

Translational tidbits

By Lev Osherovich, Senior Writer

Amgen's IBD gene hunt

Amgen Inc. is teaming up with researchers at **Massachusetts General Hospital** and the **Broad Institute of MIT and Harvard** to find new targets in inflammatory bowel disease. The partners hope an unbiased search for genetic variants that lower risk of the autoimmune disorder will uncover therapeutic entry points.

Amgen will work with teams led by Ramnik Xavier, chief of gastroenterology and director of the Center for the Study of Inflammatory Bowel Disease at MGH, and Mark Daly, an associate professor of medicine at MGH. Xavier and Daly are both senior associate members of the Broad Institute.

Inflammatory bowel disease (IBD) encompasses Crohn's disease and ulcerative colitis (UC). Genetic and tissue studies have implicated a diverse range of immunological, metabolic and gut microbial pathways in IBD.

Prior genomewide association studies by Xavier and others have identified genetic variants that strongly influence IBD risk.¹ However, not everyone carrying these risk genes becomes ill. Thus, Xavier suspects that additional, unknown genetic factors can counteract disease-associated genes and protect against IBD.

"The aim of the collaboration is to find these protective variants," said Xavier. "We will look at individuals who have not yet developed disease despite having genetic variants associated with high risk."

The team will use computational methods developed by Daly's team to re-analyze existing genomewide association data to tease out putative protective genes.

Xavier said that the work plan first involves identifying the protective genes, then categorizing them into functional categories and testing their effect in tissue culture models of IBD.

The collaborators will use materials from the Prospective Registry in IBD Study at MGH (PRISM), which stores pre- and post-treatment biopsy and fecal samples from several hundred patients with IBD.

Sasha Kamb, SVP of discovery research at Amgen, said that the project is a fishing expedition to survey the landscape of IBD genetics for potential targets. He said that the ideal target would be a druggable protein encoded by an IBD risk-reducing variant that has lower function than the wild-type protein.

"We are interested in protection against disease caused by reduced function of a gene," said Kamb. "The big win would be a relatively illuminated path to a therapeutic that starts from a protective drug target."

Kamb said that one of the biggest challenges to understanding the causes of IBD is variation in the interplay between immune activity and intestinal microbiota.

"IBD is immensely complicated, involving interactions between the immune system and the gut," said Kamb. "Host-commensal organism interactions potentially create a lot of heterogeneity between patients."

Indeed, Kamb and Xavier suspect that no two patients are likely to have exactly the same genetic and microbial risk factors and that the etiologies of IBD may prove to be highly individual.

"What is emerging is that there are many types of Crohn's disease and ulcerative colitis," said Xavier.

Financial details of the partnership are undisclosed. Amgen will gain undisclosed rights to IP arising from the collaboration.

Amgen's AMG 181, a mAb that prevents integrin $\alpha_4\beta_7$ from binding to mucosal vascular addressin cell adhesion molecule 1 (MAdCAM-1), is in Phase II testing for Crohn's disease.

In 2012, Amgen acquired deCode genetics ehf, an Icelandic genetics company. Although deCode's researchers have previously reported genetic studies of IBD, Kamb said that the Broad collaboration will operate independently of deCode.

Lakeside drug shop

Two European drug discovery centers and an Italian CRO have partnered to launch a drug screening center at a shuttered pharma facility in Constance, Germany.

The new center—**Hit Discovery Constance GmbH (HDC)**—is a joint venture between the Dortmund-based **Lead Discovery Center GmbH (LDC)**, the **Centre for Drug Design and Discovery (CD3)** in Leuven and Milan's **Axxam S.p.A.** HDC is based at a screening facility previously operated by Nycomed, which was acquired by **Takeda Pharmaceutical Co. Ltd.**

LDC is a discovery service provider spun out of **Max Planck Innovation GmbH**, the technology transfer arm of Germany's **Max Planck Society**. CD3 was set up by Belgium's **Catholic University Leuven** and the **European Investment Fund** to perform drug discovery for academic laboratories and small, regional biotechs.

"LDC had the means to run a small screening center, but we often had to rely on CROs to do assay adaptation and high throughput screening for assays with sophisticated read-out formats," said Thomas Hegendörfer, head of business development at LDC.

Hegendörfer said that LDC had previously collaborated on drug screen projects at the former Nycomed facility and wished to continue using it.

"When it became clear that Takeda was going to close it down and lay off the people, we were thinking about how to continue with access," said Hegendörfer. "We negotiated with Takeda about acquiring the entire lab" on undisclosed terms.

Having HDC operational "opens up additional possibilities to do more sophisticated screens such as with radiometric formats and high content screening under biological safety regulations," said Stefaan Allemeersch, director of business development for CD3 and managing director at HDC.

Hegendörfer said that Axxam came on board to expand the range of screening technologies for its commercial screening business.

"We had previously used Axxam as a screening partner for ion

Table 1. Selected public-private partnerships for December 2013. Public-private partnership activity ebbed as the year drew to a close. The number of notable deals in December came in at 17, dipping below 20 for the first time since July.

Source: BioCentury Archives

Companies	Institutions	Business area	Disclosed value	Purpose
Celgene Corp. (NASDAQ:CELG); Eli Lilly and Co. (NYSE:LLY); General Electric Co. (NYSE:GE)	New York City Economic Development Corp.	Other	At least \$100 million	City of New York Early-Stage Life Sciences Funding Initiative to invest at least \$100 million in early stage life science companies in the city
Not applicable	Agency for Innovation by Science and Technology; Austrian Science Fund; Danish Agency for Science, Technology and Innovation; The French National Research Agency; The Foundation for Science and Technology; Hungarian Academy of Sciences; Hungarian Scientific Research Fund; Ministry of Economy and Competitiveness; National Authority for Scientific Research; The National Centre for Research and Development; National Science Centre; Project Management Julich; Office of the Chief Scientist; Institute of Health Carlos III; European Commission	Infectious disease	€9.2 million (\$12.7 million)	Infect-ERA consortium to coordinate research projects on infectious diseases
Cardio3 BioSciences S.A. (Euronext:CARD); AdjuCor GmbH; Boston Scientific Corp. (NYSE:BSX); Contipro Biotech s.r.o.; Explora Biotech s.r.l.; Innova S.p.A.	Eberhard Karls University of Tuebingen; Fraunhofer Institute for Interfacial Engineering and Biotechnology; Royal College of Surgeons in Ireland; Trinity College Dublin; European Commission	Cardiovascular disease	€8.7 million (\$11.8 million)	Advanced Materials for Cardiac Regeneration (AMCARE) consortium to develop a bioresorbable polymeric valve tube to treat congenital heart defects
AstraZeneca plc (LSE:AZN; NYSE:AZN)	The Johns Hopkins University	Pharmaceuticals	\$6.5 million	Collaboration to focus on research projects in MedImmune LLC unit's therapeutic areas of interest
Eisai Co. Ltd. (Tokyo:4523); Eli Lilly	Alzheimer's Research UK; MRC Technology	Neurology	£3 million (\$4.9 million)	Dementia consortium to develop drug targets from academic sources
Sareum Holdings plc (LSE:SAR)	Hebei Medical University Biomedical Engineering Center	Cancer	Undisclosed	Co-development agreement for Sareum's inhibitor of aurora kinases and FMS-like tyrosine kinase 3 (FLT3; CD135)
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK)	Gustave Roussy Institute; Memorial Sloan-Kettering Cancer Center; Netherlands Cancer Institute; Princess Margaret Cancer Centre; The University of Texas MD Anderson Cancer Center; Vall d'Hebron Institute of Oncology	Cancer	Unavailable	Oncology Clinical and Translational Consortium (OCTC) to conduct Phase I/II single-agent and combination trials with GSK's early stage cancer pipeline
Amgen Inc. (NASDAQ:AMGN)	International Myeloma Foundation	Cancer	Undisclosed	Partnership to support foundation's Black Swan Research Initiative that aims to define and assess minimal residual disease (MRD) as a clinical endpoint
Ariana Pharma; Bruker Corp. (NASDAQ:BRKR)	University Hospitals of Strasbourg; University of Strasbourg	Cancer; Diagnostics	Unavailable	ExtempoNMR project to develop a tool for <i>in vitro</i> cancerous tissue diagnosis during surgical procedures
AstraZeneca; Cancer Research Technology Ltd.	Cancer Research UK	Cancer	Undisclosed	Partnership to develop the CC chemokine receptor 4 (CCR4; CD194) antagonist AZD2098 for kidney cancer
Cellular Dynamics International Inc. (NASDAQ:ICEL)	The Hamner Institutes for Health Sciences	Diagnostics	Undisclosed	Partnership to develop predictive <i>in vitro</i> screening assays for chemical, environmental and pharmaceutical toxicology assessments

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Table 1. Selected public-private partnerships for December 2013. (continued)

Companies	Institutions	Business area	Disclosed value	Purpose
Domain Therapeutics S.A.	McGill University; University of Montreal	Diagnostics	Undisclosed	Partnership to develop biosensors using GPCR technology created at University of Montreal
Johnson & Johnson (NYSE:JNJ)	Neomed Institute	Pharmaceuticals; Diagnostics	Unavailable	Partnership to jointly identify and fund early stage life science technologies from Neomed's academic and biotech partners
Merck & Co. Inc. (NYSE:MRK)	Not applicable	Pharmaceuticals	Undisclosed	Plan to create four innovation hubs to identify external early stage and late-stage R&D opportunities that the pharma could license or acquire
Neurimmune Therapeutics AG; Anelixis Therapeutics LLC	ALS Therapy Development Institute	Neurology	Undisclosed	Partnership to develop preclinical human antibodies from Neurimmune that target misfolded superoxide dismutase 1 (SOD1) to treat amyotrophic lateral sclerosis (ALS)
Not applicable	Harvard University; U.S. Army Research, Development and Engineering Command	Diagnostics	Unavailable	Partnership to advance organ-on-a-chip research to improve chemical and biological testing
Novogen Ltd. (ASX:NRT; NASDAQ:NVGN)	Weill Cornell Medical College	Cancer	Undisclosed	Partnership to develop trilexium to treat glioblastoma multiforme (GBM)

channels and GPCRs,” said Hegendörfer. “This gives them additional opportunities in the service field.”

Hegendörfer and Allemeersch said that HDC will primarily provide screening services for academic clients recruited by CD3 and LDC. HDC's team of five people is already working on two such projects.

Details about how shares in HDC are divided among the three stakeholders were not disclosed.

Public-private partnership roundup

In December, the **New York City Economic Development Corp.** launched its Early-Stage Life Sciences Funding Initiative with partners **Celgene Corp.**, **Eli Lilly and Co.** and **General Electric Co.** to drive newco formation in the city. The initiative will create a VC-managed fund to invest at least \$100 million in 15–20 early stage life science companies by 2020 (see Table 1, “Selected public-private partnerships for December 2013”).

Johnson & Johnson's Johnson & Johnson Innovation LLC and Janssen Labs units continued to expand into Canada by teaming up with the **Neomed Institute** to jointly identify and fund early stage life science technologies from Neomed's academic and biotech partners.

The deal follows a similar November collaboration in which J&J Innovation and Janssen partnered with Canada's **MaRS Innovation** to jointly identify and fund early stage life science technologies from MaRS's 16 member institutions.

Meanwhile, **Merck & Co. Inc.** is picking up the innovation center model by creating four innovation hubs in or near Boston, San Francisco,

London and Shanghai. The hubs will identify external early stage and late-stage R&D opportunities that the pharma could license or acquire.

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- Graham, D.B. & Xavier, R.J. *Trends Immunol.* **34**, 371–378 (2013)

COMPANIES AND INSTITUTIONS MENTIONED

Amgen Inc. (NASDAQ:AMGN), Thousand Oaks, Calif.
Axxam S.p.A., Milan, Italy
Broad Institute of MIT and Harvard, Cambridge, Mass.
Catholic University Leuven, Leuven, Belgium
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
Centre for Drug Design and Discovery, Leuven, Belgium
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
European Investment Fund, Luxembourg City, Luxembourg
General Electric Co. (NYSE:GE), Fairfield, Conn.
Hit Discovery Constance GmbH, Constance, Germany
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Lead Discovery Center GmbH, Dortmund, Germany
MaRS Innovation, Toronto, Ontario, Canada
Massachusetts General Hospital, Boston, Mass.
Max Planck Innovation GmbH, Munich, Germany
Max Planck Society, Munich, Germany
Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.
Neomed Institute, Montreal, Quebec, Canada
New York City Economic Development Corp., New York, N.Y.
Takeda Pharmaceutical Co. Ltd. (Tokyo:4502), Osaka, Japan