Translational tidbits

By Kai-Jye Lou, Senior Writer, and Lauren Martz, Staff Writer

Astellas bites into autophagy

Astellas Pharma Inc. and **Cancer Research UK** announced a two-year research collaboration last week that will initially focus on identifying new drug targets that could block autophagy to treat pancreatic cancer. The collaboration builds upon recent work from U.K. scientists showing that the process plays a key role in the development of some pancreatic tumors.¹

Autophagy is a process whereby cells maintain homeostasis by directing components of the cytoplasm to the lysosome to undergo degradation, freeing metabolites for use in other cellular processes. In the nutrient-deficient environment of tumors, autophagy can serve as an alternative energy source that helps cells survive and grow.

Astellas spokesperson Akiko Tanabe noted that recent studies have shown that autophagy activity is higher in pancreatic cancer than other cancers and that certain pancreatic cancers depend on autophagy to grow.

"We think blocking the autophagy pathway may help stop some pancreatic cancers," she added.

Last December, a Cancer Research UK (CRUK) research team led by Kevin Ryan of the **The Beatson Institute for Cancer Research** published mouse data in *Nature* showing that disruption of autophagy by knocking out *ATG5 autophagy related 5 homolog (Atg5)* or *Atg7* blocks the progression of premalignant pancreatic intraepithelial neoplasias into pancreatic ductal adenocarcinomas.¹ Ryan is a senior group leader at the institute and is participating in this new research partnership.

Researchers at multiple institutes already are evaluating the autophagy inhibitor hydroxychloroquine in investigator-led Phase I and Phase II trials to treat patients with pancreatic or other forms of cancer. Hydroxychloroquine inhibits autophagy by blocking autophagosome fusion and degradation.

CRUK researchers will screen for potential new targets and assess their druggability. Astellas will aid CRUK's efforts to identify potential targets and has an exclusive worldwide license to the targets identified under the collaboration that it can choose to advance. The pharma will be responsible for drug discovery and development on selected targets. CRUK's technology commercialization arm, **Cancer Research Technology Ltd.**, will be eligible for undisclosed milestones and royalties.

"The collaboration is building upon a mutual interest," said CRUK and Cancer Research Technology spokesperson Emma Rigby. "Both Astellas and the Cancer Research UK researchers have had a strong interest in autophagy."

The partners are not disclosing specific targets.

NIH SPARCs bioelectronics research

The **NIH** has announced three new Common Fund programs, including a \$248 million initiative to build proof of concept for bioelectronic peripheral neuromodulation therapies that can regulate visceral organ functions. The program provides a major boost to research funding in an area that is attracting increased interest from industry.

Bioelectronics is an emerging therapeutic area in which nanoscale, implantable electrical circuits are used to modulate peripheral nerve networks that control visceral organs.

For example, an application for peripheral bioelectronics could be an implant that detects and blocks pulmonary nerve signals that contribute to airway hyperresponsiveness.

The Stimulating Peripheral Activity to Relieve Conditions (SPARC) program will support investigators working toward four primary research objectives: developing neural circuit maps for five organ systems, creating new electrode designs, outlining surgical procedures and creating stimulation protocols. The ultimate goal of the project is to develop new neuromodulatory therapies.

"The first phase of our program is to engage the very broad research community to determine which organs to study. We want to select the organ systems in which it is most feasible to make progress based on responses from investigators," said James Anderson, director for program coordination, planning and strategic initiatives at the NIH. Another objective of the program, he said, is to coordinate storage and dissemination of the data that are collected to make them widely accessible.

Pending available funding, the NIH plans to allocate \$248 million to the SPARC program. The seven-year program will begin awarding grants in FY15, which begins this October.

At least one pharma company, **GlaxoSmithKline plc**, has also recently committed to the bioelectronics space. GSK's programs include a bioelectronics exploratory research program that is backing more than 30 academic projects, a \$50 million bioelectronics-focused venture fund and an innovation challenge to develop a rodent research platform involving a \$1 million prize.^{2,3}

Kris Famm, VP of bioelectronics R&D at GSK, told *SciBX*, "Both GSK's and NIH's programs are dependent on further advances in research tools, an area in which GSK will seek to coordinate with NIH and other funding bodies over the next few months to ensure complementary schemes, accelerated development and effective access for the global research community."

Anderson added, "The SPARC program was designed with knowledge of GSK's programs, and we have had discussions with device companies and academics in the area so that we have a good sense of what everyone is doing in the space."

Famm said that the purpose of GSK's own programs is to lay the foundation for a new treatment modality for the pharma. The aim is to identify diseases that can be treated by precision modulation of signals in peripheral visceral nerves and research the technology that will enable modulation using miniature, implantable devices.

The NIH has not disclosed the amount of funding available to the two other Common Fund programs—the 4D Nucleome and the Glycoscience programs—that will also begin next fiscal year. The 4D Nucleome program

Table 1. Selected public-private partnerships for July 2014. In July, **Intellimedix Inc.** and **Pfizer Inc.** (NYSE:PFE) partnered with the **Epilepsy Foundation** to develop drug discovery platforms for genetic forms of epilepsy, including Dravet syndrome. Separately, **AstraZeneca plc** (LSE:AZN; NYSE:AZN) partnered with the **Max Planck Institute of Molecular Physiology** to establish a cardiovascular and metabolic disease (CVMD) satellite unit to study new chemical modalities, including stabilized peptides, macrocycles and conjugation chemistry.

Source: *BioCentury Archives*

Companies	Institutions	Business area	Disclosed value	Purpose
AstraZeneca	Max Planck Institute of Molecular Physiology	Cardiovascular disease; chemistry; endocrine/metabolic disease	Undisclosed	Partnership to establish a CVMD satellite unit to study new chemistry modalities
AstraZeneca; GlaxoSmithKline plc (LSE:GSK; NYSE:GSK); Johnson & Johnson (NYSE:JNJ); Pfizer ; Takeda Pharmaceutical Co. Ltd. (Tokyo:4502); UCB Group (Euronext:UCB)	Medical Research Council	Pharmaceuticals	Undisclosed	Partnership to identify new uses for deprioritized compounds from pharma
Bayer AG (Xetra:BAYN)	University of Oxford	Genitourinary disease	Undisclosed	Partnership to discover and develop therapies to treat endometriosis and uterine fibroids
Evotec AG (Xetra:EVT)	Fraunhofer Society	Neurology; cancer	Undisclosed	Partnership to carry out drug discovery programs in CNS indications and oncology
HD Biosciences Co. Ltd.	Marshall University	Cancer	Unavailable	Partnership to develop drugs to treat cancer
ImmunID S.A.S.	Agency for Science, Technology and Research (A*STAR)	Autoimmune disease	Undisclosed	Partnership to use ImmunID's ImmunTraCkeR and ImmunIG tests to evaluate T and B cell immune repertoire diversity in the blood of patients
Ono Pharmaceutical Co. Ltd. (Tokyo:4528)	The University of Tokyo	Pharmaceuticals	Undisclosed	Partnership giving the university access to the pharma's compound library
Pfizer ; Intellimedix	Epilepsy Foundation	Neurology	Undisclosed	Partnership to develop drug discovery platforms for genetic forms of epilepsy

is developing technologies to determine the temporal and spatial DNA arrangement in cells and how that arrangement affects cell functions. The Glycoscience program is developing methods and resources to study the impact of sugar modifications on protein function.

Public-private partnership roundup

July was a quiet month for public-private partnerships, with the bulk of the activity happening outside the U.S. (See Table 1, “Selected public-private partnerships for July 2014.”)

AstraZeneca plc and the **Max Planck Institute of Molecular Physiology** partnered to establish a satellite for the pharma's Cardiovascular and Metabolic Diseases Innovative Medicines Unit. The unit will study new chemistry modalities and be located at the institute. Focus areas will include stabilized peptides, macrocycles and conjugation chemistry. AstraZeneca will be responsible for staffing, and the institute will manage and provide the facilities. Members from both parties will be part of a committee that will select, manage and oversee research projects.

AstraZeneca said that the partnership will help identify targets for cardiac regeneration, islet health and diabetic nephropathy. Financial details were not disclosed.

One of AstraZeneca's most significant public-private partnerships last year was a deal with the **Karolinska Institute** to create a similar satellite unit focused on the same therapeutic areas. The pharma is providing up to \$20 million to that center per year.

In the U.S., **Intellimedix Inc.**, **Pfizer Inc.** and the **Epilepsy Foundation** announced a three-way partnership to develop a drug discovery platform for genetic forms of epilepsy such as Dravet syndrome, a rare form of pediatric-onset epilepsy.

Intellimedix will perform gene sequencing and systems biology analysis, personalized zebrafish line development and zebrafish drug screening. Pfizer will provide its induced pluripotent stem (iPS) cell harvesting and screening capabilities through its Neusentis research unit. The foundation is providing scientific expertise and bringing in patient perspectives.

Intellimedix president and CEO Daniel Fischer said that the company has already identified several FDA-approved drugs that appear to decrease seizure activity in models of Dravet syndrome. “Two of these drugs are currently being considered for clinical trials,” he added.

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- Osherovich, L. *SciBX* **6**(14); doi:10.1038/scibx.2013.327
- Flanagan, M. *BioCentury* **21**(32), A15; Aug. 19, 2014

COMPANIES AND INSTITUTIONS MENTIONED

Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan

AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.

The Beatson Institute for Cancer Research, Glasgow, U.K.

Cancer Research UK, London, U.K.

Cancer Research Technology Ltd., London, U.K.

Epilepsy Foundation, Landover, Md.

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.

Intellimedix Inc., Atlanta, Ga.

Karolinska Institute, Stockholm, Sweden

Max Planck Institute of Molecular Physiology,

Dortmund, Germany

National Institutes of Health, Bethesda, Md.

Pfizer Inc. (NYSE:PFE), New York, N.Y.