCD had previously

shown that crude chicken mucous reduces the invasiveness of *C. jejuni* in primary human intestinal cells *in vitro*¹. Together with Prof. Stephen Carrington, also of UCD, and their teams, they have now shown that purified mucins, highly glycosylated molecules that are the main structural components of mucous, from various parts of the chicken GI tract mimic the inhibitory effect of crude chicken mucous on

Campylobacter virulence². The extent of inhibition depends on the site of origin within the avian gastrointestinal tract, with mucins isolated from the large intestine showing the greatest effect. It will now be of major importance to identify the structural differences between mucins of various origins within the chicken intestinal tract and those originating from the human gastrointestinal tract.

¹ Byrne CM, Clyne M, Bourke B. 2007. Microbiology 153:561-569

² Alemka A, Whelan S, Gough R, Clyne M, Gallagher ME, Carrington SD, Bourke B. 2010. Purified chicken intestinal mucin attenuates *Campylobacter jejuni* pathogenicity in vitro. Journal of Medical Microbiology 59, 898-903

MICROBIAL GLYCOBIOLOGY: BOOK LAUNCH

A book entitled 'Microbial Glycobiology: structures relevance and application' was launched by Dr. James J. Browne, President of NUI Galway earlier in the year. The book was edited by the late Professor Anthony P. Moran of the AGRC and NUI Galway (Editor-in-Chief), Otto Holst from the Leibniz-Center for Medicine and Biosciences Germany, Patrick J. Brennan from Colorado State University USA, and Mark von Itzstein from the Institute for Glycomics, Griffith University, Australia. This is the first comprehensive book on the subject, covering both the basic science of microbial glycobiology and how microbial

glycosylated molecules might be used in industry and biomedicine.

Among the contributors to the book were Prof. Stephen Carrington, Dr. Marguerite Clyne and Dr. Colm Reid, all investigators with the AGRC. In a chapter entitled "Microbial Interaction with Mucus and Mucins", they described how epithelial mucins are a fundamental and responsive component of the barrier at moist mucosal surfaces, that have the capacity to modulate microbial binding, penetration and colonization. The authors have outlined the

current understanding of the structural basis of mucin - microbial interactions and the cell biology underlying the biosynthesis of physiologically competent supra-mucosal gels. They conclude that although this knowledge is incomplete the current body of literature provides a sound "proof of concept" that novel antimicrobial strategies, exploiting new knowledge of such interactions, could soon be within our reach.

IN MEMORIAM

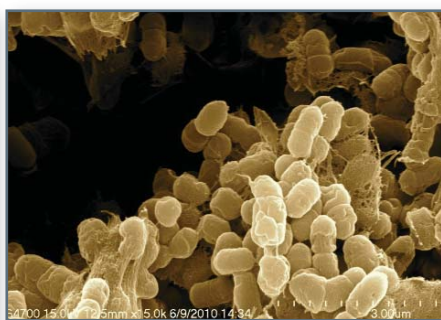
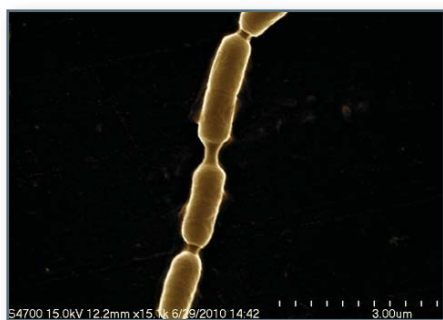


The AGRC deeply regrets the sudden and untimely death of Professor Anthony P. Moran on 30th September, 2010 aged 49 years. The news brought with it a deep sense of loss both for the Cluster, for whom Tony was a valued and highly respected colleague, and also for the Irish scientific community, to whom Tony made a valuable contribution during his distinguished career. Tony published over 170 papers in international peer-reviewed journals and 25 book chapters, and edited 4 books. He was Professor in the discipline of Microbiology in the School of Natural Sciences in NUI Galway and Adjunct Professor at the Institute for Glycomics, Griffith University, Australia. He was also an elected member of the Royal Irish Academy and a Fellow of the Royal Society of Chemistry. *Ar dheis Dé go raibh a anam.*

ENTERPRISE IRELAND INNOVATION PARTNERSHIP GRANT ON PROBIOTIC BACTERIA

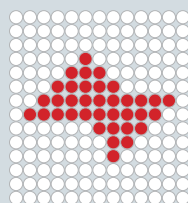
The Glycoscience Group at NUI Galway, led by Prof. Lokesh Joshi, has recently been awarded an Innovation Partnership grant by Enterprise Ireland to work in collaboration with Alimentary Health Ltd. Alimentary Health is focused on the development of gastrointestinal (GI) therapeutic and healthcare products derived from commensal gut bacteria (probiotics).

The new project will develop methods for the characterisation and selection of novel probiotic strains, that have potential to improve human health. Alimentary Health Ltd. is the foundation industry partner of the Alimentary Pharmabiotic Centre, the SFI-funded Centre for Science and Technology (CSET) based at University College Cork.



Scanning electron micrographs (i) *Lactobacillus paracasei* (ii) *Bifidobacterium longum infantis* (iii) *Faecalibacterium prausnitzii*

EU FP7 HEALTH PROJECT STARTING JANUARY 2011: GLYCOHIT



GlycoHIT

A grant of €3 million has recently been awarded under the EU Framework 7 Health programme for a collaborative project entitled "Glycomics by High-throughput Integrated Technologies: Development

and validation of complementary and integrated technologies for glycomic analysis of serum in cancer glycomarker discovery, diagnostics and glycotherapeutic monitoring" (acronym: GlycoHIT). GlycoHIT will be led by Prof. Lokesh Joshi of the AGRC and will involve 15 partners from both academia and industry with representatives from many European countries, Israel, China, Japan and the USA. Partners include Professor Pauline Rudd of NIBRT and Dr. Zohar Yakhini of Agilent Technologies, both partners in the AGRC, and Ciaran Clissman of Pintail Ltd., a project management consultancy SME based in Dublin.

THE EUROGLYCOFORUM GLYCOSYLATION AND DISEASE SUBGROUP MEETING



Among the AGRC attendees at the Euroglycoforum Glycosylation and Disease Subgroup Meeting held in University College Dublin in August were Professor Pauline Rudd of NIBRT (Organiser), Dr. Marguerite Clyne and Professor Stephen Carrington of UCD and Professor Anthony Moran and Dr. Marian Kane, Programme Manager, of NUI Galway. A variety of topics in the field of Glycosylation and Disease were discussed at the meeting. The objective of the meeting was to share current research, support existing collaborations and to facilitate potential future collaborative efforts in the field. The meeting proved extremely successful with good attendance of over 40 delegates from all over Europe (Ireland, England, Scotland, the Netherlands, Germany, Poland, Spain, Portugal, Finland and Estonia).

AGRC TECHNOLOGY PLATFORMS

Improved *in vitro* model for gut microbiology studies:

- Expanded knowledge on glycosylation and its control in the gut
- Potential targets for novel therapeutic / nutraceutical approaches

Glycoanalytical tools:

- Advances in HPLC/MS methods
- Novel HTP microarray-based glyco profiling: lectin arrays, mucin arrays, neoglycoconjugate arrays, synthetic glycan arrays
- Novel glycan binders selected using combinatorial approaches (SELEX and phage display)



Dr. Jared Gerlach of the Glycoscience Group at NUI Galway using the Agilent microarray scanner

INTERNATIONAL POSTER PRESENTATIONS

Among the posters presented by AGRC researchers at international conferences in 2010 were:

Annual Conference of the Society for Glycobiology, Florida, USA (Nov 2010)

- A comparative glycan and lectin microarray analysis of virulent and attenuated strains of *Campylobacter jejuni* at host and avian temperatures. *Authors: M Kilcoyne, ME Twomey, JQ Gerlach, AP Moran, L Joshi*
- Identification of a Gal α 1-3Gal-specific scFv through screening of a chicken scFv library. *Authors: E Starr, I Shaw, O Cox, M Kane and L Joshi*
- Method for milk oligosaccharide profiling by 2-aminobenzamide labelling and hydrophilic interaction chromatography. *Authors: K. Marino, J Lane, J L Abrahams, W Struwe, D J Harvey, MR Mariotta, R Hickey, P M Rudd*

EMBO Chemical Biology 2010, Heidelberg, Germany (Sept 2010)

- Linear and convergent synthesis of mucin O-glycan core structures for the investigation of their binding to gut bacteria. *Authors: M Hollinger, F Abraha and S Oscarson*

AGRC RELATED REVIEWS

1. A review of the ability of various dietary carbohydrates to prevent adhesion of pathogens to host cells emphasised their potential to be developed as nutraceutical ingredients, that will help to prevent infectious diseases in the human gastrointestinal tract. *Lane JA, Mehra RK, Carrington SD, Hickey, RM, 2010. The food glycome: a source of protection against pathogen colonization in the gastrointestinal tract. International Journal of Food Microbiology 142, 1-13.*
2. Recent advances in glyco-biosensors aimed at the detection and quantification of glycoconjugates or carbohydrates derived from glycoconjugates were reviewed in the context of their potential clinical, biomedical and industrial applications. *Cunningham S, Gerlach J, Kane M, Joshi L. 2010. Glyco-biosensors: recent advances and applications for the detection of free and bound carbohydrates. Analyst 135, 2471-2480.*
3. The main technologies routinely used for structural analysis of protein glycosylation were reviewed, and the complementary information that each provides described. *Marino K, Bones J, Kattla JJ, Rudd PM. 2010. A systematic approach to protein glycosylation analysis: a path through the maze. 2010 Nature Chemical Biology 6, 713-723.*

Enquiries? Comments? Suggestions?

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AGRC Partners:



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