VBI e_Connections

feature technology in the news interview

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Haselkorn gives Phi Beta Kappa lecture at VBI

What is one of the key enzymes that plants, parasites and people have in common? Robert Haselkorn, F. L. Pritzker Distinguished Service Professor of Molecular Genetics and Cell Biology at the University of Chicago and member of the National Academy of Sciences, likes to argue the case for acetyl-CoA carboxylase, one of the enzymes that living cells use to make fatty acids. On September 25, Dr. Haselkorn presented a talk, "An enzyme that is key to suppressing grassy weeds, treating parasite diseases of people, and controlling obesity," at the Virginia Bioinformatics Institute Conference Center. In the seminar, Dr. Haselkorn gave a historical overview of efforts to investigate acetyl-CoA carboxylase.

Born and raised in Brooklyn, New York, Dr. Haselkorn majored in Chemistry at Princeton University, subsequently making the transition to biochemistry for his PhD studies at the University of Harvard. Postdoctoral work at the Agricultural Research Council's Virus Research Unit, University of Cambridge, England, led to the University of Chicago, where he has worked for almost 50 years. Dr. Haselkorn's research group has been studying the molecular genetics of nitrogen fixation and photosynthesis in cyanobacteria and purple bacteria. More recently, his work has also focused on acetyl-CoA carboxylase.

Fatty acid synthesis begins in all organisms with the reaction catalyzed by acetyl-CoA carboxylase. Haselkorn started out studying how the fatty acid pathway in cyanobacteria was inhibited by herbicides but it turned out that cyanobacteria were resistant to these compounds. He therefore turned his attention to wheat. Wheat germ was chosen, according to Haselkorn, because of its widespread use as a model system for biochemical studies. Haselkorn remarked: "Piotr Gornicki in my lab was able to purify acetyl-CoA carboxylase from wheat germ and he showed that there were two isoforms of acetyl-CoA carboxylase. We subsequently demonstrated that the plastid form is sensitive to the grass-specific herbicide aryloxyphenoxypropionate." The researchers next developed a yeast expression system to look in detail at the carboxylase gene products and their ability to confer herbicide sensitivity to yeast. The work eventually allowed the researchers to identify a single amino acid in the enzyme that determines herbicide tolerance.

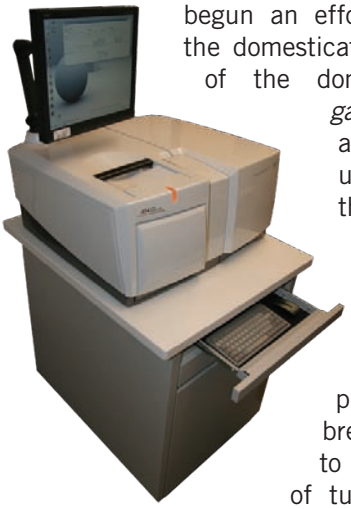
Robert Haselkorn

The yeast gene expression system was also the key to studies of the enzyme in the parasite *Toxoplasma gondii*. *T. gondii* infects cats and may lead to adverse effects on the developing fetus in pregnant women. After localizing acetyl-CoA carboxylase in *T. gondii*, Haselkorn and colleagues were able to inhibit growth of the parasite in human cells using a herbicide. Haselkorn plans to use the yeast gene expression system to screen for additional inhibitors of these parasites.

Humans have two forms of acetyl-CoA carboxylase. One form is expressed in the cytoplasm of liver and fat cells and is essential for fatty acid synthesis. The other is expressed in muscle cells and is transported to mitochondria where it is involved in the regulation of fatty acid oxidation. Haselkorn's group is cloning and expressing the human enzymes in yeast and has started work looking at how a specific compound can inhibit the muscle enzyme without affecting the liver and fat cell enzyme. Haselkorn believes this or a related inhibitor could serve as a possible drug candidate to fight obesity.

Haselkorn's talk was sponsored by the Virginia Chapter of Phi Beta Kappa, the Cooperative Leadership Institute at Virginia Tech, the Institute for Advanced Study in Virginia Tech's College of Science, and VBI.

Consortium aims to sequence turkey genome



An international consortium of researchers has begun an effort to sequence the genome of the domesticated turkey. The genetic blueprint of the domesticated turkey - *Meleagris gallopavo* - promises to transform avian experimental research and, ultimately, should help improve the quality of this commercially important source of food.

The turkey genome sequence and other genomic resources arising from the sequencing project should provide turkey breeders with the tools needed to improve commercial breeds of turkey for production traits such as meat yield and quality, health and disease resistance, fertility, and reproduction. According to the National Turkey Federation, turkey was the fourth most popular choice of meat protein for United States consumers in 2007 and an estimated 271 million turkeys will be raised in 2008.

The consortium of researchers behind this project will be instrumental in the collective annotation of the first assembly of the turkey genome as well as future versions of the sequence. The assembled and annotated genome sequence will be made freely available to the global research community and will be publicly released to GenBank, the National Institutes of Health's public repository for genetic sequences.

Otto Folkerts, associate director of technology development at the Virginia Bioinformatics Institute (VBI), remarked, "We will rapidly establish a draft sequence of the turkey genome using the Roche GS-FLX™ Titanium sequencing technology at the Core Laboratory Facility at the institute. This sequence will be of immediate interest to scientists engaged in turkey research and the starting point for our longer-term objective to sequence more than 95 percent of the turkey genome."

"Having the turkey genome sequence at hand will help uncover disease-resistance and immune-related genes that can then be targeted to improve our understanding of disease development in the context of host-pathogen interactions," said Rami Dalloul, assistant professor of animal and poultry sciences at Virginia Tech. "Such discoveries will help direct our efforts to enhance the competence of the turkey immune system and develop new, more effective disease-prevention strategies."

"The time is right to sequence the turkey genome," said Jerry Dodgson, professor of microbiology and molecular genetics at Michigan State University. "The sequence of the chicken genome is known and continues to be refined. The scientific community has established many of the experimental resources that make this project feasible. Pyrosequencing on the Roche GS-FLX platform and assembly of the sequence using the publicly available chicken sequence as a reference represents a very cost-effective approach to deliver the turkey genome sequence rapidly to the wider scientific community."

The purchase of the Roche GS-FLX™ was supported by funds from the Virginia Commonwealth Research Initiative. Funding for the pilot phase was provided by the following: the Office of the Vice President for Research, the College of Agriculture and Life Sciences, the Fralin Life Science Institute, Virginia Bioinformatics Institute -- all at Virginia Tech; and the external consortium members, the Roslin Institute, Michigan State University, University of Minnesota and Utah State University. The Consortium acknowledges Roche Applied Sciences for in-kind support.

Participant	Institution
Dave Burt	Roslin Institute, University of Edinburgh
Roger Coulombe	Utah State University
Rami Dalloul, Audrey McElroy, Ed Smith, and Eric Wong	Department of Animal and Poultry Sciences, College of Agriculture and Life Sciences, Virginia Tech
Jerry Dodgson	Michigan State University
Oswald Crasta, Clive Evans, and Otto Folkerts	Virginia Bioinformatics Institute at Virginia Tech
Rick Jensen	Department of Biological Sciences, College of Science, Virginia Tech
Kent Reed	University of Minnesota

VBI e_Connections

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Virginia Tech out to crack genetic code of turkeys

Richmond Times Dispatch — Virginia Tech, whose teams are known as the Fighting Gobblers, is leading a consortium trying to determine the genetic sequence of that Thanksgiving Day staple—the domestic turkey.

Otto Folkerts, associate director of the Virginia Bioinformatics Institute at Tech, said group members began talking turkey late last year and officially formed this spring. "What we were looking for was a big project to sink our teeth into that would show our capability," Folkerts said. "The chicken genome had been done several years ago. But the turkey is kind of the orphan of the animal genome." Also, he noted, "the Hokie Bird is our mascot, and it's no accident we decided on the turkey."

The consortium, titled the Turkey Genome Sequencing Consortium, is made up of researchers at Tech, the bioinformatics institute, the Roslin Institute in Scotland, Michigan State University, the University of Minnesota and Utah State University.

Source: Richmond Times Dispatch, November 21, 2008

Laubenbacher attends events in France, China

VBI Professor Reinhard Laubenbacher spoke at the meeting

"Discrete models of biological networks: From structure to dynamics," which was held at the Centre International de Rencontres Mathématiques (CIRM) in Marseilles, France on November 3-7, 2008. Laubenbacher's talk, "The dynamics of conjunctive Boolean networks," focused on the relationship between the properties of a dynamical system and the structure of its defining equations. Laubenbacher also attended the first joint international meeting between the American Mathematical Society and the Shanghai Mathematical Society, which was held on December 17-21 in Shanghai, China. He organized and spoke at two special sessions for the meeting – "Bioinformatics: Newly Developed Applied Mathematics and New Mathematics Arising for Biosciences" and "Combinatorics and Discrete Dynamical Systems". Following the meeting in Shanghai, Laubenbacher also delivered a lecture at Jiao Tong University.

Peccoud's work featured in IEEE magazine

The work of VBI Associate Professor Jean Peccoud and his Synthetic Biology Group was featured in the November/December 2008 edition of IEEE Intelligent Systems Magazine, the leading trade magazine for the artificial intelligence community. The article "AI and the Language of Life" highlights recent efforts by researchers to develop tools to map and create proteins along with other biological constructs in cells. The article discusses the group's efforts to help researchers find cheaper or more sophisticated ways of producing proteins by creating segments of DNA that can be analyzed or constructed similarly to the way developers work with computer code, including the development of GenoCAD, a software tool that allows the non-specialist to design and validate large-scale genetic systems for use in basic biological research or product development programs.

VBI Scientific Publications

Tyr235 of human cytosolic phosphoenolpyruvate carboxykinase influences catalysis through an anion–quadrupole interaction with phosphoenolpyruvate carboxylate

Dharmarajan L, Case CL, Dunten P, Mukhopadhyay B
FEBS J. 2008: **275**(23): 5810-5819.

Tyr235 of GTP-dependent phosphoenolpyruvate (PEP) carboxykinase is a fully invariant residue. The aromatic ring of this residue establishes an energetically favorable weak anion-quadrupole interaction with PEP carboxylate. The role of Tyr235 in catalysis was investigated via kinetic analysis of site-directed mutagenesis-derived variants. The Y235F change lowered the apparent K_m for PEP by about six-fold, raised the apparent K_m for Mn^{2+} by about 70-fold, and decreased oxaloacetate (OAA)-forming activity by about 10-fold. These effects were due to an enhanced anion-quadrupole interaction between the aromatic side chain at position 235 and PEP carboxylate. For the Y235A and Y235S changes, an elimination of the favorable edge-on interaction increased the apparent K_m for PEP by four- and six-fold, respectively, and the apparent K_m for Mn^{2+} by eight- and six-fold, respectively. The pyruvate kinase-like activity, representing the PEP dephosphorylation step of the OAA-forming reaction, was affected by the substitutions in a similar way to the complete reaction. These observations indicate that the aromatic ring of Tyr235 helps to position PEP in the active site and the hydroxyl group allows an optimal PEP-Mn^{2+} distance for efficient phosphoryl transfer and overall catalysis. The Y235A and Y235S changes drastically reduced the PEP-forming and OAA decarboxylase activities.

June Mullins

Her artistic touch will be missed by many

VBI Graphic designer June Mullins, who is retiring after serving the university as an artist and a researcher, takes some time to reflect on her winding career path that led her to VBI

"It will give me more time to work on my freelance art work," June explains. "I will be able to concentrate on my paintings and illustrations, which I've not had much time to do before."

Faculty and staff at VBI know June Mullins for her illustration and graphic design abilities. What many may not be aware of, however, is her previous scientific research experience. As she nears her retirement date from the university, Mullins has taken some time to reflect on her winding career path that eventually led her to VBI.

Although her love for art began when she was a little girl growing up in Colorado, it was a high school class that helped spark Mullins' interest in science. As an undergraduate at Colorado State University, she majored in physical science instead of art because, as she explains, "it was more marketable for job prospects, not because I liked it more than art."

Mullins has lived in Blacksburg for most of her adult life, moving to the town with her high school sweetheart and husband, Don, while he completed his Ph.D. at Virginia Tech. Apart from a few years living in Canada for her husband's postdoctoral duties, Blacksburg has been her home. She has served in several positions at the university, including as a lab technician in the Department of Dairy Science and a laboratory specialist and part-time graphic designer at the Virginia-Maryland Regional College of Veterinary Medicine. She also worked as a research associate at the Blacksburg company PPL Therapeutics, where she grew the cells which were used to create the world's first cloned pig.

Throughout her stay in Blacksburg, Mullins has consistently pursued freelance illustration projects and also completed work on her master's degree in dairy science. She used her graduate research activities as an opportunity to integrate her love of art. She created a three-dimensional drawing of the functional anatomy of the cow's cervix, which was structurally and functionally different from the model presented in scientific literature. For her thesis work, she proved that her model was more accurate by creating a three-dimensional model using serial sections, electron microscopy, and histology staining techniques. She then went on to publish an atlas of the "Illustrated Anatomy of the Bovine Male and Female Reproductive Tracts."

At VBI, Mullins has been responsible for the majority of graphic design work for the Institute, which includes creating graphics for scientific publications, designing annual reports, and creating and maintaining slide shows for VBI's common area plasma screens. She also does photography work for the Institute, helped select much of the artwork that is displayed throughout the facility, and has served on VBI's social committee.

"Of all my duties, I've enjoyed creating figures and drawings for the faculty members the most," said June. "It is more of an intellectual challenge for me and I get the opportunity to learn a lot about the projects they are working on in the process."

Mullins retires from Virginia Tech and VBI at the end of January. Although her artistic touch will be missed by many, she sees her retirement as the beginning of a new chapter of her life in Blacksburg.

"It will give me more time to work on my freelance art work," June explains. "I will be able to concentrate on my paintings and illustrations, which I've not had much time to do before."

She will also have more time to devote to her volunteer work, which includes serving as president of Blacksburg's chapter of Torch Club International, on the social justice committee and the Blacksburg United Methodist Church, and on the boards of the Montgomery County Christmas Store and 4-H.

Barry Whyte, strategic and research communications officer at VBI who oversees the Institute's public relations team, remarked: "I have had the pleasure of working with June for the past three years. June is first and foremost an outstanding artist and many at VBI will miss her creative touch. We wish her all the best for the exciting projects that she has planned for the years ahead."