

BIOWORLD® TODAY

MONDAY
MAY 10, 2010

THE DAILY BIOTECHNOLOGY NEWSPAPER

VOLUME 21, No. 89
PAGE 1 OF 6

Washington Roundup

Panel Backs Questcor Spasms Drug, but Investors Still Jittery

By Donna Young
Washington Editor

WASHINGTON – Perhaps it was the hangover from Thursday’s “2:45 p.m. Wall Street crash,” in which the Dow Jones Industrial Average spiraled nearly 1,000 points before minutes later somewhat bouncing back, that had Questcor Pharmaceuticals Inc.’s investors jittery Friday, despite an FDA panel’s support for approval of the company’s Acthar Gel (repository corticotrophin injection) as a therapy for infantile spasms.

The Union City, Calif.-based firm’s shares (NASDAQ:QCOR), whose trading had been halted Thursday pending the vote from the FDA’s Peripheral and Central Nervous System Drugs Advisory Committee, had sunk as low as 10.6 percent, before closing Friday at \$8.60, a loss of 57 cents, or 6.2 percent.

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ImmunoGen Seeking \$67.4M to Advance Cancer Compounds

By Catherine Hollingsworth
Staff Writer

With multiple trials advancing for its unpartnered cancer drug candidate lorvotuzumab, ImmunoGen Inc. is seeking to raise \$67.4 million in a stock offering priced at \$8 per share.

ImmunoGen could bring additional funds if the underwriters exercise a 30-day option to purchase up to 1.35 million additional shares to cover any overallotments. The offering is expected to close on or about May 12.

The money would fund general corporate purposes, which would include developing its pipeline.

The Waltham, Mass.-based firm has two products in the clinic that are wholly owned by the company, while its other clinical stage drug candidates are being developed under partnerships.

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Scariest Thing About Myriad Case? Frightening Investors

By Karl Thiel
BioWorld Today Columnist

There’s an old story about a man who borrows his neighbor’s kettle and later returns it with a hole in the bottom. When the neighbor complains, the man says, “First, I never borrowed your kettle. Second, there is no hole in it. And lastly, the hole was already in it when I borrowed it from you.”

It’s been a month since the decision in *Association for Molecular Pathology v. USPTO*, better known as the Myriad Genetics Inc. patent ruling that declared purified and isolated gene sequences as unpatentable, and the biotech industry finds itself engaged in various defenses and descriptions of its kettle. Having taken the position that

See Myriad, Page 5

Rethinking T Cells and Thinking

T Cells Can be Helpful, not Harmful, in Learning Tasks

By Anette Breindl
Science Editor

Most of the attention to the link between the immune system and cognitive abilities has been on the problems the former can cause for the latter. Inflammation is a culprit in brain disorders such as Alzheimer’s disease.

But new studies, published in the May 3, 2010, issue of the *Journal of Experimental Medicine* showed that some workings of the immune system can be helpful for learning as well. Specifically, in animal studies, T cells and the cytokine interleukin-4 they secreted were important during maze learning.

Senior author Jonathan Kipnis, an assistant professor

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Don’t miss this week’s *Bench Press*, inserted in this issue.

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OTHER NEWS TO NOTE

• **Adeona Pharmaceuticals Inc.**, of Ann Arbor, Mich., said it entered a corporate partnership with **Meda AB**, of Solna, Sweden, to develop flupirtine, a selective neuronal potassium channel opener, which also has NMDA receptor antagonist properties, for the treatment of fibromyalgia. Meda was granted an exclusive sublicense to all of the U.S., Canadian and Japanese patents covering the use of flupirtine for fibromyalgia in exchange for \$17.5 million, including \$2.5 million up front. The deal includes a \$5 million milestone payment to Adeona on the filing of a new drug application with the FDA for flupirtine for fibromyalgia and \$10 million on marketing approval. Adeona also is eligible to receive 7 percent royalties on sales of the drug.

• **Amicus Therapeutics Inc.**, of Cranbury, N.J., was awarded \$210,300 from the Alzheimer's Drug Discovery Foundation to evaluate small-molecule, orally delivered pharmacological chaperone compounds to treat Alzheimer's disease. Amicus has discovered an apparent link between various lysosomal enzymes and accumulation of the beta-amyloid and p-tau deposits observed in the brain of Alzheimer's patients. The ADDF's award will fund initial preclinical proof-of-concept studies for a specific pharmacological chaperone that targets one of those lysosomal enzymes.

• **Arch Biopartners Inc.**, of Toronto, said it has completed the acquisitions of Arch Biotech Inc., 1495628 AB Ltd. and 1502440 AB Ltd., which will continue to operate as separate subsidiaries of Arch. Arch said it also completed a nonbrokered private placement of \$700,000 by issuing 1.4 million common shares at 50 cents per common share. As a result of the private placement and the acquisitions, Arch said it now has 47.36 million common shares outstanding.

• **AVI BioPharma Inc.**, of Bothell, Wash., and the

Stock Movers

05/07/10

Company	Stock Change
NASDAQ Biotechnology	-2.86%
Amylin Pharmaceuticals Inc.	-8%
Bidel Inc.	+10.4%
Cardiome Pharma Corp.	-11.6%
Genoptix Inc.	-23.1%
Momenta Pharmaceuticals Inc.	-11.7%
Osteotech Inc.	-14.9%

(Biotechs showing significant stock changes Friday)

National Institutes of Health and other collaborators said new data, published last week in the *Journal of Infectious Diseases*, demonstrated the potential use of phosphorodiamidate morpholino oligomers as antimicrobial agents. The firm said the publication described preclinical studies demonstrating the in vitro and in vivo efficacy of peptide-conjugated phosphorodiamidate morpholino oligomers against the *Burkholderia cepacia* complex, which comprises 17 related species of Gram-negative bacteria, by targeting acpP, a protein known to be important for bacterial growth.

• **Cellular Dynamics International Inc.**, of Madison, Wis., and iPS Academia Japan Inc. have entered a nonexclusive licensing agreement for the iPSC patent portfolio arising out of the work of Shinya Yamanaka at the Center for iPS Cell Research and Application at Kyoto University. CDI is the first company worldwide licensed to access the key patents surrounding iPSC technology from the two stem cell pioneers, Yamanaka and James A. Thomson of the University of Wisconsin-Madison.

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AHC Media LLC

Washington Roundup

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Acthar, which is approved as a therapy to treat patients with multiple sclerosis and nephrotic syndrome, has been used off-label in the U.S. for more than 50 years to treat infantile spasms, a specific type of seizure seen in infants and children with a certain type epilepsy, known as West syndrome.

This is the second go-around by Questcor to gain the FDA's OK for the drug in infantile spasms.

Acthar has been owned by several drugmakers since it first gained FDA approval in 1952. Questcor, which acquired the rights to the drug in 2001 from Paris-based Sanofi-Aventis Group SA, submitted a supplemental new drug application to the FDA in 2006, but received a complete response letter in May 2007. Regulators, however, encouraged Questcor to try again by submitting published source data.

The FDA last week said that while Questcor had shown due diligence in obtaining the most complete data available by submitting three studies in support of Acthar's efficacy and four evaluating its safety, regulators said those data needed to be weighed carefully.

Nonetheless, the FDA's advisers Thursday voted 22 to 1 that Questcor had provided substantial evidence of Acthar's effectiveness in treating infantile spasms. The committee also voted 16 to 7 that the company has submitted evidence to support the firm's view that a two-week course of treatment with Acthar followed by a two-week tapering regimen provided sustained effectiveness.

In a 20-to-1 vote, with two abstentions, the panel also said Questcor had submitted sufficient evidence of the safety of Acthar at an effective dosing regimen.

The committee, however, was split about Acthar's adverse effects, voting 12 to 10, with one abstention, that Questcor has not yet provided evidence that the drug's side effects of infection, convulsions and hypertension are manageable and reversible.

Questcor is holding a conference call Monday with investors and analysts to discuss Acthar and the outcome of Thursday's meeting.

The FDA, which often, but not always, follows the advice of its outside experts, is expected to make a decision by June 11, the Prescription Drug User Fee Act action date.

Novartis to Pay \$72.5M to Settle Off-Label Suit

The Justice Department last week said Swiss drug and vaccine maker Novartis AG has agreed to pay \$72.5 million to settle civil False Claims Act allegations that the company had been promoting its cystic fibrosis drug TOBI off label.

The firm and Chiron Corp., which was acquired by Basel, Switzerland-based Novartis in 2006, were accused of causing false claims to be submitted to federal health care programs for certain off-label uses, such as diseases other than cystic fibrosis and for patients who did not meet the parameters of the FDA-approved cystic fibrosis indication.

Under the settlement, Novartis will pay the federal gov-

ernment \$43.5 million, plus \$29 million to various states to settle their respective claims.

The initial lawsuit was brought by former Chiron employees Robert Lalley, Courtney Davis and William Manos under the qui tam provisions of the False Claims Act, which permits whistleblowers to bring a lawsuit on behalf of the U.S. and share in any funds recovered.

The whistleblowers in the TOBI suit are sharing more than \$7.8 million, according to the Justice Department, which noted that the case specifically involved fraud against military health programs.

Lawmakers Probing J&J Drug Recall

The House Oversight and Government Reform Committee last week opened an investigation into what led to an FDA recall of more than 40 Johnson & Johnson over-the-counter pediatric medications, including Tylenol, Motrin, Zyrtec and Benadryl products. The massive recall was due to bacterial contamination in the drugs, which came to light after the FDA raised concerns about manufacturing deficiencies at J&J's Fort Washington, Pa. plant.

Reps. Edolphus Towns (D-N.Y.), chairman of the House committee, and Darrell Issa (R-Calif.), the ranking member, noted that the latest recall was the third such one in the last eight months related to the quality of drugs sold by J&J's McNeil Consumer Healthcare division.

Given McNeil's "questionable track record and consecutive recalls," the lawmakers said they are seeking to understand what prior actions the FDA took to address the drugmaker's quality control problems and what events led to the FDA's inspection of the Pennsylvania manufacturing facility.

Genentech, Shire, Novartis Warned

The FDA last week said it has warned Genentech Inc., Shire plc and Novartis AG about misleading promotional materials involving the drugmakers' products.

In a letter posted last week on the agency's website, regulators told South San Francisco-based Genentech, now part of Roche AG, that its so-called professional table-top display panels for Rituxan (rituximab) were false and misleading because they made unsubstantiated efficacy claims about the drug and omitted and minimized important risk information.

Specifically, the claims overstated Rituxan's efficacy in improving progression-free survival and providing benefits in patients with follicular non-Hodgkin's lymphoma, regulators said.

In separate letters, the FDA said certain promotional materials for Basingstoke, UK-based Shire's ulcerative colitis drugs Lialda (mesalamine) delayed-release tablets and Pentasa (mesalamine) controlled-release capsules also were misleading and made false claims.

Basel, Switzerland-based Novartis also was scolded about information on two websites about Gleevec (imatinib mesylate), which regulators said promoted unapproved uses of the drug and failed to disclose the medicine's risks. ■

ImmunoGen

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In addition to lorvotuzumab, the other wholly owned product in ImmunoGen's pipeline is Phase I IMGN388 aimed at solid tumors, for which Johnson & Johnson unit Centocor Inc. has opt-in rights.

Interim data from the dose-escalation Phase I trial that is under way are scheduled to be reported at the annual meeting of the American Society of Clinical Oncology in June.

ImmunoGen's lead partnered drug candidate, trastuzumab (T-DMI), is expected to be submitted for U.S. marketing approval this year in breast cancer. T-DMI, developed by Genentech Inc. (now part of the Roche Group) is under a collaboration agreement with Genentech.

Under that deal, Roche is responsible for the trial costs, manufacturing and marketing, while ImmunoGen collects milestone payments and royalties.

The company's next most advanced product, lorvotuzumab, is being studied as a treatment for CD56-positive solid tumors. ImmunoGen intends to report interim data at a meeting of the European Society for Medical Oncology. The expansion phase of that trial is under way, and focuses on small-cell lung cancer (SCLC), Merkel cell carcinoma (MCC) and ovarian cancer.

ImmunoGen expects to initiate a Phase I/II randomized trial evaluating lorvotuzumab mertansine for first-line treatment of SCLC by late 2010.

ImmunoGen expects to make a go/no-go decision on the initiation of pivotal testing with the compound in MCC by the end of the year based on findings in the expansion phase of the solid tumor study and on meetings with regulatory agencies.

Orphan drug designation has now been received in the EU and U.S. If ImmunoGen decides to proceed, then the pivotal trial could start in 2011.

In addition, ImmunoGen expects to report interim data at the American Society of Hematology annual meeting in December from one or both of its early stage trials being conducted in CD56-positive multiple myeloma – one assessing lorvotuzumab mertansine as a single agent and one assessing it used with lenalidomide and dexamethasone.

While at ASH, the company also expects to report data from a Phase I weekly dosing trial of SAR3419, which was licensed to Paris-based Sanofi-Aventis SA. ImmunoGen expects Phase II testing of that product candidate to begin for the treatment of non-Hodgkin's lymphoma in the second half of the year.

ImmunoGen expects two additional compounds to advance into clinical testing in 2010 through the company's collaboration with Sanofi-Aventis. It expects two to four additional product candidates to enter the clinic in 2011, including the next wholly owned ImmunoGen compound.

BT-062 for multiple myeloma, partnered with Biotest, and BIIB015 for solid tumors, partnered with Biogen Idec Inc., are still in Phase I testing.

ImmunoGen had about \$42.2 million in cash and marketable securities at the end of March.

It anticipates having cash and marketable securities of between \$33 million and \$35 million at the end of June, unchanged from previous guidance. ■

OTHER NEWS TO NOTE

• **NovaBay Pharmaceuticals Inc.**, of Emeryville, Calif., said that new preclinical data demonstrating the antiviral activity and stability of its Aganocide compounds were presented recently at the Association for Research in Vision and Ophthalmology annual meeting in Fort Lauderdale, Fla. NovaBay's Aganocide compounds are anti-infectives being developed for the treatment and prevention of antibiotic-resistant infections. Those broad-spectrum antimicrobials are in Phase II development for the treatment of conjunctivitis, or "pink eye," impetigo and catheter-associated urinary tract infections.

• **VBL Therapeutics**, of Tel Aviv, Israel, said preclinical results evaluating VB-201 for the treatment of psoriasis showed it has significant anti-inflammatory properties that are active against psoriasis. A Phase II trial is under way. Data were presented at the Society for Investigative Dermatology annual meeting in Atlanta.

CLINIC ROUNDUP

• **Cytori Therapeutics Inc.**, of San Diego, said the first clinical trial of adipose (fat) tissue-derived stem and regenerative cells (ADRCs) for the treatment of no-option chronic heart disease patients showed the procedure was safe and feasible; it demonstrated a statistically significant improvement in maximum oxygen (MVO₂) consumption and patients' aerobic capacity measured as metabolic equivalents; and it reduced the extent of infarct size in the left ventricle. The results showed absolute improvement in MVO₂ by 0.6 mL/kg/min in the treated group vs. 2.8 mL/kg/min worsening in the placebo group from baseline to six months, based on matched-pair analysis. The difference was statistically significant ($p < 0.05$). For the entire cohort of patients, mean MVO₂ improved from 16.6 mL/kg/min at baseline to 17.2 mL/kg/min at six months in cell-treated patients, and worsened from 19 mL/kg/min to 15.5 mL/kg/min in the placebo group. Shares of Cytori (NASDAQ:CYTX) fell 6 cents to close at \$5.39 Friday.

Myriad

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this outcome would be ruinous, the industry is now expecting the decision to be overturned on appeal while simultaneously claiming that it's not such a big deal. And actually, it all makes a lot of sense.

I had an interesting conversation recently with biotech patent attorney Gerry Elman, who raised a fascinating notion, perhaps philosophical, but potentially important to those who wish to communicate the aims and achievements of biotechnology. He suggested that the metaphors ingrained in our descriptions of biology subtly miscommunicate the nature of DNA and, in this case, may have changed Judge Robert Sweet's ruling – particularly since it was made as a summary judgment and Myriad wasn't allowed to argue the details of its discoveries in court.

We pretty universally talk about DNA as a storehouse of information, and the processes of translation and transcription (themselves metaphors) as ones of "reading" and "writing" that information. That pretty naturally leads one to think of DNA as fundamentally, philosophically different from all other molecules. Thus, the act of "purifying" a gene is viewed not as a complex lab process involving restriction enzymes that strip a polynucleotide out of the enormous chromosomal molecule, ridding it of all the other molecules that cling to it, and leaving you with something fundamentally different from anything you'd find in nature. Instead, it is an act of plagiarism – lifting a passage from the book of life and claiming it for yourself.

In that view, the "information" content of DNA is all that matters; the fact that a scientist has created something molecularly unique and not existing in nature – a novel chemical, clearly patentable in any other circumstance – seems as irrelevant as changing the font of a copied passage of text.

Is 'Intelligent Design' Science?

Elman suggested the further irony that this is an "intelligent design" view of DNA and life – something that the American Civil Liberties Union (ACLU), which supported the plaintiffs in the Myriad case, argued strenuously was *not* science in opposing the Dover, Pa., school board's attempt to add intelligent design to its curriculum several years ago.

Indeed, Judge Sweet explicitly framed this quasi-spiritual and seemingly extra-legal view in a footnote, noting that his opinion is based on the "unique properties of DNA that distinguish it from all other chemicals and biological molecules found in nature."

In that statement, the judge was answering a prediction made by Myriad in its brief, that (quoting Judge Sweet again) "a finding that DNA is unpatentable subject matter will . . . leave 'little to nothing' of the U.S. biotechnology industry."

Interestingly, that bit of hyperbole stands in sharp contrast to what Myriad has said since the decision – the com-

pany has assured investors that the invalidation of some claims in its BRCA-1 and BRCA-2 patents won't impact its business or its ability to protect its franchise.

So was what Myriad said before just a bit of fear mongering aimed at persuasion? Is that company just putting a brave face on a terrible situation now? Judge Sweet believes the impact of his decision is limited to gene patents alone, but I don't think everyone potentially affected by the ruling is quite so confident.

Still, the scariest thing about a world without gene patents probably isn't the lack of the patents themselves – after all, the fact that we managed to go a couple of decades without a clear legal test on patentability of genes reflects a lack of litigation in the area. The scariest thing would be to undermine the confidence of those who provide that capital that keeps the sector running. Which is why now is the time for brave talk, even in the face of uncertainty.

Bring On Bilski

The tea leaves on where this is going will become much easier to read in the coming weeks. A Supreme Court ruling in *Bilski v. Doll* is expected any time now (indeed was expected before now), and will add some clarity to how the high court views patent eligibility.

Bilski concerns the patenting of method claims, particularly business methods. The Court of Appeals for the Federal Circuit affirmed the rejection of a patent application on a method for commodity trading as being an abstraction rather than an invention. But in doing so, it devised a test for patentability that would seem to invalidate all kinds of claims by requiring that a patentable invention involve a machine or a transformation of matter. That has alarmed the biotech community – the Biotechnology Industry Organization has filed an *amicus* brief to the Supreme Court in the case – because it could have a broad impact on the industry. Just consider patents on diagnostics methods where a machine isn't specifically described and a substance isn't transformed or changed, but merely measured.

If the Supreme Court affirms *Bilski*, the industry will have more than just gene patents to worry about.

Karl Thiel, an analyst for the Motley Fool, can be reached at kthiel@qwest.net. His opinions do not necessarily reflect those of BioWorld Today. ■

CLINIC ROUNDUP

- **Dynavax Technologies Corp.**, of Berkeley, Calif., completed the first immunizations of more than 2,000 subjects enrolled in its Phase III study of Hcpisav, its hepatitis B vaccine. That starts a 12-month follow-up on those subjects and sets the study's completion for May 2011. Dynavax said that event supported its goal of a biologics license application submission in the second half of 2011.

T Cells

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of neuroscience at the University of Virginia, began to look at the relationship between the immune system and the brain, basically on a hunch.

The widespread view at the time was that the brain and the immune system were separated by an impenetrable wall.

But “the immune system patrols the CNS,” Kipnis told *BioWorld Today*. “The cells don’t go inside the brain, but they are almost there” – in the meninges, several layers of cells that line the brain and provide support and protection.

The brain, in turn, “has learned to live with the immune system in those areas.” And given that biology tends to make use of whatever is around, Kipnis reasoned that the T cells might influence the brain, and phenomena like HIV dementia or the cognitive effects of cancer treatment that is sometimes called chemo brain “could be due to [effects on] meningeal immunity.”

In their paper, Kipnis and his team first treated mice with an immunosuppressant drug that sequesters T cells, and found that a week of such treatment gave them memory deficits when they learned how to get around a maze. Treatment with a more specific antibody that prevented T cells from going into the meninges led to the same learning defects.

The T cells do not interact with neurons directly – in fact, they are prevented from any such interactions by the blood-brain barrier, and the meninges are a neuron-free zone. Instead, they secrete a cytokine, interleukin-4, that is critical for their effects.

When Kipnis and his team tested IL-4 knockout animals, they also had memory deficits; bone marrow transplantation experiments revealed that it was specifically interleukin-4 in the immune system that was important for normal learning to occur.

Interleukin-4, Kipnis said, works in “at least two” ways. First, the T cells regulate another immune cell type, meningeal myeloid cells.

When T cells are absent, the myeloid cells will develop “a severe proinflammatory phenotype,” Kipnis said.

The interleukin-4 secreted by the T cells appears to shut down the myeloid production of proinflammatory cytokines.

Interleukin-4 also crosses into the brain – either by diffusion across the innermost meningeal layer, or through as-yet unidentified transporters. And once it does, it induces a type of brain support cell known as astrocytes to secrete brain-derived neurotrophic factor, or BDNF – a factor known to play a role in brain plasticity and memory formation.

Though the work is currently at its earliest stages, “the potential practical applications are huge,” Kipnis said.

He believes the most promising strategy is most likely not to target T cells directly, given that T-cell reduction is inevitable both in diseases like HIV dementia and treatments like chemotherapy. Instead, he said, the goal should most likely be to “mimic what T cells do without actually boosting T cells,” perhaps by administering interleukin-4 therapeutically, or targeting myeloid cells in vitro.

And on the most basic level, Kipnis said, the work suggested that a re-evaluation of the interactions of the nervous system and the immune system are in order.

“For so many years,” he said, “it was thought that if you see T cells in the brain, that’s a bad thing. What we show is that no, it can be good.” ■

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CLINIC ROUNDUP

• **Nile Therapeutics Inc.**, of San Francisco, completed the dose escalation stage of an ongoing Phase II study of CD-NP in patients with acute decompensated heart failure. The study has been expanded to permit additional dose exploration prior to proceeding to larger Phase II studies. To date, 52 of the approximately 75 patients intended for inclusion in the CT005 study have been enrolled. Full data from the study are expected in late 2010.

BENCH PRESS

BIO WORLD LOOKS AT TRANSLATIONAL MEDICINE

MONDAY, MAY 10, 2010

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Researchers Analyze a Man's Full Genome for Disease Risks

From Staff Reports

Scientists at **Stanford** and **Harvard Universities** collaborated to assess the clinical usefulness of analyzing a patient's full genome for disease risks and unusual drug responses. The work brings closer to reality the concept that whole-genome sequencing might one day play a clinical role.

The authors evaluated the entire genome of a 40-year old man and compared it to several databases of disease-related gene variants. They also factored in the patient's medical and family history and statistical disease risks. As part of the work, the researchers provided the patient with genetic counseling and clinical tests relevant to his family history.

The genome analysis revealed variants associated with diseases in the man's family (osteoarthritis, vascular disease and early sudden death). It also uncovered variants linked to conditions not in his family (iron overload and thyroid and parathyroid diseases). Some variants suggested that he might have unusual responses to certain heart medications, which is meaningful in light of his risk for cardiovascular disorders.

The authors viewed their work as a proof of concept that whole-genome sequencing can yield clinically useful information for individual patients. They acknowledged that many challenges remain, including the effect of the environment, which is difficult to quantify and often changes throughout a person's life.

The paper concluded that the transition to genome-informed medical care will require an integrated team including medical and genetics professionals, ethicists and health-care delivery organizations. The analysis appeared in the May 1, 2010, issue of *Lancet*.

Hormone Mimic Effective Against PLD

A hormone mimic called Octreotide may be effective for treating polycystic liver disease (PLD) caused by ADPKD, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology*.

In addition to causing kidney failure, ADPKD also often leads to PLD, a condition characterized by multiple variably sized cysts in the liver. Octreotide mimics the somatostatin hormone that regulates the secretion of several other hormones in the body. Somatostatin exerts its effects by blocking both the formation of the chemical cyclic AMP and the secretion of fluids by cells, two factors thought to play a role in the development of kidney and liver cystic diseases.

A team of researchers led by the **Mayo Clinic College**

of Medicine designed a clinical trial to examine whether Octreotide could shrink the cyst-filled livers of patients with PLD. The randomized, double-blind, placebo-controlled trial enrolled 42 patients with severe PLD caused by ADPKD (34 patients) or autosomal dominant PLD (eight patients). (Autosomal dominant PLD is a genetic form of PLD not caused by ADPKD.) Patients received Octreotide or placebo, and treatments were administered as monthly injections.

After one year, liver volume decreased by an average of approximately 5 percent in patients taking Octreotide but slightly increased (by approximately 1 percent) in patients taking placebo. Octreotide also had an effect on the diseased kidneys of patients with ADPKD. Among those patients, total kidney volume remained practically unchanged in the Octreotide group but increased by more than 8 percent on average in the placebo group. Kidney function was similar in both groups of patients. Octreotide was well tolerated, and treated individuals reported an improved perception of bodily pain and physical activity.

Progesterone and Altered Stem Cells

Cancer researchers at **Princess Margaret Hospital** have discovered that the ovarian hormone progesterone plays a pivotal role in altering breast stem cells, a finding that has implications for breast cancer risk.

The findings, published online in *Nature*, are significant because reproductive history is among the strongest risk factors for breast cancer, researchers said. Other major known risk factors are age, genetics and breast density.

The research showed that progesterone peaks during the second half of the menstrual cycle, and starts a cross-talk between stem cells and neighboring cells that propels normal breast stem cells to expand in number, and may trigger an environment where cancer can begin.

Until now, breast stem cells were thought to be generally inactive in the adult female breast, the researchers said. In this study, the team replicated the human natural reproductive cycle in mice to determine the impact of hormones on breast stem cells. How hormones change those stem cells opens a new pathway to understanding the cell growth that begins breast cancer, and with further

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research, will open new ways of targeting stem cells, investigators said.

Milk, Renal Cancer Link Questioned

While previous research had suggested that drinking milk was related to factors that may increase the risk of renal cell cancer, results of a recent study exploiting the genetic contribution to variation in milk consumption suggested that may not be the case.

Previously reported studies suggested a connection between milk intake and renal cell carcinoma risk, and whether that represents a causal association or is the result of bias is currently unclear. Researchers at the **MRC CAiTE Center** in the department of social medicine at the University of Bristol, UK, used a genetic marker to try to untangle that observation.

From 1999 through 2003, the researchers conducted a large, hospital-based, case-control study from four central and eastern European countries. Using observational, genetic and phenotypic data, they determined whether the genetic variant at the gene MCM6 – known to be associated with lactose tolerance – may be used as a nonconfounded and unbiased marker for milk consumption's link to cancer risk.

For adult milk drinkers vs. nonmilk drinkers in the study, the difference in the odds of renal cell carcinoma was about 35 percent. However, when assessing the relationship in a more direct way by using genetic data, there was no association between the two.

The study results were published in the May 2010 issue of *Cancer Epidemiology, Biomarkers & Prevention*.

Methane Breath and Obesity

New **Cedars-Sinai** research showed obese patients who test positive for methane on their breath have a significantly higher body mass index (BMI) than their peers.

The study, presented recently at Digestive Disease Week in New Orleans, is the first in humans to show a link between the presence of methane-producing bacteria in the gut and elevated BMI, indicating that bacteria may play a role in obesity.

In the study, 58 patients ages 18 to 65 with BMIs between 30 and 60 were given a breath test to determine if methane was present. About 20 percent of those patients tested methane-positive. The methane-positive patients had a BMI of up to 7 points higher than those patients who did not show methane on their breath tests. BMI is used as a measurement that correlates with obesity. A methane-positive test indicates the patient has certain bacteria in the gut that produce the gas.

Previous research by the Cedars-Sinai GI Motility Program has shown that methane from methane-producing bacteria can slow the gut down. That could play a role in explaining why obese patients with the methane type of bacteria have a higher BMI since methane, by slowing the gut, could increase calorie harvest, researchers said.

Another Dark Chocolate Benefit

Researchers at **Johns Hopkins** have discovered that a compound in dark chocolate may protect the brain after a stroke by increasing cellular signals already known to shield nerve cells from damage.

Ninety minutes after feeding mice a single modest dose of epicatechin, a compound found naturally in dark chocolate, the scientists induced an ischemic stroke by essentially cutting off blood supply to the animals' brains. They found that the animals that had preventively ingested the epicatechin suffered significantly less brain damage than the ones that had not been given the compound.

While most treatments against stroke in humans have to be given within a two- to three-hour time window to be effective, epicatechin appeared to limit further neuronal damage when given to mice 3.5 hours after a stroke. Given six hours after a stroke, however, the compound offered no protection to brain cells.

Clumping Breast-Milk Cells

New research led by **McGill University** researchers helped explain why breast-milk cells lose their structure, causing them to clump up in strange ways and sometimes become cancer tumors. The researchers discovered how one particular gene regulates epithelial cells – cells that normally form in sheets and are polarized to enable the transport of molecules in a single direction. It's that loss of polarity that is thought to play an important role in breast tumor development.

By using mouse models, investigators discovered that the cells do not form neat structures when the gene malfunctions.

The research, published in *Genes and Development*, showed that if the gene is reintroduced into a tumour, polarity can be restored. The investigators pointed out that the gene functions by working with more than 40 various proteins, of which only one, a scaffold protein, has been identified.

Serotonin's Role in IBS

Serotonin is commonly associated with brain neurology, but a **Mayo Clinic** research team has identified a number of genetic variants in serotonin genes that impact irritable bowel syndrome (IBS).

The Mayo team used high-throughput technology to study nearly 400 tagged single-nucleotide polymorphisms (SNPs) in more than 20 serotonin-related genes, and found a number of previously unknown IBS associations. The conclusion: Many more serotonin-related SNPs were implicated in IBS than first thought. The implicated genes relate to serotonin synthesis, metabolism and receptors. The researchers also found IBS may be caused by multiple genes – not just one or a few – and there may be distinct as well as overlapping molecular mechanisms that cause diarrhea and constipation, two major symptoms of IBS.

The findings were presented at Digestive Disease Week 2010 in New Orleans.