

## The NIDDK iNFORMER Newsletter - July/August 2011



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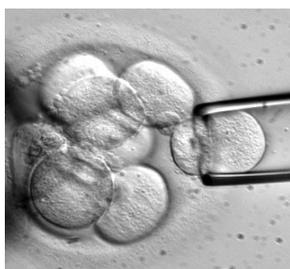
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### Special points of interest:

Summer double issue!

- Glycomics initiative
- ES cell court case update
- German *E. coli* outbreak
- Summer picnic date announced!



Read about the latest developments in the court case over human ES cell research on page 2.



Report on the Consortium for Functional Glycomics meeting. Page 3



An overview on the recent deadly outbreak of *E. coli* in Germany on page 3.



Meet June & July's new NIDDK fellows on page 4.



The **iNFORMER**, is a monthly newsletter published by the Fellows Advisory Board (FAB) in collaboration with the NIDDK Fellowship Office. If you would like to participate in writing newsletter articles or have questions or comments, please contact any of the following members.

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## Events Calendar

Thurs Sept 1st	Nancy Nossal Fellowship applications due
Tue Sept 13th	NIDDK Fellows' Awards Ceremony & Picnic
Tue-Wed Sept 20th-21st	ACS careers workshop

## Fellowship Office news

**NIDDK Awards Ceremony and summer picnic** on September 13, Tuesday 2:30 pm – 8:30 pm. For ticket details: Please contact Shauna Clark or Matt Wenham.

### American Chemical Society Workshop on September 20 & 21

**Bldg 10, 9:30 Am – 5:00 PM**  
**Career Workshop for Fellows in Lipsett Auditorium**  
**ALL About CAREER CAREER! -**  
 Launching your Career: A Workshop for Postdocs  
 Workshop geared toward your career  
 Starting your job search  
 Non-Traditional Career Options  
 Acing the Job Interview  
 Meeting Expectations –Your First Year on the Job  
 Scheduled Resume Review and Practice Interviews  
 Registration Link: <http://fs21.formsite.com/ACSPostdoc/form6/index.html>

### Congratulations FARE WINNERS!

The Fellowship Office is delighted to acknowledge the 15 winners of the 2012 FARE Award Competition from NIDDK. Congratulations to the following for their excellent scientific contributions. We are very proud.

- Nicholas Anthis 2) Alta Berger 3) Anna Burkart 4) Suchismita Chandran 5) Joshua Chappie 6) Ling Chin Hwang 7) Qihuang Jin 8) Yanfen Liu 9) Pushpa Mudiyansele 10) Nicholas Noinaj 11) Harish Ramanathan 12) Edina Rosta 13) Guelaguetza Vazquez-Ortiz 14) Chaochen Wang 15) Lifeng Wang

### NIDDK Office of Fellow Recruitment and Career Development Office

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## Prometheus reprieved by Matt Wenham

*Conclusion reached in ES cell suit—research to continue*



**US District Court for the District of Columbia Chief Judge Royce C. Lamberth (left) and Drs James Sherley and Theresa Deisher, plaintiffs in the case (below).**

Regular readers of *The Informer* will recall that the November 2010 issue covered the ongoing case before the US District Court that sought to bring a halt to federally-funded research on human embryonic stem cells (hESC). Two adult stem cell researchers, James Sherley and Theresa Deisher, had sued the federal government over NIH funding guidelines for ES cell research introduced by the Obama administration, claiming that the 2009 rules violated a federal law banning the destruction of embryos. Now the court has issued a final ruling on the suit, bringing the two-year saga to a potential close.

In August 2010, the judge hearing the case, DC Circuit

Chief Judge Royce Lamberth, issued an injunction against the NIH funding further hESC research while he considered the Sherley-Deisher suit. The Department of Health and Human Services, NIH's parent agency, immediately appealed the injunction, with the appeal court staying the injunction and allowing grant money to continue flowing. In April, the Court of Appeals for the DC circuit overturned Lamberth's original injunction, returning the full case to the lower court for judgement.

On July 27, Judge Lamberth issued his judgement in a 38-page opinion, which agreed with the appeals court's decision that the allegedly-violated law - the Dicker-Wicker amendment - was

creating demand for the cells.

Supporters of hESC research rejoiced at the decision, although many remained sanguine in their views on the future security of research programs. The plaintiffs still retain the ability to appeal the decision to the appeals court, where legal commentators said it would likely be heard by the same three judge panel that struck down the original injunction, and was therefore unlikely to succeed. If this were to occur, an appeal to the US Supreme Court would be possible, meaning that an ultimate decision on the future of hESC research could be two to three years away. Harvard Medical School hESC researcher and recent NIH WALs lecturer, George Church, summed up the caution felt by many in the field. "I hope we're done for now, but nothing surprises me anymore."

sufficiently ambiguous in its definition of the word 'research' as to allow the NIH to fund work on hESC, providing it did not fund the derivation of such cells. Lamberth said that he was bound to abide by the higher court's ruling, although his opinion demonstrated that he was less than convinced by the appellate judges' reasoning. "This Court has become a grudging partner in a bout of 'linguistic jujitsu'", he said, although he did also rule against the plaintiffs' claims that research on hESC put embryos in general at risk by



## The sweet promise of glycobiology by Michelle Bond

Carbohydrates are essential cellular modifications conferring specific biological activity to the proteins and lipids on which they reside. The fundamental importance of these glycans is underscored by their roles in nearly every biological process, including critical cellular functions such as

recognition, endocytosis, and signaling (Figure 1). Moreover, carbohydrates are recognized as likely players for virtually every human disease and play critical roles in processes ranging from host-pathogen recognition and infection to axon regeneration.

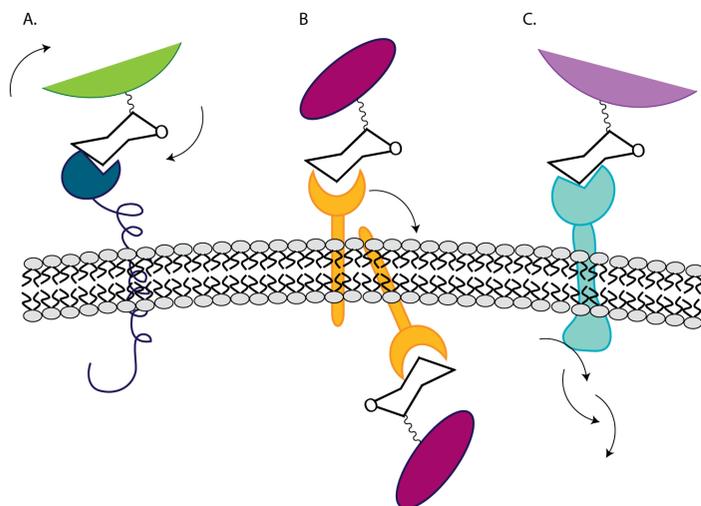
Despite the importance of

glycans in cellular functions and the ubiquity of glycoconjugates (glycoproteins and glycolipids) are found on the cell surface, in the extracellular milieu, in the cytosol, and in the nucleus), the molecular details governing both glycan synthesis and the role of carbohydrates in biological

processes has remained underexplored until recently. Progress toward defining the molecular details of glycan synthesis and carbohydrate recognition has been elusive because of the inherent complexity of carbohydrates:

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**Glycobiology cont.**



**Figure 1.** Glycans attached to a cell (A and C) or protein (B) are important for cellular recognition (A), endocytosis (B) and signaling (C). (A) Glycans facilitate leukocyte “rolling” along the endothelial cell surface. (B) Scavenger Receptor C-type Lectin and dendritic cell-specific ICAM3 grabbing nonintegrin can serve as both cell adhesion molecules and endocytic receptors through carbohydrate recognition. (C) The proliferating B cell lectin (Prolectin) can bind glycans and initiate signaling cascades.

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...they are synthesized in a non-linear, non-templated fashion and their ultimate composition is largely determined by the concentration of the monosaccharides and enzymes available within an individual cell. These complexities precluded the use of traditional synthetic techniques and analytical methods, necessitating new technologies and methodologies for studying glycans both *in vitro* and *in vivo*.

Acknowledging glycobiology as a critical frontier for understanding disease progression, pathogen invasion, and other topics related to health, the National Institute of General Medical Sciences (NIGMS) recognized that an integrated approach bridging diverse disciplines would expeditiously advance the fundamental understanding of carbohydrates in biological systems. In 2001, through a “Glue Grant” (U54) from the NIGMS, the Consortium for Functional Glycomics (CFG) brought together 30 scientists

in fields ranging from genetics and molecular biology to immunology and synthetic chemistry. Expanding to over 550 participating investigators in 2011, the CFG has made significant progress toward understanding the paradigms by which protein-carbohydrate interactions mediate cellular communication.

Through collaborative efforts, the CFG has produced a valuable set of resources, including glycan and gene arrays, a reagent bank, and knockout mice (many of which were highlighted at the recent CFG meeting at the NIH entitled “Glycan-Binding Proteins in Cell Communication”, July 27-29, 2011). With at least 50% of all polypeptides being modified by carbohydrates and around 2% of the genome encoding for proteins that are involved in glycan biosynthesis, degradation, and transport, these resources are critical for advancing, arguably, nearly every field of the biological sciences. Although the complexity of glycomics may have once deterred scientists from considering carbohydrates beyond the table sugar used to sweeten their morning coffee, the cutting-edge technology and significant advances in methodologies expands the potential impact of

glycoscience and glycomics significantly. For more information about the CFG and the broad reach of glycobiology, visit <http://www.functionalglycomics.org>.

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**Deadly German *E. coli* outbreak is over—at least for now** by Matt Wenham

The European outbreak of a deadly strain of *E. coli*, which led to the deaths of 52 people (all but two in Germany), has been declared over, almost two months after it started. German health authorities began noticing a sharp increase in cases of hemolytic

uremic syndrome (HUS) in mid-May, quickly determining that the cause was infection with a pathogenic strain of the bacteria, known as enterohemorrhagic *E. coli* (EHEC).

Most strains of *E. coli* are harmless commensal bacteria,

found in the digestive tracts of all people. However, in certain strains, the acquisition of genes coding for protein toxins results in them becoming pathogenic to humans, producing symptoms such as abdominal cramps and diarrhea. Perhaps the best

known pathogenic strain is *E. coli* O157:H7, which has caused numerous food borne illness outbreaks in the US as a result of the contamination of foods such as spinach and hamburger meat.

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## *E. coli* outbreak cont.

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EHEC bacteria produce the harmful Shiga toxin, which is internalized by the epithelial cells of the gut and inhibits protein synthesis by cleaving ribosomal RNA. The most severe complication of EHEC infection is HUS, which is characterized by the destruction of red blood cells and kidney failure. A complicating factor is that treatment with antibiotics – the usual course of action for *E. coli* infections – may actually worsen a patient's condition.

In the German case, doctors in the city of Hamburg noticed an increase in HUS cases in May and notified the German center for disease control, the Robert Koch Institute (RKI).

Investigators at the RKI initially thought they may be dealing with a new serotype of EHEC, after ruling out O157 as the cause. However, subsequent studies revealed that a rare serotype, O104:H4 was the culprit. The epidemiological investigation to find the source of the bacteria lurched from food product to food product; initial warnings that Spanish cucumbers were responsible (later found to be wrong) saw a collapse in trade of Spanish produce and a diplomatic spat between the two countries. A subsequent theory pointed the finger at German-grown sprouts, which was later revised to pinpoint the seeds used to grow the plants, imported from Egypt during 2009 and 2010. According to

European food safety officials, the ultimate origin of the bacteria remains an open question, although the farm which grew the seeds was the most likely source. On July 26, the RKI declared the outbreak officially over, as no new infections had been reported for three weeks, the pathogen's incubation period. During the outbreak, more than 4000 people were sickened by the bacteria.

Across Europe, attention is now turning to the way the outbreak was investigated, how the authorities responded to the crisis and what the longer-term implications may be. Critics said the RKI was too quick to lay blame for the contamination source, with Spanish farmers seeking

compensation from the German government for their lost income. In their defense, RKI officials said they were obliged to warn the public as soon as a potential source became clear. EHEC experts are also concerned that the bacteria may re-emerge, as the reservoir for the strain and the actual route of contamination have not yet been determined. Tim Eckmanns from the RKI summed up the work ahead for researchers in the field, saying "we need to find where this pathogen is hiding". No doubt the effects of this latest outbreak will be felt for some time to come.

## Welcome New Fellows!



The following fellows joined NIDDK in the last two months: (top: L to R)

**Madoka Chinen**

Visiting Fellow - Japan  
PhD, Kumamoto University  
Laboratory of Cellular and Developmental Biology (Lei group) Bldg 50

**Chen Du**

Visiting Fellow - Germany  
PhD, Heidelberg University  
Genetics of Development and Disease Branch (Mueller group) Bldg 10

**Anton Gorkovskiy**

Visiting Fellow - Russia  
PhD, Moscow State University  
Laboratory of Biochemistry and Genetics (Wickner group)

**Sameh Soliman**

Visiting Fellow - Egypt  
PhD, Faculty of Science, Alexandria University  
Laboratory of Bioorganic Chemistry (Kovac group)

**Antonino Baez-Rogelio**

Visiting Fellow- Mexico  
Ph.D., National Autonomous University of Mexico  
Biotechnology Core ( Shiloach group)

(lower: L to R)

**Koji Fujita**

Visiting Fellow - Japan  
PhD, Yokohama-city university graduate school of medicine  
Liver Diseases Branch ( Rotman group)

**Amit Kumar**

Visiting Fellow, Pre-doc  
B.Tech, IIT, India  
Biotechnology Core ( Shiloach group)

**Hettiarachchige Perera**

IRTA  
PhD, Cleveland State University  
Laboratory of Bioorganic Chemistry (Bewley group)

**Dalya Lateef**

IRTA  
PhD, Tuskegee University  
Diabetes, Endocrinology and Obesity ( Reitman group)

**Sijung Yin**

IRTA  
PhD, Boston University  
Laboratory of Molecular Biology (Krause group)