



KU Technology Transfer

Promoting Innovation to Benefit Society

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KU Lawrence Campus Life Sciences: The Tradition Continues

The tradition of collaboration between life science research and industry dates back more than 40 years on the Lawrence Campus. KU has built steadily on its foundation of research, innovation and entrepreneurship in the life sciences, and keeps the Kansas economy and society in its vision of the future as it plans new research centers.

Past: Founding the Tradition, Takeru Higuchi

In 1980, Bayh-Dole Act facilitated transfer of technology arising from government-funded research by assigning ownership of the intellectual property to the institution. However, at KU the culture of moving life science research to the marketplace formed over a decade prior to the landmark legislation.

In 1967, Takeru Higuchi, widely recognized as the "Father of Physical Pharmacy" was persuaded to join the KU faculty. New facilities for his research were part of the package. Almost immediately, Alejandro Zaffaroni offered Higuchi an enticing prospect - to start a company called Alza in Palo Alto. Higuchi preferred to remain in Lawrence.

Therefore, Alza operated out of Lawrence for five years, in the building next door to McCollum laboratories that today bears Higuchi's name. Dipivefrin or Propine® (dipivaloyl epinephrine) was developed by Takeru Higuchi at Alza/INTERx, with some of the work done at KU. The product was eventually sold through Allergan in Irvine, CA. Higuchi also held the patents through Alza—with much of the work done here at KU—on the Alza osmotic drug delivery systems. After breaking from Alza in 1972, Higuchi started INTERx as a drug delivery company. Merck bought INTERx in 1981.

The KU Center for Bioanalytical Research, founded by Higuchi and colleagues in 1983, actually articulated the drive to move basic research to marketable technologies, to benefit the public, in its mission statement. In 1986, a phenytoin prodrug, fosphenytoin, developed by Distinguished Professor Valentino Stella, was licensed to pharmaceutical powerhouse, Merck. It was eventually marketed and sold by Pfizer as Cerebyx®. Dr. Stella was also a co-inventor of Viread® (tenofovir disoproxil fumarate), an anti-viral drug used in the treatment of HIV-1. In 1989, the KU Center for Drug Delivery Research was founded and began developmental research on sulfobutylether- β -cyclodextrin, a drug-solubilizing compound discovered by Professor Stella and Roger Rajewski, a native of Victoria, KS. In 1993, CyDex was incorporated to license and commercialize modified cyclodextrins.

Present: KU Technologies Benefit Today's Society

KU's portfolio of life science technologies keeps growing, resulting in new licenses and start-up companies.

CyDex's Captisol® Enables Two New Drugs by Pfizer

Pfizer recently has brought two new Captisol®-enabled drugs to the market. Vfend® (voriconazol) is an anti-fungal drug and Geodon (ziprasidone) is an anti-schizophrenia drug. The success of these new drugs is expected to increase awareness of the benefits and availability of cyclodextrin technologies. CyDex also is developing Captisol-enabled versions of several generic drugs to improve their safety and efficacy.

Guilford's AQUAVAN® Injection Completes Phase II Clinical Trials

ProQuest's acquisition of the PHOS™ prodrug chemistry platform, developed by Professors Stella, Gunda Georg and colleagues at KU's Center for Drug Delivery Research, led to the preclinical development of the PHOS™ prodrug of propofol, the world's leading injectable anesthetic. The water-soluble PHOS™ prodrug of propofol was licensed to Guilford Pharmaceuticals in March 2000 and the product is now named AQUAVAN® Injection. Guilford recently announced the completion of Phase II clinical trials in the U.S. AQUAVAN® Injection may provide several significant clinical benefits compared to the lipid-based formulation of the parent compound. These may include reduced risk of bacterial contamination and injection site pain; improved stability and ease of use; and elimination of the elevation of blood lipid levels.

Check It Out

NIH Roadmap for Medical Research:
<http://nihroadmap.nih.gov/>

KU Partners in Innovation
<http://www.research.ku.edu/techtran/partners/>

KU Start-up Companies
<http://www.research.ku.edu/techtran/startup/index.shtml>

KU Technologies Available for Licensing
<http://www.research.ku.edu/techtran/lictech/kulc.shtml>

Information for KU Inventors
<ftp://www.research.ku.edu/pub/tt/invdisc.doc>

The KU Technology Transfer newsletter is published bi-monthly through the KUTTNEWS list serve. This newsletter is distributed to interested KU faculty and staff, economic development organizations and others interested in learning about KU innovations.

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Leave the subject line blank. The message should contain one line, 'unsub'
Do not add a signature line or attachments.

Pinnacle Technologies Licenses Glutamate Sensor

Pinnacle Technologies of Lawrence, KS, has licensed KU's implantable glutamate sensor, developed by George Wilson, distinguished professor of chemistry. Pinnacle's sensors will be used to study in animals the neurotoxic role of l-glutamic acid in neurological disorders. The device is one of a suite of implantable sensors that monitor blood levels of various substances. Dr. Wilson's implantable glucose sensor is currently being studied for human use by an east coast company.

West Nile Virus Vaccine Disclosed

Vladimir Yamshchikov, professor of molecular biosciences, has developed a vaccine for West Nile virus. Potential uses include vaccination of military personnel or public groups that may be exposed to the virus and may develop viral encephalitis; vaccination of horses, which are highly susceptible to the West Nile infection and often contract fatal encephalitis; and immunization of susceptible bird species in zoological establishments.

NIH-sponsored Research Produces Possible New Compounds for Cancer Therapy

Brian Blagg, professor of medicinal chemistry, and associates have disclosed new compounds that inhibit Hsp90, a molecular chaperone. Numerous proteins required for cancerous growth are dependent on Hsp90 for their conformational maturation. *In vitro* evaluations have shown the new compounds to be potent inhibitors of Hsp90.

New technologies in the Neurosciences

■ **ACTIFIER II.** Steven M. Barlow, Ph.D., Don Finan, Ph.D., and Rick Konopacki, M.S.E.E., have developed a new biomedical instrument for studies of biomechanics, sensorimotor entrainment, and electrophysiology of the orofacial system during non-nutritive sucking in preterm babies at risk for neurologic impairments and developmental disabilities. ■ **N-Trainer.** Barlow and Finan also have developed a new biomedical instrument system that works in conjunction with the Actifier II to provide a therapeutic method for stimulating and entraining motor pattern development in the human orofacial system. ■ **OroStiff.** Barlow and Raj Vantipalli, M.S., have developed a new biomedical instrument system that samples oral tissue stiffness in patients with progressive neuromotor disease, such as Parkinson's disease.

Future: The Promise of New Research Centers

The KU Office of Technology Transfer and Intellectual Property works closely with designated research centers at the University and external economic development organizations to bridge the gap between technology discovery and commercial applications.

High Throughput Screening Laboratory (HTS) Gains Additional Facilities

Newly located at the Lawrence Life Science Research Facilities, 15th and Wakarusa Drive in Lawrence, the KU High Throughput Screening Laboratory is poised to speed identification of compounds with potential as drugs. HTS technology vastly reduces time required to identify leads for drug discovery. The KU-HTS facility, developed as part of an NIH grant, began operations at the end of 2002 with the acquisition of 100,000 drug-like small molecules and the installation of a fully automated screening system. Currently KU-HTS researchers are developing screening capabilities for diverse biochemical and cell-based assays. KU has since dedicated the entire upper level (6,500 sq. ft.) of its new Life Sciences Research Laboratories to the core HTS facilities. Dr. Qi-Zhuang Ye is director of the HTS facility. Dr. Gunda Georg, distinguished professor of medicinal chemistry, is the principal investigator of the NIH/COBRE grant.

Picking up the Pace of Developing New Drug Compounds: KU CMLD

The National Institutes of Health (NIH) has awarded a \$9.57 million grant to the University of Kansas that will help establish a Combinatorial Methodology and Library Development Center of Excellence at KU, or KU-CMLD. The award to KU is part of an NIH initiative, called Roadmap for Medical Research, aimed at speeding the progress of research discoveries from lab bench to bedside. The KU center is one of only four such NIH-funded centers in the nation.

Jeffrey Aubé, professor of medicinal chemistry, is the project leader for the effort. "Today," said Aubé, "a technique called combinatorial chemistry is quickening the pace of molecule-building. Instead of making compounds one at a time, the combinatorial chemist makes collections of molecules -- 30, 96, 1,000, even a million -- at a time. "Identifying a molecule with drug potential amid all the candidates is like finding a needle in a haystack," Aubé said. "It's common for a medicinal chemist to synthesize about 10,000 different molecules before a single drug reaches the bedside."

Structural Biology Center (SBC)

Phase I (12,000 sq. ft.) of KU's Structural Biology Center (SBC) is under construction now with a projected completion date of August 2004. Phase II construction to house proteomics and protein analysis, will encompass 17,000 total sq. ft. and will be completed in the fall. A proposal has been submitted for Phase III, which will house a Molecular Library Center within its 20,000 sq. ft. Benefits from the SBC and its new equipment will include learning what proteins do and how they do it, a better understanding of life processes, designing new drugs, attracting first-rate scientists to KU, and attracting high-tech research companies to Lawrence and the region. In the future, the SBC will incorporate the High Throughput Screening (HTS) Laboratory, core labs of the Center of Excellence in Chemical Methodologies and Library Development (CMLD), and a wide-ranging set of tools for drug discovery.

