Vascular Magnetics, the first start-up company to be spun off by The Children’s Hospital of Philadelphia, has raised $7 million to advance development of an innovative drug delivery system to treat peripheral artery disease. Vascular Magnetics recently announced that Devon Park Bioventures, of Wayne, Pa., is the sole investor in this Series A financing agreement.

Vascular Magnetics was co-founded in 2010 by Robert J. Levy, M.D., William Rashkind Endowed Chair of Pediatric Cardiology at Children’s Hospital, and Richard S. Woodward, Ph.D. Vascular Magnetics has an exclusive license to the technology invented by Levy’s cardiology research team at Children’s Hospital.

“It’s exciting to see that one of our hospital’s research discoveries has attracted investors to move it toward commercial development,” Philip R. Johnson, M.D., chief scientific officer, at Children’s Hospital, said. “This work can have multiple benefits—directly to patients receiving a new treatment, and also to children whose lives will be improved by future research supported by revenue generated by this technology.”

The drug delivery system at the heart of the company’s work is called vascular magnetic intervention. The system combines biodegradable, magnetic drug-loaded particles with a magnetic targeting catheter and a device that creates a uniform magnetic field. The system, which Levy has tested in animals, guides the particles to the walls of arteries narrowed by peripheral artery disease (PAD). At the disease site, the particles remain in place, slowly biodegrading and releasing the drug paclitaxel, which prevents re-obstruction of the artery.

Vascular magnetic intervention could fill an important unmet need in treating PAD, in which blocked arteries, primarily in the legs, exact a heavy toll in some 30 million older adults in North America and Europe. Diabetes patients and smokers are particularly affected by this painful, debilitating condition, which is responsible for the majority of amputations performed in this country. Drug-eluting stents, currently used in heart disease, are less effective in PAD. Magnetic intervention could deliver more effective doses of drugs than the standard drug-eluting stents, and could be used to re-administer drugs as needed, Dr. Levy said.

As a new platform technology, vascular magnetic intervention could also be adapted to delivering other agents, such as therapeutic genes or cells, and has potential utility in treating heart conditions in children, Dr. Levy added. In the near future, Vascular Magnetics will complete preclinical development of its technology, and plans to conduct its first clinical trial in 2014, in adult patients.
Approval of Skin Cancer Drug Leads to Medulloblastoma Treatment Hopes

For more than 15 years, Tom Curran, Ph.D., FRS, deputy scientific director at CHOP Research, has worked toward a cure for medulloblastoma, the most common form of malignant brain tumor in children. While medulloblastoma can currently be treated through surgery, chemotherapy, and radiation, patients often suffer debilitating side effects. And those patients who are not successfully treated, or whose tumors return, face an extremely low cure rate.

However, the FDA’s recent approval of a drug to treat a form of skin cancer in adults could have wide-ranging implications in the fight against medulloblastoma and other pediatric cancers. Erivedge (vismodegib), developed by Genentech and Curis Inc., was recently approved to treat metastatic basal cell carcinoma (BCC), a form of skin cancer, in adults.

Erivedge, much like the compounds Dr. Curran and his team have been investigating, works by inhibiting the hedgehog (HH) pathway, which plays a critical role during the development of the cerebellum. Because Erivedge is the first HH drug to receive an FDA nod, its approval could lead to approvals for other compounds that share a similar mechanism of action.

Dr. Curran’s Pathway

Dr. Curran began working on medulloblastoma treatments after meeting a number of younger patients with the disease in 1995. One patient’s story, a 16-year-old boy who had undergone radiation and surgery to treat his tumor, particularly affected Dr. Curran.

The treatments had “severely impaired” the patient’s quality of life, Dr. Curran said. Because of damage to his cerebellum the boy had difficulty walking normally, and the radiation he had received was affecting his ability to learn. The boy, who had a great sense of humor, “was seeing the rest of his class progress while he was falling behind,” Dr. Curran said.

Dr. Curran, who has a background in brain development and cancer research, decided then that he wanted to develop a drug that could help patients without the many negative side effects.

One molecular target Dr. Curran has focused on is the sonic hedgehog (SHH) signaling pathway, which is crucial for normal development of the cerebellum and has been shown to play an important role in medulloblastoma and other cancers. Dr. Curran identified the SHH pathway as an ideal target for medulloblastoma therapies following the finding that patients with Gorlin syndrome, a disorder caused by a mutation in a gene associated with the SHH pathway, are predisposed to these brain tumors. Gorlin syndrome is also associated with a “very high instance” of BCC, according to Dr. Curran.

The mutation affects the PTCH1 transmembrane protein that acts as a receptor for SHH, and in the absence of SHH maintains inactivity of the SHH pathway by repressing Smoothened (Smo), another transmembrane protein. The PTCH1 mutation results in an inappropriately active SHH pathway, leading to increased expression of genes that influence neuronal progenitor cell proliferation.

Dr. Curran’s team engineered an animal model of medulloblastoma that precisely mimics the characteristics of disease through the PTCH1 mutation to investigate whether suppressing the overactive SHH signaling could cause tumor regression. They evaluated the effect of HhAnTag, a SHH pathway inhibitor developed to block the SHH pathway by binding to Smo.

Isolated by Lee Rubin, Ph.D., director of Translational Medicine at the Harvard University Stem Cell Institute, while he was working at Curis Inc., HhAnTag acts in a similar way to the naturally occurring SHH pathway inhibitor cyclopamine but is more effective and far less toxic. The study team found that treatment with HhAnTag drastically decreased tumor proliferation and increased tumor apoptosis in the models of medulloblastoma, and long-term treatment eliminated all tumors. In later studies, the team found that this agent was also active against medulloblastomas in which the SHH pathway was active even though they lacked known mutations in the pathway.

Erivedge Approval Raises Hopes

The recent FDA approval of Erivedge, which Genentech developed under an agreement with Curis, to treat BCC in adults is an important first step for hedgehog pathway signaling inhibitors, and could eventually lead to other approvals.

“Our understanding of molecular pathways involved in cancer, such as the Hedgehog pathway, has enabled the development of targeted drugs for specific diseases,” Richard Pazdur, M.D., director of the Office of Hematology and Oncology Products in the FDA’s Center for Drug Evaluation and Research said.

“This approach is becoming more common and will potentially allow cancer drugs to be developed more quickly. This is important for patients who will have access to more effective therapies with potentially fewer side effects,” Pazdur added.

The recent approval of Erivedge “justifies everything we do,” Dr. Curran noted, adding that it was a rare privilege “to have an idea or concept that can lead to an approved drug.”
Gene Chip Pinpoints New Target to Prevent Heart Disease

A large international study indicates that anti-inflammatory drugs may become a new tool for preventing and treating coronary heart disease, the leading global cause of death. In investigating a specific gene variant linked to inflammation and heart disease, the researchers used the Cardiogchip, a gene analysis tool designed by Brendan J. Keating, Ph.D., a researcher in the Center for Applied Genomics at Children's Hospital, and co-author of the study.

Scientists already knew that inflammation is associated with atherosclerosis, the buildup of fatty deposits on artery walls that causes coronary heart disease (CHD), but until now no one had identified an inflammatory agent causing the disease. Likewise, it was unknown whether a drug targeted at reducing inflammation might treat CHD.

The current study focused on the interleukin-6 receptor (IL6R), a signaling protein found in the blood that increases inflammatory responses. “This study provides robust evidence that IL6R is implicated in coronary heart disease,” said Dr. Keating. “Furthermore, our analysis showed that an existing anti-inflammatory drug, acting on this receptor, may offer a new potential approach for preventing CHD.”

The study, which recently appeared in The Lancet, was performed by the IL6R Mendelian Randomisation Analysis Consortium, an international research team led by Dr. Juan Pablo Casas, Professor Arnon D. Hingorani, and Dr. Daniel I. Swerdlow, all of University College London in the U.K. The study was a meta-analysis of data from 40 existing studies that included nearly 133,500 participants from the U.S. and Europe. Mendelian randomization is a research method that uses knowledge of genes and biological mechanisms to predict likely effects of a new drug before conducting a clinical trial.

A companion study in the same issue of The Lancet, by the IL6R Genetics Consortium and Emerging Risk Factors Collaboration, found that a genetic variant in the IL6R gene, which carries the code for the IL6R protein, dials down inflammation and thus lowers the risk of heart disease.

The study in which Keating participated focused on SNPs (single nucleotide polymorphisms) single-base changes in the IL6R gene that codes for the IL6R protein.

Among the research team’s tools was a DNA array, the IBC Human CVD BeadChip, also called the Cardiogchip, created by Keating in 2006 and since used in many large gene studies. That chip contains DNA markers for 2000 gene variants implicated in cardiovascular disease.

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New Research Administration Fellow Selected

The Office of Postdoctoral Affairs recently announced the selection of the research administration fellow for the first half of 2012. Rudy Fuentes, Ph. D., a postdoctoral fellow in the laboratory of Mortimer Poncz, M.D., began the administration fellowship in early February.

The Research Administration Fellowship is a part-time, unpaid, six-month program that fellows complete concurrently with their research duties. The overall goal of the fellowship is to provide the fellow with a broad overview of CHOP Research Administration through rotations with administrative directors in the fellows’ areas of interest.

Rudy began his time at CHOP in 2005, as a research assistant in Dr. Poncz’s laboratory in the Division of Hematology, studying the production of functional platelets after infusing mature megakaryocytes in a murine model. An article published on this work in the Journal of Clinical Investigation, and a presentation given at the 2009 American Society of Hematology meeting, brought Rudy a number of accolades. Now in his second year of postdoctoral training in Dr. Poncz’s laboratory, Rudy is working to complete a manuscript in collaboration with investigators from the University of Pennsylvania Center for Targeted Therapeutics & Translational Nanomedicine.

Originally from El Salvador, Rudy is the first member of his family to receive an advanced degree. After earning his bachelor’s from SUNY at Old Westbury, Rudy entered the pharmacology program in Biomedical Graduate Studies at the University of Pennsylvania, receiving his doctorate in 2010.

Rudy is currently working with the Office of Responsible Research Training on the development of a pilot training proposal, the Pediatric Translational Research Course (PTRC). Designed to provide scientists with the essential skills and knowledge to perform pediatric translational research, the PTRC is aligned with the Hospital’s commitment to foster the training of innovative pediatric researchers. During his time as the Research Administration fellow Rudy plans to provide support for the PTRC pilot, which is tentatively scheduled to launch in 2014.

For more information about the Research Administration Fellowship, visit https://intranet.research.chop.edu/display/deptpda/Research+Administration+Fellows or contact David Taylor at taylord@email.chop.edu.
Flaura K. Winston, M.D., Ph.D., director of the Center for Injury Prevention and Research (CIRP) at The Children’s Hospital of Philadelphia, recently told a House committee that, despite advances in preventing and treating traumatic brain injury, “we’re just beginning to understand the biomechanics of brains.”

Traumatic brain injury (TBI) is the leading cause of injury-related death in children, causing more than 6,000 deaths and hospitalizing 60,000 children and adolescents every year. “Each day more than 125 children die or are hospitalized with a TBI caused by largely preventable events – such as car crashes and sports- with high costs to families and to society,” according to Dr. Winston.

In addition to being the founder of CIRP, Dr. Winston’s pioneering research has focused on preventing child occupant and teen driver deaths and injuries in motor vehicle crashes. On March 19 along with several other TBI experts, Dr. Winston testified before the House Energy and Commerce Committee’s Subcommittee on Health. The hearing was held to give committee members a chance to assess the state of TBI prevention, treatment, recovery, related research and federal efforts to address TBI.

Saying that the “brain is the organ that is least able to heal,” Dr. Winston stressed the need for continued research to prevent and treat pediatric brain injuries. “New and improved child-focused strategies will only emerge from investments in basic and translational biomechanical, behavioral, and medical research to inform new safety products and their testing,” Dr. Winston said.

However, she added, while many pediatric brain injuries are preventable, the science behind treating those injuries that do occur is limited, because most research has focused on adults. “Children are not small adults,” Dr. Winston explained.

Indeed, recent developments have led researchers to question the traditional belief that children are more resilient than adults. For example, researchers have seen a connection between an increase in disabilities and mild TBI in teenagers, Dr. Winston said.

Noting that federal funding has been “crucial” to brain injury research, Dr. Winston called on the National Institutes of Health (NIH) and other agencies to continue to invest in TBI research. “We need to build up our scientific foundation,” Dr. Winston said.

The costs of TBI were also raised during the hearing. On average, the yearly cost of children dying from TBI is $29 billion and $53 billion for those who are hospitalized,” Dr. Winston testified, adding that the average medical cost for children hospitalized with TBI is $40,000.

“That’s a lot of helmets,” Dr. Winston said.

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CHOP Researcher Highlights Brain Injury Research, Prevention in House Testimony

The CHOP Research Institute announces the 2012 solicitation for its internal award competition, the Foerderer Fund for Excellence. Awards will commence July 1, 2012. Clinical, translational and basic research projects are eligible.

Foerderer Awards are designed to allow on-going research to move into new and productive areas, or allow investigators to apply new research techniques toward novel investigations. Projects should have the potential to develop preliminary data to support extramural applications. Proposals involving collaborative research between different groups at The Children’s Hospital of Philadelphia are encouraged. Applicants may request up to $50,000.

Eligibility: Individuals based at Children’s Hospital with faculty appointments at the University of Pennsylvania are eligible to apply.

Clinical and postdoctoral fellows are also eligible to apply. If the potential applicant does not hold a faculty appointment, a letter of endorsement from the relevant Chief or Chair is required to be submitted with the application.

Deadline: April 12, 2012, 4:00 p.m. No extensions will be granted.

Submission: Electronic submission through eSPA will be required. Visit https://intranet.research.chop.edu/display/deptspbm/FoerdererGrants-2012 for complete details.

Questions may be directed to Michael Campbell at campbellm@chop.edu or 215-590-0664.
Behind the Scenes: Research Finance

In your day-to-day work supporting or conducting research at CHOP, you may not see the multiple teams behind the scenes working to ensure research runs more smoothly and efficiently. What are these groups? What do they do? The “Behind the Scenes” series is designed to enhance the research community’s understanding of the administrative support provided to investigators. Take a moment to learn about CHOP Research’s administrative resources and consider how they might benefit your research endeavors.

In this issue, Research Finance director Steve Wiley gives a look behind the scenes at what her group does to support CHOP Research.

What is the overall goal of your department?
Research Finance provides support and services regarding the financial aspects of grants and contracts.

What do you manage for the research community?
We manage the flow of grant dollars into the Research Institute that funds our Principal Investigators’ research. We manage all financial reporting as required by the sponsors who fund the research, as well as the financial systems that account for our funding. In addition, we manage all financial audits of research funds that are conducted externally and internally.

How to you ease or improve things for investigators?
Our department manages the flow of sponsor funds into the institution, allowing our investigators to focus on their research. We are responsible for managing financial compliance to ensure that research can continue without interruption.

How is the department structured?
We have three groups within Research Finance. Bethann Kurek leads the day-to-day operations group. This includes closing out grants, submitting final financial reports to our sponsors, ensuring that sponsor funds are received by the Research Institute, invoicing sponsors, and processing invoices and check requests for payment for the Research Institute. This group is also responsible for the direct interaction with internal and external auditors.

Luz Arrison leads the Financial Cost Analysis group, which prepares the Research Institute’s monthly financial statements, reviews and analyzes the budget, prepares the Research Institute’s fiscal year budget, manages time and effort reporting, and manages Endowed Chairs as well as Institutional Development Funds.

Alin Anton leads our financial application systems team, which is responsible for managing Lawson and Business Objects as it relates to the Research Institute. In addition, the Lawson infrastructure is managed here where grant activity numbers are set up and maintained including all of the security that allows investigators to access grant reports through Business Objects.

How many people work in the department?
There are 23 people in Research Finance.

What types of projects does your group typically work on?
Research Finance works on a broad array of projects that is not only research-specific but spans the organization with a focus on financial applications and control.

What does someone in your group tackle on a typical day?
A normal day would include closing out a grant, invoicing a sponsor; establish a Lawson activity number for a new grant, and preparing financial analysis for senior leadership.

Is there a special project the department is working on this year?
This fiscal year, we are required to submit our Indirect Cost Proposal to the Department of Health and Human Services. This will set our indirect cost rate for the next several years. This is necessary for the financial support of the Research Institute’s infrastructure. We are also involved in making more efficient the financial close-out of our grant funding. Additionally, we are working with the institution as a whole on an Electronic Content Management project that will transform Accounts Payable into a paperless function. Research Finance is also part of the eResearch Business Objects reporting universe design that will enhance and marry our pre- and post-award reporting.

What recent accomplishment is your group most proud of?
One of our proud accomplishments was implementing Lawson Grant Management System, which is integrated with Lawson Payroll as well as Lawson Human Resources systems and is uniquely designed for healthcare organizations. Grants Management allows us to allocate Research payroll information across single and multi-funded grant activities according to our business design while automating our grant management processes. In addition, time and effort reporting to federal government is generated from Lawson Grants Management reducing the labor-intensive manual spreadsheet analysis needed for sponsor reporting.

What do you want the research community to know about your work?
Research Finance is here to help and support our investigators. We are here to ensure financial compliance and safeguard the research assets.

What is a common misperception about your department?
One misuse is that Research Finance establishes the rules and regulations regarding grant spending. We are here to ensure compliance with the guidelines of our sponsors and ensure appropriate stewardship of the funding.

What is unique about what your department offers compared to similar departments at other institutions?
One thing that sets us apart is that Research Finance is responsible for financial planning and analysis for the Research Institute. Additionally, we manage the institutional funds that support research such as Endowed Fund and Institutional Development funds. In many other Institutions, Research Finance only focuses on grants.

How is your work influenced by the work of departments focused on supporting clinical care?
One influence is the cost of patient care services. This impacts patient care rates that we negotiate with government. This ultimately impact grants where there are patient care expenses charged for services provided by the clinical care areas.

Is there anything your department does that might surprise people?
Research Finance has a small group that focus on financial information systems. This group is not only responsible for managing Research financial data within Lawson Financials and Business Objects Reporting but also troubleshoot technical systems issues, user security, system enhancements, testing and validating system upgrades.

What is the most satisfying part of your job?
The most satisfying part to me is that we are here to support the Research community. All sponsored project funding comes through Research Finance. When you see what our investigators are doing, it really makes you feel good to be a part of this community.
Research Buyers Have Moved to Wanamaker Building

The Hospital’s Supply Chain has now centralized its procurement operations and on March 12 all buyers – for both the Hospital and Research Institute – will be located in the Wanamaker Building.

The move of the Research Institute’s buyers will not impact procurement services or the level of customer service provided by the Supply Chain. The contact information for buyers and their assignments for research will also remain the same:

Arun Nair - 267-426-0215
• ARC Floors: 8, 9, 10, 11
• CTRB Floors: 3, 4, 9, 11
• Main Building

Thankappan Nair - 215-590-4814
• ARC Floors: 1, 3, 7, 12, 13
• CTRB Floors: 2, 5
• 3535 Floors 12-15 and 3550 Market St.

Brenda Saunders-Tilley - 215-590-3990
• ARC Floors: 2, 4, 5
• CTRB Floors: 6 & Animal Facilities
• Wood Building and 3535 Market St. Floors 8-11

The centralization of services will also allow for access to nine senior buyers as well as customer service professionals who can quickly resolve any issues concerning orders.

Procurement operations will be located on the 8th floor (Office 8045) of Wanamaker. If you have any questions about the operations, please contact Regina Council, Procurement Operation Manager, at councilr@email.chop.edu or at 267-426-0119.

Faculty Mentoring Workshops - Coming This Spring!

Registration is now open for the “Developing Effective Research Mentoring Strategies” workshop series co-hosted by CHOP and UPenn. Faculty at all levels with an interest in optimizing their skills as scientific mentors should attend.

Two workshops are being offered:

• Mentoring Research Trainees in bench Science/Laboratory Setting
  Monday, May 7, 2012
  3 to 5 p.m.
  Colket Translational Research Building, Room 1200A/B (1st Floor)

• Mentoring Research Trainees in a Clinical Research Environment
  Tuesday, May 8, 2012
  8 to 10:30 a.m.
  Colket Translational Research Building, Room 1200A/B (1st Floor)

The workshops will be facilitated by Christine Pfund, Ph.D., a faculty member of the Wisconsin Program for Scientific Teaching and author of Entering Mentoring: A Seminar to Train a New Generation of Scientists (http://www.hhmi.org/resources/labmanagement/downloads/entering_mentoring.pdf).

Space is limited. Register now for one of the two workshops at http://www.research.chop.edu/dems. A program description and session objectives can also be found on the registration website. Questions about this event may be directed to williamsw@email.chop.edu.

Congratulations to our 2012 CHOP Research Poster Day Award Winners

The Research Institute celebrated its 22nd Annual CHOP Research Poster Day on February 22, 2012, with over 115 cutting-edge research posters on display in the Colket Translational Research Building (CTRB). This event recognizes the outstanding research conducted at CHOP each year, and honors our exceptional trainee participants.

This year, 40 individuals were selected by our faculty judges to receive awards for their outstanding Poster Day presentations in the patient-oriented research and laboratory-based tracks. Winners can be viewed at the following site https://intranet.research.chop.edu/display/deptrrt/Poster+Day+2012.

For more information about CHOP Research Poster Day and to review abstracts submitted for the event, please visit http://www.research.chop.edu/posterday. Additional information and photos from the event will be placed on this site within the next week.