

# Biotech SMART Report

*Summarized Multipurpose Articles on Research and Technology (SMART)*



## BIOTECHNOLOGY INDUSTRY RESEARCH ASSISTANCE PROGRAM

*A program of*

Department of Biotechnology, Ministry of Science and Technology, Government of India

In partnership with ABLE and BCIL

April - June 2010

Volume: 04

## Biotech SMART Report

(Summarized Multipurpose Articles on Research and Technology)

Biotech SMART Report is a Quarterly publication from BIRAP, a programme of DBT, Govt. of India which is dedicated to nurture, incubate and discover innovative research in the Biotechnology Industry.

The Report is an assemblage of updated news reports from company websites, e-newspapers, e-magazines and market report updates in the area of Biotechnology for a period of 03 months from 01 April 2010 to 30 June 2010.



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**Published by:**

**BIRAP**

A – 254, 3<sup>rd</sup> & 4<sup>th</sup> Floor, Bhisam Pitamah Marg,

Defence Colony New Delhi – 110024 I N D I A

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DEO, BIRAP

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## Section A: Agriculture

### Headline 1: Agriculture's next revolution -- perennial grain -- within sight

**Published by:** Science Daily

**Date of Publication:** June 24, 2010

**Source:** <http://www.sciencedaily.com>

Earth-friendly perennial grain crops, which grow with less fertilizer, herbicide, fuel, and erosion than grains planted annually, could be available in two decades, according to researchers writing in the current issue of the journal *Science*.

Perennial grains would be one of the largest innovations in the 10,000 year history of agriculture, and could arrive even sooner with the right breeding programs, said John Reganold, Washington State University (WSU) Regents professor of soil science and lead author of the paper with Jerry Glover, a WSU-trained soil scientist now at the Land Institute in Salina, Kansas.

"It really depends on the breakthroughs," said Reganold. "The more people involved in this, the more it cuts down the time."

Published in *Science's* influential policy forum, the paper is a call to action as half the world's growing population lives off marginal land at risk of being degraded by annual grain production. Perennial grains, say the paper's authors, expand farmers' ability to sustain the ecological underpinnings of their crops.

"People talk about food security," said Reganold. "That's only half the issue. We need to talk about both food and ecosystem security."

Perennial grains, say the authors, have longer growing seasons than annual crops and deeper roots that let the plants take greater advantage of precipitation. Their larger roots, which can reach ten to 12 feet down, reduce erosion, build soil and sequester carbon from the atmosphere. They require fewer passes of farm equipment and less herbicide, key features in less developed regions.

By contrast, annual grains can lose five times as much water as perennial crops and 35 times as much nitrate, a valuable plant nutrient that can migrate from fields to pollute drinking water and create "dead zones" in surface waters.

"Developing perennial versions of our major grain crops would address many of the environmental limitations of annuals while helping to feed an increasingly hungry planet," said Reganold.

Perennial grain research is underway in Argentina, Australia, China, India, Sweden and the United States. Washington State University has more than a decade of work on perennial wheat led by Stephen Jones, director WSU's Mount Vernon Research Center. Jones is also a contributor to the *Science* paper, which has more than two dozen authors, mostly plant breeders and geneticists.

The authors say research into perennial grains can be accelerated by putting more personnel, land and technology into breeding programs. They call for a commitment similar to that underway for biologically based alternative fuels.

## Headline 2: Organic Pesticides Not Always 'Greener' Choice, Study Finds

**Published by:** Science Daily

**Date of Publication:** June 23, 2010

**Source:** <http://www.sciencedaily.com>

Consumers shouldn't assume that, because a product is organic, it's also environmentally friendly.

A new University of Guelph study reveals some organic pesticides can have a higher environmental impact than conventional pesticides because the organic product may require larger doses.

Environmental sciences professor Rebecca Hallett and PhD candidate Christine Bahlai compared the effectiveness and environmental impact of organic pesticides to those of conventional and novel reduced-risk synthetic products on soybean crops.

"The consumer demand for organic products is increasing partly because of a concern for the environment," said Hallett. "But it's too simplistic to say that because it's organic it's better for the environment. Organic growers are permitted to use pesticides that are of natural origin and in some cases these organic pesticides can have higher environmental impacts than synthetic pesticides often because they have to be used in large doses."

The study, which is published in the journal *PLoS ONE*, involved testing six pesticides and comparing their environmental impact and effectiveness in killing soybean aphids -- the main pest of soybean crops across North America.

The two scientists examined four synthetic pesticides: two conventional products commonly used by soybean farmers and two new, reduced-risk pesticides. They also examined a mineral oil-based organic pesticide that smothers aphids and another product containing a fungus that infects and kills insects.

The researchers used the environmental impact quotient, a database indicating impact of active ingredients based on such factors as leaching rate into soil, runoff, toxicity from skin exposure, consumer risk, toxicity to birds and fish, and duration of the chemical in the soil and on the plant.

They also conducted field tests on how well each pesticide targeted aphids while leaving their predators -- ladybugs and flower bugs -- unharmed.

"We found the mineral oil organic pesticide had the most impact on the environment because it works by smothering the aphids and therefore requires large amounts to be applied to the plants," said Hallett.

Compared to the synthetic pesticides, the mineral oil-based and fungal products were less effective, as they also killed ladybugs and flower bugs, which are important regulators of aphid population and growth.

These predator insects reduce environmental impact because they naturally protect the crop, reducing the amount of pesticides that are needed, she added.

"Ultimately, the organic products were much less effective than the novel and conventional pesticides at killing the aphids and they have a potentially higher environmental impact," she said. "In terms of making pest management decisions and trying to do what is best for the environment, it's important to

look at every compound and make a selection based on the environmental impact quotient rather than if it's simply natural or synthetic. It's a simplification that just doesn't work when it comes to minimizing environmental impact."

### **Headline 3: Bt cotton linked with surge in crop pest**

**Published by:** Science Daily

**Date of Publication:** May 14, 2010

**Source:** <http://www.scidev.net>

[BEIJING] Scientists are calling for more thorough risk assessments for genetically modified crops after they discovered a surge in pests in a region planted with Bt cotton.

Their fifteen-year study surveyed a region of northern China where ten million small-scale farmers grow nearly three million hectares of Bt cotton, and 26 million hectares of other crops. It revealed widespread infestation with mirid bug (*Heteroptera Miridae*), which is destroying fruit, vegetable, cotton and cereal crops. And the rise of this pest correlated directly with Bt cotton planting.

Bt cotton is a genetically engineered strain, produced by the biotechnology company Monsanto. It makes its own insecticide which kills bollworm (*Helicoverpa armigera*), a common cotton pest that eats the crop's product — the bolls.

Planting Bt cotton slashes farmers' pesticide requirements and increases cotton yield. It has been adopted worldwide, with about 16 million hectares — about 50 per cent of world cotton cultivation — now Bt cotton.

#### *In northern China 95 per cent of cotton is the Bt variety.*

The scientists, from the Chinese Academy of Agricultural Sciences, and the China National Agro-Technical Extension and Service Center, monitored insecticide use on cotton farms for 15 years. After the first five years, they also monitored mirid bug numbers at 38 locations.

They watched the farms gradually become a source of mirid bug infestations, in parallel with the rise of Bt cotton. The bugs, initially regarded as occasional or minor pests, spread out to surrounding areas, "acquiring pest status" and infesting Chinese date, grape, apple peach and pear crops.

Before Bt cotton, the pesticides used to kill bollworm also controlled mirid bugs. Now, farmers are using more sprays to fight mirid bugs, said the scientists.

"Our work shows that a drop in insecticide use in Bt cotton fields leads to a reversal of the ecological role of cotton; from being a sink for mirid bugs in conventional systems to an actual source for these pests in Bt cotton growing systems," the authors wrote in their paper, published yesterday in the journal *Science* (13 May).

Although Bt cotton is well-researched, few studies examine the knock-on effect on other pests, said the scientists.

"This study is the first report of a landscape-level emergence of non-target pests," said co-author, Kongming Wu, adding that the study highlights a "critical need" to explore the complex ecological impacts of Bt crops.

"Crops are the first level in the food chain," he told *SciDev.Net*. "When people make it uneatable to certain insects, we need to understand how it might affect the whole ecosystem."

The team concluded that more comprehensive risk management "may be crucial to help advance integrated pest management and ensure sustainability of transgenic technologies".

#### **Headline 4: Scientists harness 'good' fungi to boost staple crops**

**Published by:** Science Daily

**Date of Publication:** June 15, 2010

**Source:** [http:// www.scidev.net](http://www.scidev.net)

Rice has been made to grow five times faster, and potatoes to require much less fertiliser, using a technique that introduces fungi to the roots of the crops.

Although some fungi can cause disease in crops, others — known as mycorrhizal fungi — live in harmony with them, with both the plant and the fungus deriving benefit.

Fungi are known for extracting nutrients, such as phosphate, from the soil around a plant, which the plant can then use. The fungus, in turn, receives sugars produced by the plant through photosynthesis.

But so far, studies of this phenomenon have been done in temperate regions — with little evidence that these fungi could help improve crops such as rice, which grow in other climates.

Ian Sanders, a biologist at the University of Lausanne, Switzerland, said recent research has shown that the fungi can have a major impact on yield in the acidic soils of tropical regions.

"There, phosphate fertiliser gets bound to the soil which makes it difficult for crops to extract it without fungal help," he told *SciDev.Net*. Harnessing this process could become increasingly important, with global soil phosphate shortages predicted to occur in the coming decades.

Sanders' team used traditional, non-GM approaches to breed fungi (*Glomus intraradices*) containing beneficial genes, and inoculated rice with them.

The genes aided the exchange of nutrients between the fungi and the rice roots, leading to five-fold faster rice growth, the researchers reported in *Current Biology* last week (10 June).

The research was conducted in Swiss greenhouses that mimicked tropical conditions, so field tests are still needed to confirm that this would work in rice on large scale.

Sanders is also collaborating with researchers from the National University of Colombia on field trials of economically important crops such as potato and cassava.

So far, the results are promising: the same amount of potato can be grown with less than a third of the phosphate fertiliser normally applied.

*Field test results on cassava are expected within the next couple of years.*

Roland Buresh, a principal scientist at the International Rice Research Institute specialising in nutrient management, said: "The fungi require the presence of oxygen for growth. They might be able to grow

well in a rice nursery, but they are unlikely to thrive after transplanting into submerged rice soils with limited soil aeration, so the benefits might be less for rice on submerged soils.

"The technique would not be expected to change the growth duration of a rice variety and enable more rice crops to be grown in a year."

Last month (23 May) two research teams reported independently in *Nature Genetics* their discovery of a gene — OsSPL14 — that can increase rice yield by as much as ten per cent.

### **Headline 5: Soil fertility key to African green revolution**

**Published by:** Science Daily

**Date of Publication:** May 24, 2010

**Source:** <http://www.scidev.net>

Replenishing soil fertility with mineral and organic fertilisers could triple cereal crop yields in tropical Africa and achieve an African green revolution, says Pedro A. Sánchez from the Earth Institute.

Staple crop yields have not risen from one tonne per hectare in most of tropical Africa since the 1960s. The problem, according to Sánchez, is decades of farming without adequate fertiliser that have "stripped the soils of the vital nutrients needed to support plant growth".

The eighty 'Millennium Villages', set up in 2005 across ten African countries to promote community-led development, show the extent to which better soil fertility improves yields. Through mineral fertiliser applications, improved cultivars and the latest agronomic knowledge, maize yields have surpassed three tons per hectare in 78 per cent of village households, says Sánchez.

And at a national level, Malawi's fertiliser subsidy scheme — that gives farmers two-thirds off the market price of mineral fertilisers — has increased maize production from 0.8 tonnes per hectare in 2005 to 2.2 in 2007. The scheme has transformed the country from a receiver of food aid to a food exporter and donor, says Sánchez.

To build on these initial successes, African countries must now focus on adding organic fertilisers to their soils. "Only organic fertilisers add carbon, feed soil microbes and help to retain soil moisture", writes Sánchez. The best way of applying them, he adds, is to grow leguminous trees that capture nitrogen from the air and transfer it to the soil.

Such 'nitrogen-fixing' trees could capture 50–100 kilogrammes of nitrogen per hectare per year in tropical Africa — similar to the amount added by mineral fertilisers. They have the added benefit of providing fuel wood.

But to establish the nitrogen-fixing system, farmers have to forgo one crop, which makes it unattractive to most farmers in tropical Africa. Governments could overcome the hurdle by subsidising nitrogen-fixing trees, suggests Sánchez.

### **Headline 6: With Fungi on Their Side, Rice Plants Grow to Be Big**

**Published by:** Science Daily

**Date of Publication:** June 11, 2010

**Source:** <http://www.sciencedaily.com>

By tinkering with a type of fungus that lives in association with plant roots, researchers have found a way to increase the growth of rice by an impressive margin. The so-called mycorrhizal fungi are found in association with nearly all plants in nature, where they deliver essential nutrients -- specifically phosphate -- to plants in return for sugar. The findings are nevertheless a surprise, according to researchers reporting online on June 10th in *Current Biology* because there has been little evidence thus far to suggest that crop plants actually respond to the fungi.

"Global reserves of phosphate are critically low, and because the demand for phosphate goes hand in hand with human population expansion, it is predicted that there will be major shortages in the next few decades," said Ian Sanders of the University of Lausanne in Switzerland. "Unfortunately, most of our important crop plants do not respond strongly, if at all, to inoculation with these fungi. This is especially so for rice, the most globally important food plant. There are no clear reports that rice benefits from inoculation with mycorrhizal fungi."

That is, until now. In fact, the researchers started with a strain of mycorrhizal fungus of the species *Glomus intraradices* that clearly didn't benefit rice. They then took advantage of the fungus's unusual genetics. A single fungal filament can contain genetically distinct nuclei. Those distinct nuclei can fuse together, mixing genes up in different combinations, and fungal spores can also end up with different complements of genes, the new research shows. As such, the supposedly clonal fungi maintain a degree of genetic variation that had been overlooked.

"It turns out we can very simply manipulate their genetics to produce fungi that induce up to a five-fold growth increase in this globally important food plant," Sanders said.

The genetic changes that the researchers produced in the fungi led to changes in the activity of important genes in the rice, they report. Those affected genes are known to be involved in establishing the mutually beneficial relationship between plant and fungus and in the transport of phosphate at the interface between fungus and plant.

Sanders emphasized that the genetic manipulation the researchers undertook didn't involve any insertion of new genes into the fungal genome. It rather relied on the same biological processes of genetic exchange and segregation that normally take place in the fungus. "What we have done with these fungi is not much different from what plant breeders, and farmers before them, have done to improve crops," he said. "The only difference is that the genetics of these fungi is a little bit more unusual, and no one thought it worth doing."

On a cautionary note, Sanders did emphasize that the plants they studied were grown in a greenhouse in Switzerland under conditions that only mimicked those found in the tropics. "This is clearly not at all the same environment as a rice plant growing in a real paddy field," he said. It remains to be seen whether the same growth benefits will apply in practice.

"However," Sanders said, "our study clearly shows that the potential is there to manipulate the genetics of the fungus to achieve greater crop yields."

## Section B: Healthcare & Clinical Research

### Headline 1: Therapeutic Potential of Embryonic Stem Cells

**Published by:** Science Daily

**Date of Publication:** June 21, 2010

**Source:** <http://www.sciencedaily.com>

*Are stem cells ready for prime time?*

The therapeutic potential of embryonic stem cells has been an intense focus of study and discussion in biomedical research and has resulted in technologies to produce human induced pluripotent stem cells (hiPSCs). Derived by epigenetic reprogramming of human fibroblasts, these hiPSCs are thought to be almost identical to human embryonic stem cells (hESCs) and provide great promise for patient-tailored regenerative medicine therapies. However, recent studies have suggested noteworthy differences between these two stem cell types which require additional comparative analyses.

Scientists at Children's Memorial Research Center at Northwestern University Feinberg School of Medicine investigated the expression of key members of the Nodal embryonic signaling pathway, critical to maintaining pluripotency, in hiPSC and hESC cell lines. Nodal is an important morphogen -- a soluble molecule that can regulate cell fate -- in embryological systems that requires tight regulatory control of its biological function.

The group's results demonstrated slightly lower levels of Nodal and Cripto-1 (Nodal's co-receptor) and a dramatic decrease in Lefty (Nodal's inhibitory regulator) in hiPSCs compared with hESCs, suggesting less regulatory control of cell fate in reprogrammed stem cells. Based on these findings, additional work addressed the implications associated with the epigenetic reprogramming of hiPSCs and examined a global comparative analysis of 365 microRNAs (miRs) in hiPSC vs. hESC lines.

The data revealed 10 highly expressed miRs in hiPSCs with greater than 10-fold difference, which have been shown to be cancer related. Collectively, these data demonstrate cancer hallmarks expressed by hiPSCs, which will require further elucidation for their impact on clinical applications, especially with respect to the fate of precancerous stem cells.

The paper is published online in the Journal of Cellular Physiology. The authors are Sergey Malchenko, Vasil Galat (two first authors), Elisabeth A. Seftor, Elio F. Vanin, Fabricio F. Costa, Richard E.B. Seftor, Marcelo B. Soares and Mary J.C. Hendrix (two senior authors), Cancer Biology and Epigenomics Program (SM, EAS, EFV, FFC, REBS, MBS and MJCH) and Developmental Biology Program (VG). This research was supported by the National Cancer Institute (MJCH), the National Heart, Lung and Blood Institute (VG), the Maeve McNicholas Memorial Foundation (FFC), and the Medical Research Institute Council.

### Headline 2: New Combination Effective Against Pancreatic Cancer: Substance in Broccoli Supports Cancer Therapy, Study Finds

**Published by:** Science Daily

**Date of Publication:** June 16, 2010

**Source:** <http://www.sciencedaily.com>

The new cancer medication sorafenib looks promising. Sorafenib is used for advanced liver and kidney cancer and also appears to be effective against cancer stem cells in pancreatic cancer. A team led by Professor Dr. Ingrid Herr, Head of the Department of Molecular Oncosurgery, a group of the Department of Surgery at Heidelberg University Hospital, (Managing Director: Professor Dr. Markus W. Büchler) in cooperation with the German Cancer Research Center, tested the new substance in mice and pancreatic cancer cells. It inhibits resistant tumor stem cells and is also especially effective in combination with sulforaphane, an organic compound found in broccoli.

*The results have been published online in the medical journal Cancer Research.*

About 12,900 people in Germany develop pancreatic cancer every year. The disease is frequently noticed too late and very few people survive the diagnosis longer than one year. In particular, early precursor cells of the tumor known as cancer stem cells are responsible for uncontrollable growth of the cancer, metastasization to other organs, and recurrence shortly after surgery. They are extremely resistant to conventional therapy and are the focus of new treatment strategies.

### **Headline 3: Sequence and Structure Key to Prion Disease Transmission**

**Published by:** Science Daily

**Date of Publication:** June 14, 2010

**Source:** <http://www.sciencedaily.com>

Prion diseases are lethal neurodegenerative disorders that include Creutzfeldt-Jakob disease (CJD) in humans and bovine spongiform encephalopathy (BSE; commonly known as mad cow disease) in cows. A team of researchers, led by Adriano Aguzzi and Christina Sigurdson, at UniversitätsSpital Zürich, Switzerland, has generated data in mice that provides greater understanding of the factors that determine how easy it is for prion diseases to be transmitted to a new host species.

This information provides new insight into a highly important food safety issue; dietary exposure to beef contaminated with the BSE agent is believed to have caused nearly 200 cases of variant CJD in humans.

The key infectious agent in prion diseases is PrP<sup>Sc</sup>, a highly aggregated form of the cellular prion protein (PrP<sup>C</sup>). The ease with which prions from different species can be transmitted to a new host species varies dramatically. The team found that transmission between species with the same protein building block at position 170 in PrP<sup>C</sup> was relatively easy while it was relatively difficult between those species with different building blocks at that position.

As this protein building block influences the structure of the PrP<sup>C</sup> protein, the authors suggest that local structure of PrP<sup>C</sup> affected by the protein building block at position 170 might have a triggering role in prion transmissibility between different species.

#### **Headline 4: Obstacles to Stem Cell Therapy Cleared**

**Published by:** Science Daily

**Date of Publication:** June 13, 2010

**Source:** <http://www.sciencedaily.com>

Researchers at Lund University have come up with a new technique to prevent tumours developing in connection with stem cell transplantations.

The results have been published in the scientific journal Proceedings of the National Academy of Sciences.

"When you develop, for example, nerve cells for transplantation, you always get a small contamination of immature stem cells," explains Johan Jakobsson, head of research group at the Department of Experimental Medical Science.

#### ***These immature stem cells can lead to tumours -- an unacceptable side-effect.***

"We have developed a technique that enables us to eliminate immature stem cells and thus create safer stem cell transplantations."

The researchers have transplanted the stem cells into mice with Parkinson's disease. The results are very promising: there are far fewer tumours and the cells that survive are the correct type of nerve cells.

#### ***The technique uses a specially designed virus.***

"We use the virus to genetically modify the cells, which means that we can see which ones we want and which ones we don't want. You could say that we hijack one of the cell's gene regulation systems, microRNA. The cell itself tells us when it is mature; it is black when it is immature and turns green when it has completed its development."

It is relatively simple to isolate, cultivate, preserve and genetically modify stem cells. If transplanted into humans they could replace damaged tissue in the nervous system and support other cells that work to heal a brain injury.

"For us this is a major step. Previously tumours have always developed with this type of transplantation. Now we have shown that this can be avoided," says Johan Jakobsson.

At Lund University collaborations are underway on stem cell therapy, for example, for Parkinson's disease, diabetes, stroke, leukaemia and breast cancer. The research community has set the goal of making stem-cell based treatment effective and safe for at least one of the diseases within the next 10 years.

"Our technique could in theory be used for all these diseases," says Johan Jakobsson. The next step is to conduct experiments on human cell lines.

*This project is collaboration within the Bagadilico research network.*

## **Headline 5: New Type of Human Stem Cell May Be Easier to Manipulate**

**Published by:** Science Daily

**Date of Publication:** June 11, 2010

**Source:** <http://www.sciencedaily.com>

Researchers from the Massachusetts General Hospital Center for Regenerative Medicine (MGH-CRM) and the Harvard Stem Cell Institute have developed a new type of human pluripotent stem cell that can be manipulated more readily than currently available stem cells. As described in the June 4 Cell Stem Cell, these new cells could be used to create better cellular models of disease processes and eventually may permit repair of disease-associated gene mutations.

"It has been fairly easy to manipulate stem cells from mice, but this has not been the case for traditional human stem cells," explains Niels Geijsen, PhD, of the MGH-CRM, who led the study. "We had previously found that the growth factors in which mouse stem cells are derived define what those cells can do, and now we've applied those findings to human stem cells."

The first mammalian embryonic stem cells (ESCs) were derived from mice and have proven very useful for studying gene function and the impact of changes to individual genes. But techniques used in these studies to introduce a different version of a single gene or inactivate a particular gene were ineffective in human ESCs. In addition, human ESCs proliferate much more slowly than do cells derived from mice and grow in flat, two-dimensional colonies, while mouse ESCs form tight, three-dimensional colonies. It is extremely difficult to propagate human ESCs from a single cell, which prevents the creation of genetically manipulated human embryonic stem cell lines.

In previous work, Geijsen and his colleagues demonstrated that the growth factor conditions under which stem cells are maintained in culture play an important role in defining the cells' functional properties. Since the growth factors appeared to make such a difference, the researchers tried to make a more useful human pluripotent cell using a new approach. They derived human induced pluripotent stem cells (iPSCs) -- which are created by reprogramming adult cells and have many of the characteristics of human ESCs, including resistance to manipulation -- in cultures containing the growth factor LIF, which is used in the creation of mouse ESCs.

The resulting cells visibly resembled mouse ESCs and proved amenable to a standard gene manipulation technique that exchanges matching sequences of DNA, allowing the targeted deactivation or correction of a specific gene. The ability to manipulate these new cells depended on both the continued presence of LIF and expression of the five genes that are used in reprogramming adult cells into iPSCs. If any of those factors was removed, these hLR5- (for human LIF and five reprogramming factors) iPSCs reverted to standard iPSCs.

"Genetic changes introduced into hLR5-iPSCs would be retained when they are converted back to iPSCs, which we then can use to generate cell lines for future research, drug development and someday stem-cell based gene-correction therapies," says Geijsen. He is an assistant professor of Medicine at Harvard Medical School and a principal faculty member of the Harvard Stem Cell Institute.

Co-authors of the Cell Stem Cell paper are lead author Christa Buecker, MGH-CRM and Harvard Stem Cell Institute (HSCI); Hsu-Hsin Chen, PhD, Laurence Dahern, and Konrad Hochedlinger, PhD,

MGH-CRM and HSCI; Patricia Okwieka, MGH-CRM; Jose Polo, PhD, MGH Cancer Center; Lei Bu, PhD, MGH Cardiovascular Research Center; Tahsin Stefan Barakat and Joost Gribnau, PhD, University Medical Center, Rotterdam, The Netherlands; and Andrew Porter, PhD, Imperial College London, U.K. The study was supported by grants from the National Institutes of Health, the Dutch Science Organization, the Gottlieb Daimler and Karl Benz Foundation and the National Science Council of Taiwan.

## **Headline 6: Ancient Viral Invasion Shaped Human Genome**

**Published by:** Science Daily

**Date of Publication:** June 06, 2010

**Source:** <http://www.sciencedaily.com>

Scientists at the Genome Institute of Singapore (GIS), a biomedical research institute of the Agency for Science, Technology and Research (A\*STAR), and their colleagues from the National University of Singapore, Nanyang Technological University, Duke-NUS Graduate Medical School and Princeton University have recently discovered that viruses that 'invaded' the human genome millions of years ago have changed the way genes get turned on and off in human embryonic stem (ES) cells.

The study provides definitive proof of a theory that was first proposed in the 1950s by Nobel Laureate in physiology and medicine, Barbara McClintock, who hypothesized that transposable elements, mobile pieces of the genetic material (DNA), such as viral sequences, could be "control elements" that affect gene regulation once inserted in the genome.

This finding is an important contribution to the advancement of stem cell research and to its potential for regenerative medicine. Led by GIS Senior Group Leader Dr Guillaume Bourque, the study was published in Nature Genetics on June 6, 2010.

Through the use of new sequencing technologies, the scientists studied the genomic locations of three regulatory proteins (OCT4, NANOG and CTCF) in human and mouse embryonic stem (ES) cells. Interestingly, while the scientists found a lot of similarities, they also found many differences in the methods and the types of genes that are being regulated in humans. In particular, it was discovered that specific types of viruses that inserted themselves in the human genomes millions of years ago have dramatically changed the gene regulatory network in human stem cells.

"This study is a computational and experimental tour de force. It provides undeniable evidence that some transposable elements, which are too often dismissed as merely junk DNA, are key components of a regulatory code underlying human development," said Dr Cedric Feschotte, Associate Professor of the University of Texas Arlington.

The comparisons between the human and mouse model system in the study of gene regulatory networks help to advance the understanding of how stem cells differentiate into various cell types of the body. "This understanding is crucial in the improved development of regenerative medicine for diseases such as Parkinson's disease and leukaemia," said Dr Bourque. "Despite the advantages of using mouse ES cells in the study of gene regulatory networks, further research must focus more

directly on human stem cells. This is due to the inherent challenges of converting the results of studies done from one species to that of the next. More research will need to be done in both human and non-human primate stem cells for findings on stem cells to be used in clinical application.”

Prof Raymond L. White, PhD, Rudi Schmid Distinguished Professor of Neurology, University of California said, “The paper reports very exciting new findings that establish a new and fundamentally distinct mechanism for the regulation of gene expression. By comparing the genomes of mouse with human, the scientists were able to show that the binding sites for gene regulatory factors are very often not in the same place between the two species. This by itself would be very surprising, but the investigators go further and demonstrate that many of the sites are imbedded within a class of DNA sequences called “transposable” elements because of their ability to move to new places in the genome. There are a number of such elements believed to be the evolutionary remnants of viral genomes, but it was very surprising to learn that they were carrying binding sites for regulatory elements to new locations. These changes in regulation would be expected to create major changes in the organisms which carry them. Indeed, many think that regulatory changes are at the heart of speciation and may have played a large role in the evolution of humans from their predecessors. This is likely to be a landmark paper in the field.”

Dr Eddy Rubin, Director of the U.S. Department of Energy Joint Genome Institute and Director of the Genomics Division at Lawrence Berkeley National Laboratory in Berkeley added, “This study using a comparative genomics strategy discovered important human specific properties of the regulatory network in human ES cells. This information is significant and should contribute to helping move the regenerative medicine field forward.”

## **Headline 7: Insulin Pills For Diabetes Finally In Clinical Trials**

**Published by:** Science Daily

**Date of Publication:** June 03, 2010

**Source:** <http://www.sciencedaily.com>

After years of research and anticipation, insulin pills that could make it easier for millions of patients worldwide to manage diabetes are finally moving ahead in clinical trials and a step-closer to the medicine cabinet. That's among the topics highlighted in a two-part cover story on drug manufacturing in the current issue of Chemical & Engineering News (C&EN), ACS' weekly newsmagazine.

C&EN Senior Correspondent Ann Thayer notes that drug manufacturers have tried for years to develop oral insulin without much success. Insulin is a peptide hormone that people with diabetes currently take by injection to bring their blood sugar to within normal levels. But doing so requires uncomfortable, inconvenient injections that can make patients reluctant to use the drug frequently enough to adequately control their blood sugar. An oral form of insulin could help solve this problem. However, stomach acids and enzymes easily destroy insulin and other protein-based drugs. Scientists have had difficulty finding an effective way to eliminate this problem.

They've responded to this challenge by developing special coatings for insulin pills that prevent stomach acid from destroying them. Scientists also are using additives that make it easier for the

intestine to absorb large molecules like insulin. After years of setbacks, signs of success may be at hand. Several insulin pills are now in various stages of clinical trials, and proof of concept may allow them to move into late-stage and more rigorous clinical testing. Only time will tell, however, whether these much-anticipated pills will make it to the market.

### **Headline 8: Detecting cancer related enzyme**

**Published by:** Scientist Live

**Date of Publication:** June 02, 2010

**Source:** <http://www.scientistlive.com/>

An enzyme implicated in osteoporosis, arthritis, atherosclerosis and cancer metastasis – cathepsin K -- eluded reliable detection in laboratory experiments in the past. Now, a research team at the Georgia Institute of Technology has developed an assay that reliably detects and quantifies mature cathepsin K using a technique called gelatin zymography.

"This assay is important because researchers and pharmaceutical companies need a dependable method for sensitively detecting a small amount of cathepsin K and quantifying its activity to develop inhibitors to the enzyme that can fight the diseases while minimising side effects," said Manu Platt, an assistant professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University.

Cathepsin K is required to maintain adequate calcium levels in the body, but it can be highly destructive because it has the ability to break down bone by degrading collagen and elastin.

Platt described the cathepsin K detection protocol in the June issue of the journal *Analytical Biochemistry*. This research was funded by new faculty support from Georgia Tech, and the Facilitating Academic Careers in Engineering and Science Scholars (FACES) and Summer Undergraduate Research in Engineering (SURE) programs at Georgia Tech.

The benefits of this assay over existing techniques are numerous, according to Platt. The major advantage of this protocol, he said, is the definitive knowledge that mature cathepsin K is being detected in cells and tissues -- and not its immature form or one of the other 10 cathepsin varieties: B, H, L, S, C, O, F, V, X or W.

Another advantage of this technique is that it is more sensitive and less expensive than current, less reliable techniques. The new assay allows cathepsin K to be detected in quantities as small as a few femtomoles and does not require antibodies, which can be expensive and cannot be used across different species.

"In our experiments we were able to detect mature cathepsin K activity in quantities as small as 3.45 femtomoles with zymography, which was 10 to 50 times more sensitive at detecting the enzyme than conventional Western blotting," noted Platt, who is also a Georgia Cancer Coalition Distinguished Cancer Scholar.

In addition, zymography allowed the researchers to measure the activity of the enzyme, whereas Western blotting just measured its presence.

To detect mature cathepsin K with gelatin zymography, Platt and Georgia Tech undergraduate student Weiwei Li first separated the enzymes present in cells by their molecular weights. This allowed them to distinguish the mature form of cathepsin K from the immature form and other cathepsin varieties.

Then, to verify the identity and presence of mature cathepsin K, the team activated the enzymes in the gel. They created the perfect acidic environment for cathepsin K to thrive and added inhibitors to block the activity of all enzymes except mature cathepsin K.

To validate the cathepsin K activity detected in the laboratory experiments, Platt and Georgia Tech undergraduate student Zachary Barry developed a computational kinetic model of the enzyme's activity. By solving a system of differential equations, they were able to calculate the concentrations of immature, mature and inactive cathepsin K present at all times during the experimental procedure.

"It is more challenging to work with enzymes than proteins because enzymes have to be functional, which means they have to be folded correctly to be active," explained Platt. "The model suggested that even after the slight denaturation and refolding required by our assay, the cathepsin K activity determined by zymography reflected what happens in nature and was not an artifact of the experimental procedure."

The model also predicted something unexpected -- the inactive form of cathepsin K commonly purchased from supply houses contained 20 percent mature enzyme.

"Cathepsins are implicated in many different diseases and the value of this assay is that it enables the measurement of previously undeterminable cathepsin activity in normal and diseased cells and tissues," noted Platt.

With this assay, Platt's team is currently investigating whether cathepsin K activity is different in the cells of individuals with metastatic and non-metastatic breast and prostate cancers, and the role of cathepsin K in cardiovascular diseases, such as stroke, in children with sickle cell anemia. They are also examining whether cathepsin K plays a role in the inflammation associated with HIV.

"This research should provide new information on a number of existing pathophysiological conditions where cathepsin K activity had been previously undetectable," added Platt.

## **Headline 9: AstraZeneca Announces Results Of Recentin HORIZON II Phase III Trial In Metastatic Colorectal Cancer**

**Published by:** Scientist Live

**Date of Publication:** June 01, 2010

**Source:** <http://www.scientistlive.com/>

AstraZeneca announced the top-line results of the HORIZON II Phase III study evaluating RECENTIN (cediranib) for the first-line treatment of metastatic colorectal cancer (mCRC). Cediranib met the co-primary endpoint of improving progression-free survival (PFS) but showed no improvement in overall survival (OS).

The adverse events associated with cediranib during this study were broadly consistent with previous studies. HORIZON II is the second of two pivotal studies of cediranib in first-line mCRC. In March, the

HORIZON III study of cediranib plus chemotherapy versus bevacizumab plus chemotherapy did not meet the primary endpoint of PFS.

Based on the results of these two trials, AstraZeneca does not intend to file regulatory submissions in first-line mCRC.

The results of a Phase III study evaluating cediranib for the treatment of recurrent glioblastoma (REGAL) are expected soon. In addition, AstraZeneca is currently examining whether cediranib may have applications in a number of different tumour types.

Data from HORIZON II and HORIZON III will be submitted to a forthcoming medical congress.

## **Headline 10: Breakthrough in Stem Cell Culturing**

**Published by:** Science Daily

**Date of Publication:** May 31, 2010

**Source:** <http://www.sciencedaily.com>

For the first time, human embryonic stem cells have been cultured under chemically controlled conditions without the use of animal substances, which is essential for future clinical uses. The method has been developed by researchers at Karolinska Institutet and is presented in the journal Nature Biotechnology.

Embryonic stem cells can be turned into any other type of cell in the body and have potential uses in treatments where sick cells need to be replaced. One problem, however, is that it is difficult to culture and develop human embryonic stem cells without simultaneously contaminating them. They are currently cultured with the help of proteins from animals, which rules out subsequent use in the treatment of humans. Alternatively the stem cells can be cultured on other human cells, known as feeder cells, but these release thousands of uncontrolled proteins and therefore lead to unreliable research results.

A research team at Karolinska Institutet has now managed to produce human stem cells entirely without the use of other cells or substances from animals. Instead they are cultured on a matrix of a single human protein: laminin-511.

"Now, for the first time, we can produce large quantities of human embryonic stem cells in an environment that is completely chemically defined," says professor Karl Tryggvason, who led the study. "This opens up new opportunities for developing different types of cell which can then be tested for the treatment of disease."

Together with researchers at the Harvard Stem Cell Institute, the researchers have also shown that in the same way they can culture what are known as reprogrammed stem cells, which have been converted "back" from tissue cells to stem cells.

Laminin-511 is part of our connective tissue and acts in the body as a matrix to which cells can attach. In the newly formed embryo, the protein is also needed to keep stem cells as stem cells. Once the embryo begins to develop different types of tissue, other types of laminin are needed.

Until now, different types of laminin have not been available to researchers, because they are almost impossible to extract from tissues and difficult to produce. Over the last couple of decades, Karl

Tryggvason's research group has cloned the genes for most human laminins, studied their biological role, described two genetic laminin diseases and, in recent years, even managed to produce several types of laminin using gene technology. In this latest experiment, the researchers produced the laminin-511 using recombinant techniques.

### **Headline 11: [Novavax Announces Publication of a Pre-clinical Study with Its Pandemic 2009 H1N1 Influenza Virus-Like Particle \(VLP\) Vaccine](#)**

**Published by:** Medical news

**Date of Publication:** May 15, 2010

**Source:** <http://www.medicalnewstoday.com>

Novavax, Inc. (Nasdaq: NVAX) announces the first report of a vaccine protecting ferrets against the 2009 pandemic H1N1 virus has been published in the journal Vaccine May 12, 2010 online issue. Scientists from Novavax and the Centers for Disease Control and Prevention (CDC) based in Atlanta, GA, under a collaborative agreement, co-authored the scientific report.

Novavax produced a 2009 H1N1 influenza VLP vaccine and delivered it to the CDC in less than four (4) weeks following the April 24, 2009 announcement of the strain of the H1N1 influenza for vaccines. CDC scientists immunized ferrets with 3.75, 7.5, or 15.0 mcg dose of 2009 H1N1 influenza VLP vaccine or a placebo then boosted with a second dose after three (3) weeks. The H1N1 influenza VLP vaccine was highly immunogenic and all vaccinated animals, even in the lowest 3.75 mcg dose group, developed hemagglutination inhibition (HI) antibody titers of 1:40 or higher, which is considered a protective level of immunity. Vaccinated animals were challenged with nasal exposure of live H1N1 influenza virus isolated. Three (3) days post challenge, animals immunized with the 15 mcg dose of the H1N1 influenza VLP vaccine had no detectable virus recovered in nasal washes and showed no signs of disease. In contrast, control animals that received no vaccine were not protected from virus replication and became ill.

Dr. Rahul Singhvi, President and CEO of Novavax, stated: "This study demonstrated in real time the ability of our influenza VLP technology to respond quickly with an effective vaccine in the face of an influenza pandemic. We are pleased with the publication of this important study."

The published report concludes: "this study demonstrates that effective immunity to H1N1 pandemic virus can be achieved in ferrets by VLP vaccination, resulting in significant protection and viral clearance from the upper and lower respiratory tracts. Recombinant VLP vaccines are non-infectious and have advantages in safety and manufacturing. They circumvent problems like slow growth, unpredictable yields, and mutations during host adaptation. Thus, rapid response immunization strategy for pandemic influenza outbreaks could include the preparation of VLP vaccine for prevention of disease in people."

### **Headline 12: [Viruses against cancer](#)**

**Published by:** Scientist Live

**Date of Publication:** May 05, 2010

**Source:** <http://www.scientistlive.com/>

Particular parvoviruses normally infect rodents, but they are also infectious for human cells. However, they do not cause any disease symptoms in humans. Most importantly, these viruses have an astonishing property: They kill infected tumour cells without causing any damage to healthy tissue. Therefore, scientists in the teams of Jean Rommelaere and Jörg Schlehofer at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have been investigating over the past years whether these viruses can be used as weapons against cancer.

Many different viruses have been tested before in cancer therapy, particularly for treating those types of cancer for which there are no effective established treatment methods. The DKFZ researchers realised early on that parvovirus H-1 has important advantages over other viruses. Now they have been the first to prove that malignant glioblastomas regress completely as a result of treatment with these viruses.

The treatment experiments were conducted in rats who had received brain tumour cells by implantation. Once the resulting brain tumours had reached a specified size, the animals were given parvoviruses, either by direct injection into the tumour or via the blood stream. In those animals in which the viruses had been injected directly into the tumour, the tumours shrank visibly after only three days and even disappeared completely in eight of twelve animals treated. The rodents survived without any symptoms, while untreated control animals suffered from severe disease symptoms within three weeks following tumour cell implantation. In the intravenously treated group, tumours regressed completely in six of nine animals. The animals have survived for more than one year now without any symptoms or late side effects of therapy.

The researchers found no infection-related damage in the nervous tissue surrounding the tumour. The viruses did not spread to the whole organism. Although parvovirus DNA was detectable in all organs after several days following virus transfer, this was only for a short time. The viruses had infected healthy cells, but these did not produce a new virus generation. However, in the tumour tissue, the viruses reproduced and viral protein production was detected only in these cells. In rats that did not bear tumours, the viruses did not reproduce. Thus, it appears that the presence of cancer cells is a necessary condition for the parvoviruses to reproduce.

After the positive results of these experiments the DKFZ researchers are convinced that parvoviruses are suitable candidates for use in cancer treatment. Professor Jean Rommelaere summarizes the reasons why: "Parvovirus H-1 does not cause any disease symptoms in humans. Since we are normally not immune against rodent viruses, it is not immediately eliminated by the human immune system after injection. Parvoviruses kill tumours due to natural properties so that their genetic material does not need to be genetically manipulated like herpes viruses, polio viruses or adenoviruses, which have been used in other studies. Moreover, they do not incorporate their genetic material into the host cell's genome, so we need not fear that they might 'accidentally' boost growth-promoting genes."

Rommelaere's colleague, Jörg Schlehofer, adds two more qualities that could be decisive for therapy of glioblastomas, in particular: "Parvoviruses pass the blood brain barrier so that they can be administered via the blood stream. In addition, they reproduce in cancer cells, which is particularly

important for successful treatment of glioblastoma with its diffuse growth. Thus, the second generation viruses reach and eliminate even those cancer cells that have already settled at some distance from the primary tumour."

### **Parvovirus therapy to be tested in clinical trial**

The promising results in the animal model have encouraged the DKFZ scientists, jointly with Dr. Karsten Geletneky of the Neurosurgery Department of Heidelberg University, to plan a clinical trial on the treatment of advanced glioblastomas. Glioblastoma is considered the most threatening type of brain tumour; only about half of those affected survive the first year after diagnosis. Even innovative drugs that have been made available recently can prolong survival only marginally. Therefore, new treatment approaches for this type of cancer are urgently needed.

Preparing such a trial is a tremendous effort. Thus, large amounts of virus have to be produced under controlled conditions for toxicological tests. Therefore, even a large institute like DKFZ could not afford financing a transfer of these results into clinical practise. Continuation of viral therapy development was made possible only by funds from Munich-based company Oryx. The company aims to provide funds for the development of therapeutically effective substances into clinically applicable drugs in an early stage.

Many of the required toxicological data have already been obtained and submitted to the drug approval authority by the researchers so that they expect to be able to admit the first patients to the trial by the end of the year. In addition, DKFZ and Oryx have recently signed another agreement: Oryx will also get involved in the development of a parvovirus therapy against pancreatic cancer.

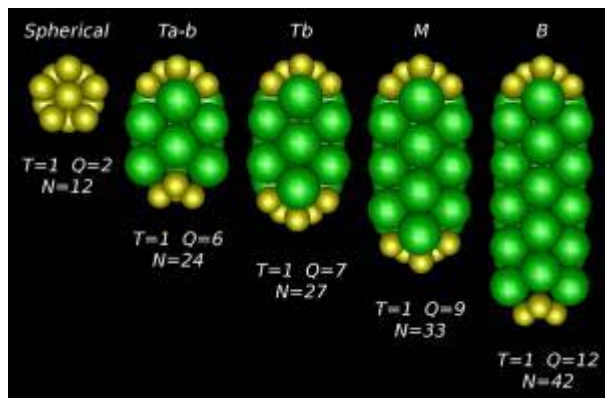
### Headline 1: Physical Model Describes Structures of Viral Capsids

**Published by:** Science Daily

**Date of Publication:** June 21, 2010

**Source:** <http://www.sciencedaily.com>

The genetic material of viruses is shielded by a protective protein covering called a capsid. The UB researchers David Reguera and Antoni Luque, of the Department of Fundamental Physics, have uncovered the strict selection rules that define capsid structure in spherical and bacilliform viruses, which they report in two papers published in the *Proceedings of the National Academy of Sciences* and the *Biophysical Journal*.



*Gallery of the bacilliform structures proposed by the physical model for the different sizes of alfalfa mosaic virus. (Credit: Image courtesy of Universidad de Barcelona)*

The main conclusion of the study is that viral capsids can only adopt a finite range of radii, lengths and protein numbers, making it possible to calculate and characterize all of their possible structures. "This model marks an important step towards understanding the viral assembly process and opens the way for controlling this process for applications in biotechnology, such as gene therapy, and applications in nanotechnology, for example in the creation of nanoscale moulds with highly precise dimensions for designing nanostructures," explains David Reguera.

Viral capsids are formed through a process of self-assembly governed by a universal physical principle: energy minimization. Based on this knowledge, it was possible to identify the potentially optimal architectures of viral capsids; that is, those structures which minimize the energy requirement. As Reguera explains, "we have found that the well-defined geometry observed in different spherical and bacilliform viruses is a product of free-energy minimization in the interaction between the different structural units of which the capsid is composed."

Since the 1960s scientists have known that spherical viruses adopt a clearly defined structure with icosahedral symmetry, formed by groups of six and five proteins (hexamers and pentamers, respectively), similar to the panel structure of a football, for example. In the case of bacilliform viruses, however, the structure had not been clearly identified. The results of this new study suggest that the capsids of bacilliform viruses are generally formed by a tube-like central body, the ends of which are closed by icosahedral caps centred on one of the three axes of symmetry. These structures are similar to those of fullerenes and carbon nanotubes and have the advantage of being highly stable and resistant.

Reguera and Luque, with support from the researcher Roya Zandi, of the University of California, applied a simple physical model and found that the local energy is minimal for bacilliform capsids formed by a specific, discrete number of proteins distributed in a cylindrical body of hexamers and closed by isocahedral caps centred along the 5-, 3- and 2-fold axes.

The study corroborates the existence of this type of viral structure and, with the complimentary geometric model, serves as the basis for reproducing the architecture of spherical and bacilliform viruses *in vivo* and *in vitro* and for making informed predictions. The models have been successfully applied to several known viruses and confirm many of the hypotheses from earlier studies regarding the structure of the alfalfa mosaic virus, which adopts different lengths depending on the quantity of genetic material contained. Given that the different lengths correspond to the rules set out in the model, it has been possible to obtain definitive models of the finite possible structures.

## **Headline 2: Bacteria Converted Into 'mini-Factories' For Biofuels and Vaccines**

**Published by:** Science Daily

**Date of Publication:** June 11, 2010

**Source:** <http://www.sciencedaily.com>

Scientists at the University of Kent and University College Cork have manipulated simple bacteria into constructing internal compartments where biofuels and vaccines can be produced.

These micro-compartments eventually occupy almost 70 percent of the available space in a bacteria cell, enabling segregation of metabolic activities and, in the era of synthetic biology, representing an important tool by which defined micro-environments can be created for specific metabolic functions.

Martin Warren, Professor of Biochemistry at the School of Biosciences, University of Kent, explained: 'Synthetic biology is really exciting because we can produce some important and useful products that can be difficult and expensive to make using traditional chemistry techniques. Bacteria can make these things very easily and in large quantities if we develop bacteria with the right characteristics to do so efficiently.

'What we often do is to make sure that the desired product is made within one or more tiny compartments that already exist inside the bacteria. This means that the process doesn't get caught up or slowed down by everything else that is going on in the cell and so is much more efficient.'

It is envisaged that these micro-compartments could be modified for the synthesis of ethanol or even hydrogen gas, which could reduce the human need for many oil-derived products, including certain medicines. The team is currently working on ways to produce new antibiotics within these compartments.

Michael Prentice, Professor of Medical Microbiology at the University College Cork, said: 'Using these compartments, simple bacteria like E.coli can make chemicals that would normally be deadly for them. The bacteria are partially protected because the chemicals are being made within compartments inside their cells. We are working on ways to use these 'factories' to produce substances that will kill other harmful bacteria.'

The research was funded by the Biotechnology and Biological Sciences Research Council (BBSRC) and Science Foundation Ireland.

### **Headline 3: How RNA Viruses Copy Themselves: Hijack Cellular Enzyme to Create Viral Replication Factories on Cell Membranes**

**Published by:** Science Daily

**Date of Publication:** May 30, 2010

**Source:** <http://www.sciencedaily.com>

Nihal Altan-Bonnet, assistant professor of cell biology, Rutgers University in Newark, and her research team have made a significant new discovery about RNA (ribonucleic acid) viruses and how they replicate themselves.

Certain RNA viruses -- poliovirus, hepatitis C virus and coxsackievirus -- and possibly many other families of viruses copy themselves by seizing an enzyme from their host cell to create replication factories enriched in a specific lipid, explains Altan-Bonnet. Minus that lipid -- phosphatidylinositol-4-phosphate (PI4P) -- these RNA viruses are not able to synthesize their viral RNA and replicate. The key structural components on cell membranes, lipids often serve as signaling molecules and docking sites for proteins.

Viral replication is the process by which virus particles make new copies of themselves within a host cell. Those copies then can go on to infect other cells. An RNA virus is a virus that has RNA, rather than DNA, as its genetic material. Many human pathogens are RNA viruses, including SARS virus, West Nile virus, HIV, and the ones Altan-Bonnet has been studying.

As reported in the May 28, 2010 issue of *Cell*, Altan-Bonnet and her co-researchers for the first time have uncovered that certain RNA viruses take control of a cellular enzyme to design a replication compartment on the cell's membrane filled with PI4P lipids. Those lipids, in turn, allow the RNA viruses to attract and stimulate the enzymes they need for replication. In uninfected cells, the levels of PI4P lipids are kept low, but in virally infected cells those levels increase dramatically. The findings by Altan-Bonnet and her colleagues not only open several possibilities for preventing the spread of various viral infections, but also may help to shed new light on the regulation of RNA synthesis at the cellular level and potentially on how some cancers develop.

"The goal of the virus is to replicate itself," notes Altan-Bonnet. "For its replication machines to work, the virus needs to create an ideal lipid environment which it does by hijacking a key enzyme from its host cell."

Altan-Bonnet and her team also were able to identify the viral protein (the so-called 3A protein in poliovirus and coxsackievirus infections) that captures and recruits the cellular enzyme (phosphatidylinositol-4-kinase III beta). Additionally, her lab was able to impede the replication process by administering a drug that blocked the activity of the cellular enzyme once it had been hijacked. Drug therapies to prevent viral replication potentially also could be targeted to prevent the hijacking of the enzyme.

Once that enzyme is hijacked, cells are prevented from normally operating their secretory pathway, the process by which they move proteins to the outside of the cell. In many cases, the impeding of that process can result in the slow death of the cell, leading to such problems as cardiac and vascular complications in those infected with the coxsackievirus and neurological damage in those with poliovirus.

Utilizing their recent findings, Altan-Bonnet and her team now plan to investigate PI4P dependence in other viruses as well as the role other lipids may play in different virus families. For example, the SARS virus also requires a lipid-rich environment for its replication, so her lab now is working with SARS researchers on determining what lipid is necessary for that virus's replication. In addition, they will be examining the role of lipids in regulating RNA synthesis in cells, potentially providing new insight into some of the cellular mutations that occur in cancer.

"Given that a lot of what we know about cellular processes historically comes from the study of viruses, our studies may provide insight into the novel roles lipids play in regulating the expression of genetic material in cells," notes Altan-Bonnet.

Altan-Bonnet's research into RNA replication is supported with grants from the National Science Foundation and the Busch Foundation.

#### **Headline 4: New Weapon against Highly Resistant Microbes within Grasp**

**Published by:** Science Daily

**Date of Publication:** May 28, 2010

**Source:** <http://www.sciencedaily.com>

An active compound from fungi and lower animals may well be suitable as an effective weapon against dangerous bacteria. We're talking about plectasin, a small protein molecule that can even destroy highly resistant bacteria . Researchers at the Universities of Bonn, Utrecht, Aalborg and of the Danish company Novozymes AS have shed light on how the substance does this. The authors see plectasin as a promising lead compound for new antibiotics.

*These results will be published in Science journal on 28th May.*

More and more bacteria are becoming resistant to normal antibiotics. This is especially true for the methicillin-resistant *Staphylococcus aureus* (MRSA). Most of the pharmaceutical weapons are now useless against these MRSA strains . According to estimates, as many as every second patient in the USA treated by intensive-care medicine comes down with an MRSA infection.

Plectasin could shift the balance of power back in the doctors' favour. But how exactly does the little protein molecule do that? The Bonn researchers in Dr. Tanja Schneider and Professor Hans-Georg Sahl's team have answered these questions together with Danish and Dutch colleagues. Thus plectasin disrupts the forming of the cell wall in bacteria so that the pathogens can no longer divide.

## **Headline 5: Revealing the Metabolic Activity of Microbial Communities: New Method for Tracing Carbon Flux**

**Published by:** Science Daily

**Date of Publication:** May 27, 2010

**Source:** <http://www.sciencedaily.com>

Microbial communities are performing important functions all around us -- from the earth in our flowerpots to the human gut. Now researchers have developed a method for studying the metabolic functions of microbial communities in detail. It is now possible for the first time, thanks to a new algorithm developed at the UFZ, to use the incorporation of stable carbon isotopes into proteins to investigate natural remineralisation processes in much greater detail, to identify relevant key species and to study the way they interact in complex decomposition processes.

The new Protein-SIP technique makes it possible to measure carbon flux in microbial communities very accurately, say researchers from the Helmholtz Centre for Environmental Research (UFZ), the Max Planck Institute for Infection Biology and the Universities of Oslo and Greifswald writing in *Molecular and Cellular Proteomics*.

Although in the past it was possible to identify species with metabolic activity using DNA or RNA analyses, the new method can also identify carbon flux and therefore food chains within a microbial community. This means that it is now possible to analyse the interaction between individual groups of micro-organisms within a community.

Microbiologists all over the world are currently working hard to explore the world of bacteria living on and in the human body. The scope of potential applications is huge and could range from forensic medicine and simpler medical diagnosis to entirely new treatments. However, simply identifying the genes is not enough, because bacteria do not live on their own, but in large communities. "It's like a city with lots of people. Imagine a fire breaks out. Normally, fire-fighters would deal with it, but if there are no fire-fighters around, other people have to step in to prevent disaster," explains Dr Ingo Fetzer of the UFZ. "But who is responsible for what within these microbial communities?" This is an important question that scientists are only just starting to investigate." And it is not just human gut flora that are at issue. Microbes are tiny organisms that, unseen by the human eye, control all the major biological processes on earth -- from the global carbon cycle to the remineralisation of organic material and the breakdown of harmful substances.

The number of species of higher organisms on the planet is estimated to be between five and 100 million. There are only vague conjectures about the number of species of micro-organisms. This means that researchers have to concentrate on just a few species. So how is it possible to identify the key organisms within the microbial communities? In order to answer this question more easily, researchers at the Helmholtz Centre for Environmental Research combined the use of stable isotopes with protein measurements using mass spectrometry and bioinformatics.

In the new method, microbial communities are fed a carbon source containing the heavy, non-radioactive isotope  $^{13}\text{C}$  as well as normal carbon,  $^{12}\text{C}$ . The two isotope masses differ by 1.0035 atomic mass units. Because they are stable isotopes, the method is also known as Stable Isotope Probing (SIP). Once the bacteria have consumed the isotope-marked substrate, the  $^{13}\text{C}$  atoms are

incorporated into the bacterial proteins. The bacteria that make use of the substrate itself incorporate the <sup>13</sup>C first. Other species of bacteria only make use of metabolites from the first group and incorporate less <sup>13</sup>C into their proteins and do so later.

For the analysis, the proteins of all the bacterial species from a sample are extracted and cut into specific fragments using the enzyme trypsin. The fragments are analysed using a mass spectrometer to determine the amino acid sequence of the peptides. When compared with a genome database, this reveals a peptide's origin, i.e. the bacterium it comes from. Peptides are protein fragments -- organic compounds containing a number of amino acids. These consist primarily of carbon and nitrogen, which are two of the basic building blocks of all molecules within organisms and are therefore passed on even in mixed microbial cultures. In a second step, the researchers calculate the level of <sup>13</sup>C incorporation. The <sup>13</sup>C level then provides an elegant, direct and accurate measure of the metabolic activity of the species in question.

"We first tested this key technology in 2008 in a joint project conducted by two UFZ departments to analyse the metabolic activity of one specific species of bacteria within a mixed culture. We have been studying the structure and function of the microbial communities involved in the breakdown harmful substances for years. But it is only with the advent of the new mass spectrometers and their more accurate measurements that we have been able to achieve a breakthrough in developing the method," says project coordinator Dr Martin von Bergen from the Department of Proteomics

Now it is possible to calculate the level of <sup>13</sup>C incorporation into the peptides using the decimal places of the peptide masses. The researchers make use of the 0.0035 deviance in atomic mass units over and above the theoretically precise figure of 1.000 atomic mass units between <sup>12</sup>C and <sup>13</sup>C. Since there are more than 20 carbon atoms in a peptide, the decimal places are shifted over around 0.07 atomic mass units. Prof. Hauke Harms from the Department of Environmental Microbiology is very pleased with the new method: "Our new algorithm will make research work much easier in future. The method offers great potential for studying communities, which are at the heart of microbial ecology."

With support from the German Research Foundation (DFG) and the EU, researchers will now identify the key organisms in the breakdown of environmental pollutants such as benzene and polycyclic hydrocarbons in the absence of oxygen. "In conjunction with other techniques, Protein-SIP is a very good tool for investigating the food web involved in the breakdown of benzene, for example. Protein-SIP is already being used in projects with national and international partners to identify the metabolic activities of methane bacteria from oil deposits and the methane cycle in marine sediments," Dr Hans Richnow (Department of Isotope Biogeochemistry) adds. These projects are of relevance for securing energy supplies and conserving the quality of the environment.

The Protein-SIP method makes it possible to trace the carbon flux within mixed bacterial cultures. Other potential applications include the treatment of biofilms, such as those used in sewage works, and the optimisation of biogas generation processes and the analysis of the human intestine. The next step for the Leipzig-based researchers is to examine the relationship between the intestinal bacteria of termites and earthworms and their host organisms.

## **Headline 6: Chemical Compound Effective in Destroying Antibiotic-Resistant Biofilms**

**Published by:** Science Daily

**Date of Publication:** April 8, 2010

**Source:** <http://www.sciencedaily.com>

Researchers at North Carolina State University have found a chemical compound that, when used in conjunction with conventional antibiotics, is effective in destroying biofilms produced by antibiotic-resistant strains of bacteria such as the Staphylococcus strain MRSA and Acinetobacter. The compound also re-sensitizes those bacteria to antibiotics.

Infections from antibiotic-resistant bacteria such as MRSA are especially difficult to get rid of because the bacteria can attach to surfaces and then create biofilms, sticky layers of cells that act as a shield and prevent antibiotics from destroying the bacteria underneath. While a limited number of existing antibiotics may destroy part of the biofilm, enough bacteria survive to create a recurring infection as soon as antibiotic therapy stops, and over time the surviving bacteria build resistance to that antibiotic.

NC State chemist Dr. Christian Melander had already shown that combining a compound made from a class of molecules known as 2-aminoimidazoles with antibiotics was effective in dispersing the biofilms created by certain bacterial strains. The next step was to see if this combination could remove resistant bacteria from surfaces.

"The problem with biofilms is that even if you treat with effective antibiotics, they never succeed in completely dispersing the biofilm and killing the bacteria on the surface they've stuck to," Melander says. "This is especially exacerbated when the bacteria are antibiotic-resistant. Basically, if you are trying to treat a multi-drug resistant bacterial infection, you need to worry about both the bacteria forming a biofilm and disarming their antibiotic resistance genes."

Melander and his team, in collaboration with NC State biochemist John Cavanagh, found that pre-treating the bacteria with their compound and then introducing the antibiotic penicillin one hour later increased the penicillin's effectiveness 128-fold, even when the bacteria was penicillin resistant. The antibiotics also provided a 1,000-fold enhancement to the ability of the 2-aminoimidazole to disperse biofilms.

The researchers' results were published online March 8 in the journal *Antimicrobial Agents and Chemotherapy*.

"We had two goals in mind -- to overcome antibiotic resistance and to disperse biofilms," Melander says. "This compound cooperates with conventional antibiotics, overcoming an infectious threat that would otherwise persist if treated with either agent individually."

The Department of Chemistry is part of NC State's College of Physical and Mathematical Sciences, and the Department of Biochemistry is a part of the College of Agriculture and Life Sciences

## **Headline 7: Flu Jab for Bacteria**

**Published by:** Science Daily

**Date of Publication:** April 6, 2010

**Source:** <http://www.sciencedaily.com>

Viruses can wreak havoc on bacteria as well as humans and, just like us, bacteria have their own defence system in place, explains Professor John van der Oost, at the Society for General Microbiology's spring meeting. Uncovering the workings of the bacterial "immune system" could be used to keep industrial microbes at peak performance.

Professor van der Oost and his team at Wageningen University in the Netherlands have spent the last three years working out the molecular details of the immune system called CRISPR that is present in bacteria. The recently discovered CRISPR defence system differs from the immune system in higher organisms in that acquired immunity can be passed down future generations. This means bacterial offspring are protected from viral attack even before they are exposed to the invading virus.

Specific bacterial proteins recognise infectious viruses, called bacteriophages, by detecting foreign DNA. These proteins take the viral DNA and insert it into the bacterial genome at very specific locations. "Storing the information in this way gives the bacteria a lasting 'memory' of the harmful virus that subsequently confers immunity- much like our own immune systems," said Professor van der Oost. Upon future attack by the same virus, the DNA sequence of the invader is quickly recognised and destroyed by the bacteria.

Understanding the exact mechanisms of the CRISPR defence system could have big economic rewards for industry. "We can exploit this system and expose bacteria to artificial or modified bacteriophages whose DNA could be stored. This would be exactly like giving them a flu jab and protect them against a real attack in the future. For industrially-important bacteria this could be a great cost-saving method to reduce viral infections that may compromise yields of bacterial products. It's a classic example of vaccinating the workforce to increase its productivity."

## Section D: Nano Technology

### **Headline 1: Asymmetric Nanostructures for Early and More Accurate Prediction of Cancer**

**Published by:** Science Daily

**Date of Publication:** June 24, 2010

**Source:** <http://www.sciencedaily.com>

Researchers at the nanotechnology research centre imec (Leuven, Belgium) have demonstrated biosensors based on novel nanostructure geometries that increase the sensitivity and allow detecting extremely low concentrations of specific disease markers. This paves the way to early diagnostics of for example cancer by detecting low densities of cancer markers in human blood samples.

Functionalized nanoparticles can identify and measure extremely low concentrations of specific molecules. They enable the realization of diagnostic systems with increased sensitivity, specificity and reliability resulting in a better and more cost-efficient healthcare. And, going one step further, functionalized nanoparticles can help treat diseases, by destroying the diseased cells that the nanoparticles bind to.

Imec aims at developing biosensor systems exploiting a phenomenon known as localized surface plasmon resonance in noble metal (e.g. gold and silver) nanostructures. The biosensors are based on optical detection of a change in spectral response of the nanostructures upon binding a disease marker. The detection sensitivity can be increased by changing the morphology and size of the noble metal nanostructures. The biosensor system is cheap and easily extendable to multiparameter biosensing.

Imec now presents broken symmetry gold nanostructures that combine nanorings with nanodiscs. Combining different nanostructures in close proximity allows detailed engineering of the plasmon resonance of the nanostructures. More specifically, imec targeted an optimization of both the width of the resonance peak and the resonance shift upon binding of the disease marker. With respect to these parameters, the new geometries clearly outperform the traditional nanospheres. Therefore, they are better suited for practical use in sensitive biosensor systems.

"With our bio-nano research, we aim at playing an important role in developing powerful healthcare diagnostics and therapy. We work on innovative instruments to support the research into diseases and we look into portable technologies that can diagnose diseases at an early stage. We want to help the pharmaceutical and diagnostic industry with instruments to develop diagnostic tests and therapies more efficiently;" said Prof. Liesbet Lagae, program manager HUMAN++ on biomolecular interfacing technology.

Some of these results were achieved in collaboration with the Catholic University of Leuven (Leuven, Belgium), Imperial College (London, UK) and Rice University (Houston, Texas).

### **Headline 2: Nanoparticles: Peering Into the Never-Before-Seen**

**Published by:** Science Daily

**Date of Publication:** June 17, 2010

**Source:** <http://www.sciencedaily.com>

Scientists can now peer into the inner workings of catalyst nanoparticles 3,000 times smaller than a human hair within nanoseconds.

The findings point the way toward future work that could greatly improve catalyst efficiency in a variety of processes that are crucial to the world's energy security, such as petroleum catalysis and catalyst-based nanomaterial growth for next-generation rechargeable batteries. The work was performed in a collaborative effort by Lawrence Livermore National Laboratory and the University of California at Davis.

Using a new imaging technique on Lawrence Livermore's Dynamic Transmission Electron Microscope (DTEM), researchers have achieved unprecedented spatial and temporal resolution in single-shot images of nanoparticulate catalysts.

The DTEM uses a laser-driven photocathode to produce short pulses of electrons capable of recording electron micrographs with 15-nanosecond (one billionth of a second) exposure time. The recent addition of an annular dark field (ADF) aperture to the instrument has greatly improved its ability to time-resolve images of nanoparticles as small as 30 nanometers in diameter.

"Nanoparticles in this size range are of crucial importance to a wide variety of catalytic processes of keen interest to energy and nanotechnology researchers," said UC Davis' Dan Masiel, formerly of LLNL and lead author of a paper appearing in the journal, *ChemPhysChem*. "Time-resolved imaging of such materials will allow for unprecedented insight into the dynamics of their behavior.

"Previously, particles smaller than 50 nanometers could not be resolved in the 15-nanosecond exposure because of the limited signal and low contrast without ADF aperture. But by using DTEM's ADF, almost every 50-nanometer particle and many 30-nanometer ones became clearly visible because of the fast time resolution and high contrast.

"The stark difference between these two images clearly demonstrates the efficacy of annular dark field imaging when imaging samples with feature sizes near the resolution limit of DTEM," Masiel said.

The new technique makes it easier to discern significant features when compared to bright field pulsed imaging. It allows for vastly improved contrast for smaller particles, widening the range of catalyst systems that can be studied using DTEM.

DTEM can record images with six orders of magnitude higher temporal resolution than conventional TEM and can provide important insights into processes such as phase transformations, chemical reactions and nanowire and nanotube growth.

Co-authors include LLNL's Bryan Reed, Thomas LaGrange, Geoffrey Campbell, Ting Guo and Nigel Browning. The work was funded by the Department of Energy's Office of Science, Office of Basic Energy Sciences, Materials Sciences and Engineering Division.

### **Headline 3: [Scientist Speaks on New Discoveries](#)**

**Published by:** Science Daily

**Date of Publication:** June 16, 2010

**Source:** <http://www.sciencedaily.com>

Scientists who work at the atomic and molecular levels -- nanoscale -- have to think big. After all, it is at this level where everything happens.

Alexandra Navrotsky, Distinguished Professor at the University of California, Davis, and Director of its Nanomaterials in the Environment, Agriculture, and Technology Organized Research Unit, has studied the properties of nanoparticles throughout her career. She presented her findings in Knoxville, Tenn., at the Goldschmidt Conference, hosted by the University of Tennessee, Knoxville, and Oak Ridge National Laboratory.

"Nanoparticles are everywhere. You eat them, drink them, breathe them, pay to have them, and pay even more to get rid of them," Navrotsky said. Nanomaterials science deals with particles that are about one billionth of a meter long.

During the conference, Navrotsky spoke on recent discoveries she and Ph.D. student Chengcheng Ma made on the thermodynamic properties of transition metal oxides such as insulators and superconductors.

Navrotsky's research group found that the thermodynamic driving force -- the energy needed for oxidized reactions -- depends strongly on particle size. The ease with which these materials change their oxidation state is important in all kinds of applications, for example, the catalytic splitting of water for the production of hydrogen and oxygen, the metabolism of microorganisms and the evolution of mineral deposits.

Since chemical and biological reactions occur on the surface of a particle, these activities are enhanced at the nanoparticle scale. An understanding of the way nanoparticles react under certain temperatures and other conditions can be applied to many areas of science, including communication technology; agricultural technology; environmental remediation; interactions in the oceans, atmosphere, and biosphere; and biotechnology for medicine and health.

For example, the thermodynamics at the nanoscale in a battery affects its voltage output, so understanding this principle can help scientists make a more efficient battery.

## Section E: Pharmaceuticals

### Headline 1: APP Pharma to sell generic breast cancer drug

**Published by:** The Associated Press

**Date of Publication:** June 29, 2010

**Source:** <http://www.businessweek.com>

APP Pharmaceuticals Inc. will join Mylan Inc. and Teva Pharmaceutical Industries Ltd. in marketing generic versions of AstraZeneca PLC's breast cancer drug Arimidex.

APP Pharmaceuticals said Tuesday it will immediately start selling 1-milligram tablets of anastrozole in the United States after the Food and Drug Administration granted marketing approval to Fresenius Kabi Oncology Ltd. Both businesses are units of Germany's Fresenius Kabi Pharmaceutical Holding Inc.

The drug is used to treat some forms of breast cancer in postmenopausal women. APP Pharmaceuticals said 2009 U.S. sales of Arimidex totaled about \$917 million.

Mylan also said Tuesday it received regulatory approval to sell a generic version of Arimidex. On Monday, the FDA approved Teva's version of the drug.

### Headline 2: Data shows no increased risk of cardiovascular events associated with Symlin treatment in patients with type 2 diabetes

**Published by:** PharmaBiz

**Date of Publication:** June 29, 2010

**Source:** <http://www.pharmabiz.com>

Amylin Pharmaceuticals, Inc. announced results from an analysis of an integrated database of clinical studies that showed no increased risk of cardiovascular (CV) events associated with Symlin (pramlintide acetate) injection use compared to a pooled comparator group treated with either placebo or rapid-acting insulin. These findings were presented at the 70th Annual Scientific Sessions of the American Diabetes Association (ADA) in Orlando, Florida.

The meta-analysis included five completed, randomized, controlled clinical trials of 16 to 52 weeks' duration, and was based on the US Food and Drug Administration's (FDA's) recent guidance for evaluating CV risk in new type 2 diabetes agents. The primary endpoint for this analysis was occurrence of primary major adverse CV events (MACE). The 95 per cent confidence interval for the estimated risk ratio for the primary endpoint was 0.55 to 1.34. With the upper limit below the FDA-specified threshold of 1.8, this suggests that there is no increase in CV risk associated with Symlin use.

"People with diabetes are two to four times more likely to develop cardiovascular disease because of increased risk factors such as high blood pressure, lipid disorders and obesity," said Orville G. Kolterman, M.D., senior vice president, chief medical officer at Amylin. "Symlin is an important tool for many patients who struggle to achieve their glucose control targets, despite their best efforts with

insulin. These safety analyses confirm our findings from individual clinical studies and provide additional insight into the CV safety profile of Symlin use in type 2 diabetes."

In this integrated analysis, 1,434 Symlin subjects and 582 pooled comparator subjects were treated for a total of 957 and 359 patient-years of exposure, respectively. Subjects in both groups received at least one type of insulin, and in some cases, oral antidiabetic agents. The mean age (56-57 years), body mass index (32-33 kg/m<sup>2</sup>), and blood sugar as measured by A1C, a measure of average blood sugar over three months, (9.0-9.1 per cent) were comparable between the treatment groups.

The primary endpoint was occurrence of primary major adverse CV events (MACE), including CV mortality, myocardial infarction, stroke, acute coronary syndrome hospitalization, and urgent revascularization procedures. The relative risk between the Symlin and pooled comparator groups was 0.86 (95 percent confidence interval: 0.55-1.34). The hazard ratios for primary MACE ranged from 0.88 to 0.93, depending on the analysis method (95 percent confidence interval: 0.56-1.38). Additional analyses of narrower and broader MACE definitions resulted in similar findings with the upper limit of the 95 percent confidence interval below 1.8 for most CV endpoints and analysis methods. These data suggest that Symlin treatment in patients with type 2 diabetes is not associated with an increased risk of CV adverse events.

The findings from this meta-analysis are further supported by an analysis of post-marketing reports, which have not revealed evidence of a signal for CV risk in an estimated cumulative exposure of 67,540 patient-years since the launch of Symlin in 2005.

Taken at mealtime, Symlin is the first and only amylin mimetic for use in patients with diabetes treated with mealtime insulin. Symlin is a synthetic analog of human amylin, a naturally occurring hormone that is made in the beta cells of the pancreas, the same cells that make insulin. In patients with type 2 diabetes who use insulin, and in patients with type 1 diabetes, those cells in the pancreas are either damaged or destroyed, resulting in reduced secretion of both insulin and amylin after meals. The use of Symlin contributes to glucose control after meals.

The SymlinPen (pramlintide acetate) pen-injector is an easy way for patients to use Symlin and offers convenient pre-filled Symlin administration with simple, dial-up dosing to improve mealtime glucose control. The SymlinPen1 20 features fixed dosing to deliver 60 or 120 micrograms of Symlin per dose. The SymlinPen 60 features fixed dosing to deliver 15, 30, 45, or 60 micrograms of Symlin per dose.

Amylin Pharmaceuticals is a biopharmaceutical company dedicated to improving lives of patients through the discovery, development and commercialization of innovative medicines.

### **Headline 3: AstraZeneca and MMV Join Efforts in the Fight against Malaria**

**Published by:** WorldPharma News

**Date of Publication:** June 29, 2010

**Source:** <http://www.worldpharmanews.com>

AstraZeneca and Medicines for Malaria Venture (MMV) announced a collaborative agreement designed to identify novel candidate drugs for the treatment of malaria. The agreement will initially allow MMV access to AstraZeneca's extensive compound library. MMV will seek to identify promising

compounds with the potential to treat malaria, including drug resistant strains of the disease. AstraZeneca CEO David Brennan announced the collaboration at the Fortune/TIME/CNN Global Forum in Cape Town, South Africa.

Globally, malaria caused an estimated 863,000 deaths in 2008, mainly amongst vulnerable populations in the developing world. Today's malaria drugs require courses of treatment lasting days or even weeks and follow-up can be difficult in many malaria-endemic countries. In some cases the disease has begun to develop resistance to existing drugs - a problem exacerbated, in part, by failure to complete courses of treatment. MMV works to discover, develop and deliver new, effective and affordable anti-malarial drugs with simpler dosing regimens thereby encouraging patient compliance and helping reduce the risk of resistance developing. The ultimate goal is to find a one-dose cure for malaria.

Under the terms of the agreement, scientists working with MMV will screen 500,000 compounds in AstraZeneca's unique library for activity against *P. falciparum*, the most lethal of malaria parasites. Prof. V. Avery at the Eskitis Institute for Cell and Molecular Therapies at Griffith University in Brisbane, Australia will conduct the screening on behalf of MMV. Promising compounds identified through the screening process will be starting points for antimalarial drug discovery projects. These compounds will be progressed through a discovery cascade at AstraZeneca's R&D facility in Bangalore, India, with the aim of identifying suitable candidates for clinical testing.

David Brennan, AstraZeneca's CEO said: "Our experience with infection research, and indeed with all of our R&D efforts, has taught us that we will only find solutions to today's global health challenges through collaborative efforts. Opening up our compound library to MMV is an important step toward addressing the enormous unmet medical needs of the developing world. AstraZeneca is committed to being part of the solution and we look forward to working with MMV and all those with a stake in global health."

Tim Wells, MMV's Chief Scientific Officer said: "AstraZeneca has had a long standing interest in neglected disease, and we are delighted to be able to collaborate with the centre in Bangalore on this exciting project in malaria. The screening of their library will give us some new unique starting points. However, the additional advantage is the Indian perspective: India has millions of cases of malaria per year, and in addition has a balance between *Plasmodium falciparum* and *Plasmodium vivax*. Understanding and eliminating Indian malaria is one of the keys to eliminating malaria worldwide."

#### About MMV

Medicines for Malaria Venture, a not-for-profit public-private partnership, was established as a foundation in Switzerland in 1999. It is dedicated to the reduction of the malaria burden in disease-endemic countries with the discovery, development and delivery of new, effective and affordable antimalarial drugs. Our vision is a world in which these innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria, and help to ultimately eradicate this terrible disease.

MMV is currently managing the largest portfolio of antimalarial R&D projects ever assembled; almost 60 antimalarial projects in partnership with over 130 pharmaceutical, academic, and endemic-country partners in 44 countries. In 2009, in collaboration with partners, MMV launched its first ever product -

a sweet-tasting, paediatric formulation, Coartem® Dispersible. Two other MMV-supported artemisinin combination therapies, Eurartesim® and Pyramax®, have been submitted to the EMA for regulatory approval. Seven further potential medicines are in clinical development. For more information please visit: [www.mmv.org](http://www.mmv.org).

#### **Headline 4: New SIMPONI® (Golimumab) Data Shows Sustained Efficacy in the Treatment of Rheumatoid Arthritis**

**Published by:** WorldPharma News

**Date of Publication:** June 23, 2010

**Source:** <http://www.worldpharmanews.com>

Findings from an open-label, uncontrolled long-term extension of a Phase 3 registration trial demonstrated efficacy of SIMPONI in patients with moderately to severely active rheumatoid arthritis despite methotrexate therapy at two years. Results showed that reductions in signs and symptoms and improvements in physical function were maintained over two years with subcutaneous injections of SIMPONI® (golimumab) 50 mg or 100 mg once every four weeks. These data were presented at the 2010 European League Against Rheumatism (EULAR) Annual Congress.

#### **Long-term efficacy observed over two years**

Findings from the GOLimumab FOR Subjects With Active RA Despite MTX (GO-FORWARD) study, demonstrated that patients with active rheumatoid arthritis despite methotrexate therapy sustained positive responses to SIMPONI through week 104. A total of 444 patients 18 years of age and older were randomized to one of four treatment groups: placebo plus methotrexate (group one), SIMPONI 100 mg plus placebo (group two), SIMPONI 50 mg plus methotrexate (group three), and SIMPONI 100 mg plus methotrexate (group four). At week 16, patients with less than 20 percent improvement in swollen and tender joint counts in groups one, two and three entered early escape. At week 24, patients in group one crossed over to SIMPONI 50 mg plus methotrexate. At week 52, the trial was unblinded and patients could be dose-escalated from SIMPONI 50 mg to SIMPONI 100 mg based on clinical judgment.

The findings showed that 70 of 133 patients in group one, 60 of 133 patients in group two, 57 of 89 patients in group three and 51 of 89 patients in group four achieved at least 20 percent improvement in arthritis symptoms (ACR20) at week 104. Of the patients with improved physical function as measured by the Health Assessment Questionnaire (HAQ  $\geq$  0.25) at week 24, 43 of 47 patients in group one, 50 of 57 patients in group two, 52 of 60 patients in group three and 53 of 60 patients in group four maintained improvement.

"Our findings add to the growing body of evidence supporting the sustained efficacy of golimumab in the treatment of rheumatoid arthritis patients over time," said Edward C. Keystone, M.D., professor, Department of Rheumatology, University of Toronto/Mount Sinai Hospital, Toronto, Canada, lead investigator. "For patients with active rheumatoid arthritis, these data provide important insights in the treatment of this debilitating disease."

Patients also experienced improvement in disease activity at two years as measured by DAS28 (CRP) response. At week 104, 93 of 133 patients in group one, 80 of 133 patients in group two, 69 of 89 patients in group three and 65 of 89 patients in group four experienced improvements in disease activity. Improvements were also demonstrated in the number of tender and swollen joints. The median percent improvement in swollen joint counts of 133 patients in groups one and two was 75 percent and 56 percent respectively, and of 89 patients in groups three and four was 83 percent and 86 percent respectively. The median percent improvement in tender joint counts of 133 patients in groups one and two was 71 percent and 60 percent respectively and of 89 patients in groups three and four was 81 percent and 79 percent, respectively.

### **About the GO-FORWARD Trial**

GO-FORWARD is a placebo-controlled, double-blind, Phase 3 registration trial that demonstrates the efficacy and safety of an anti-TNF $\alpha$  agent in patients with active rheumatoid arthritis despite methotrexate therapy. The co-primary endpoints were percentage of patients achieving ACR 20 response at week 14 and improvement from baseline in HAQ at week 24. For the trial extension, analyses were based on intent-to-treat population with last observation carried forward for missing data.

Through two years, serious adverse events per 100 patient-years were 15, 27, 16 and 25 in the placebo plus methotrexate, SIMPONI 100 mg plus placebo, SIMPONI 50 mg plus methotrexate and SIMPONI 100 mg plus methotrexate treated patients, respectively, and serious infections per 100 patient-years were 2, 6, 4 and 6, respectively. Active tuberculosis was reported in two patients: one patient in the SIMPONI 50 mg plus methotrexate group and one patient in the SIMPONI 100 mg plus methotrexate group. There were sixteen malignancies; two patients in the methotrexate plus placebo group, three patients in the SIMPONI 100 mg plus placebo group, six patients in the SIMPONI 50 mg plus methotrexate group and five patients in the SIMPONI 100 mg plus methotrexate group. Three patients in the SIMPONI 100 mg plus placebo group died (sepsis, fulminant hepatic failure and complicated respiratory distress) and one patient in the SIMPONI 100 mg plus methotrexate group died (circulatory insufficiency).

### **About SIMPONI**

SIMPONI is a human monoclonal antibody that targets and neutralizes excess tumor necrosis factor (TNF)- $\alpha$ , a protein that when overproduced in the body due to chronic inflammatory diseases can cause inflammation and damage to bones, cartilage and tissue. The first once-monthly subcutaneous anti-TNF- $\alpha$  therapy, SIMPONI is approved for the treatment of moderately to severely active rheumatoid arthritis, active psoriatic arthritis and active ankylosing spondylitis, and is available either through the SIMPONI SmartJect<sup>®</sup> autoinjector or a prefilled syringe.

Centocor Ortho Biotech Inc. developed and discovered SIMPONI and has exclusive marketing rights to the product in the United States. Following regulatory approvals, Schering-Plough will assume exclusive marketing rights outside the United States except in Japan, Indonesia and Taiwan, where

SIMPONI will be co-marketed by Mitsubishi Tanabe Pharma Corporation and Janssen Pharmaceutical Kabushiki Kaisha; Hong Kong, where SIMPONI will be exclusively marketed by Janssen-Cilag; and China, where SIMPONI will be exclusively marketed by Xian-Janssen.

### **About Rheumatoid Arthritis**

Rheumatoid arthritis is a chronic and debilitating disease that affects more than three million people in Europe. Signs and symptoms of RA include pain, stiffness and motion restriction in multiple joints. Because RA is a progressive disease, it can cause permanent joint deformity and severe disability if not diagnosed early or if initial treatment is delayed. RA can occur at any age, but is most common in adults 30-50 years old and is two to three times more prevalent in women than in men. The cause of RA is unknown, although genetic factors may contribute to the disease.

### **About MSD**

Today's MSD is a global healthcare leader working to help the world be well. MSD is a tradename of Merck & Co., Inc., with headquarters in Whitehouse Station, N.J., U.S.A. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. MSD. Be well. For more information, visit [www.msd.com](http://www.msd.com).

## **Headline 5: [New Use for Old Drugs in Treating Hepatitis C](#)**

**Published by:** Science Daily

**Date of Publication:** June 09, 2010

**Source:** <http://www.sciencedaily.com>

Common drugs used to treat conditions such as diabetes and obesity could be used to successfully treat hepatitis C virus infection.

Research led by the University of Leeds has found drugs such as anti-diabetic drug Metformin and AICAR, used to combat obesity, can prevent the hepatitis C virus from replicating in the body.

Hepatitis C virus affects an estimated three per cent of the world's population and there are four million carriers of the virus in Europe alone. The virus affects the liver and recovery rates are low: only around 40 per cent of hepatitis C sufferers will fully recover, with others developing cirrhosis and in many cases, liver cancer.

"We're very excited about these findings," says Professor Mark Harris from the University's Faculty of Biological Sciences. "These drugs are already on the market, and whilst substantial clinical trials still need to take place before they can be used to treat hepatitis C infection, we think it could be an enormous step forward in the battle against the virus."

Drugs such as Metformin and AICAR work by stimulating an enzyme called AMP kinase (AMPK) which regulates energy within our cells -- the very enzyme that hepatitis C virus represses to enable it to replicate.

AMPK's usual function is to conserve the energy balance in cells, which it does by temporarily shutting down the production of lipids (fats) and membranes when it senses an increase in energy requirements. Professor Harris and his team have now shown that the hepatitis C virus switches off AMPK so that the cell continues production of lipids and membranes, both of which are vital to its survival.

"You'd expect AMPK to be activated when a cell becomes infected by a virus, because it would sense the increase in energy required to enable the virus to replicate. In such cases, AMPK would shut down certain functions of the cell temporarily until the cell's energy is rebalanced," says Prof Harris. "We found that hepatitis C virus, because it needs lipids and membranes, causes the opposite to happen."

Building on this finding, the research team were able to examine how cells would react when treated with common drugs that stimulate AMPK. They found that in infected cells, the drugs were able to halt virus replication, enabling cells to clear the infection.

The research was supported by the Wellcome Trust, the Medical Research Council and the Biotechnology and Biological Sciences Research Council. A patent has been filed on the discovery and the team will shortly embark on a small-scale clinical trial with The University of Nottingham. This will provide a greater evidence base upon which future clinical trials can be based.

## **Headline 6: Pharma Company clarifies on effects of Gardasil vaccine**

**Published by:** The Hindu

**Date of Publication:** April 09, 2010

**Source:** <http://www.hinduonline.com>

MSD Pharmaceuticals Private Limited, the company that markets Gardasil in India, has said that the vaccine can help prevent cervical, vulvar and vaginal cancers and genital warts caused by the HPV (human papilloma virus) types 6, 11, 16 and 18, as also some protection against 10 additional cervical cancers.

### **'Ten years of research'**

"Gardasil is the result of over 10 years of research and development. As part of the rigorous scientific vaccine clinical development programme, clinical trials evaluating the efficacy and safety of the vaccine have included more than 25,000 women from 33 countries from around the world," a statement issued by the company said in response to criticism of its clinical trials in India reportedly carried out in an unethical manner.

In India, the Indian Academy of Paediatrics Committee on Immunization (IAPCOI) stated that the HPV vaccine was of public health importance and recommended giving it prior to sexual debut.

### **U.S. recommendations**

In 2006, the United States Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices recommended that girls and women between 11-26 years be vaccinated with an HPV vaccine such as Gardasil, the statement said.

While it is difficult to determine the exact number of doses administered, since its launch in 2006, more than 55 million doses of the anti-cancer vaccine have been distributed worldwide as part of the global fight against HPV diseases.

### **Robust surveillance**

The statement claimed that MSD has established a robust surveillance programme to monitor the long-term safety, efficacy and duration of protection of people vaccinated with Gardasil.

### **Analyses**

"MSD monitors vaccine safety by conducting analyses of adverse events reported to MSD, and we share these adverse event analyses with regulatory and medical authorities around the world.

### **Preliminary studies**

"Preliminary studies conducted to date have encouragingly demonstrated that there is no waning of protective immunity at five years following vaccination.

"MSD is conducting long-term follow-up studies to confirm whether immunity to HPV disease is long-lasting," the statement said.

While no vaccine or medicine is completely without risk, leading international health organisations throughout the world — including the Drug Controller-General of India, World Health Organisation (WHO), the CDC, Health Canada, the European Medicines Agency (EMA), and the Australia Therapeutic Goods Administration (TGA), among others — have reviewed all of the safety information available to them about Gardasil and continue to recommend its use, the statement added.

## **Headline 7: Patient Trial of Personalized Two-Drug Therapy for Brain Tumors Launched**

**Published by:** The Hindu

**Date of Publication:** April 08, 2010

**Source:** <http://www.hinduonline.com>

Patients suffering from recently diagnosed malignant brain tumors called glioblastoma multiforme or a rare variant called gliosarcoma may be eligible to participate in a Phase II clinical trial at Cedars-Sinai Medical Center that combines two innovative drugs.

Cedars-Sinai's Cochran Brain Tumor Center is the only site in California and one of only 13 in the nation offering this experimental therapy through the Brain Tumor Trials Collaborative (BTTC) based at M.D. Anderson Cancer Center in Houston.

Glioblastoma multiforme is a highly aggressive, treatment-resistant brain tumor. Even with standard therapies - surgery, chemotherapy and radiation - patient survival averages less than 15 months.

The two anticancer drugs, Avastin® (bevacizumab) and Tarceva® (erlotinib), work through different molecular mechanisms to attack brain tumors. Avastin inhibits vascular endothelial growth factor (VEGF), a protein that contributes to the formation of blood vessels that tumors need for growth. Tarceva is designed to prevent tumor growth by blocking a signal pathway that controls cell division by binding to a cancer cell membrane receptor called epidermal growth factor (EGFR).

Although single-agent targeted therapies have not produced significant improvements in treating glioblastomas, laboratory experiments and studies in animals suggest that a combination approach may have greater impact. This two-drug combination is also in clinical trials for the treatment of other cancers, including non-small cell lung cancer and renal cell carcinoma. While all glioblastoma multiforme tumors share certain characteristics, they are not all genetically alike. This patient trial is specifically designed for those whose tumor cells have "unmethylated MGMT promoter." This provides an especially strong study of the effects of the new two-drug approach because these tumors are resistant to the type of chemotherapy typically prescribed for patients with glioblastoma.

"Unmethylated MGMT promoter" means that a gene involved in repairing damaged tumor DNA is highly active in the tumor cells. When this gene, MGMT (O6-methylguanine-DNA methyltransferase), is functioning in cancer cells, it makes the tumor resistant to certain types of chemotherapy - including temozolamide, which is often used to treat glioblastoma - because it helps repair the damage the drug inflicts. On the other hand, if the gene is "silenced" (blocked) - through a process called methylation - the tumor will be more vulnerable to temozolamide.

The two-drug therapy will be administered after standard treatment with temozolamide and radiation therapy. Because radiation has been found to increase activation of certain molecular factors that the two drugs target, it is theorized that radiation therapy may stimulate a greater antitumor effect from the drugs.

The mission of the Brain Tumor Trials Collaborative "is to develop and perform hypothesis-based, state-of-the-art clinical trials in a collaborative and collegial environment, emphasizing innovation and meticulous attention to protocol compliance and data quality." The group is led by researchers at M.D. Anderson Cancer Center in Houston and includes investigators at Cedars-Sinai and 11 other cancer research and treatment centers across the nation.

## Section F: Energy & Environmental

### Headline 1: Research cruise unveils new deep-sea coral, rockfish fields

**Published by:** PhysOrg

**Date of Publication:** June 23, 2010

**Source:** <http://www.physorg.com>

A federal research cruise off the Olympic Peninsula coast has revealed new deep-sea boulder fields peppered with bright sponges, small corals and rockfish.

The National Oceanic and Atmospheric Administration (NOAA) cruise, which returned last week from the Olympic Coast National Marine Sanctuary, was the first in a series of summer cruises looking for new deep-water rocky habitats and deep-sea coral fields.

Using high-tech underwater vehicles that take video and still photos, researchers examined critters in the depths, including petite corals, bright-green sponges and a variety of fish.

"See that little fish tucked into the sponge?" said Elizabeth Clarke, of the Northwest Fisheries Science Center, who was among the lead scientists on the cruise. "Using this technology, you really catch them unawares in their environment and get such a great view of the spatial relationship between the habitat, the invertebrates and the fish."

The cruise searched for lush deep-sea coral colonies, suspected of being important fish habitat. Researchers chose boulder fields more than 300 feet deep, where corals normally thrive. Their underwater cameras revealed a world absent of large corals, but still thick with other species.

"Although we didn't encounter the dense coral fields that I would have liked to see," said Edward Bowlby, research coordinator at the sanctuary and chief scientist on the cruise, "it was quite beautiful to see these underwater boulder fields and all the associated invertebrates, crinoids (sea lilies), sponges and fishes."

Moreover, bouts of bad weather and high seas made it too dangerous to deploy equipment four out of the six days they were sampling.

Despite the absence of coral, the researchers found an abundance of yellow rockfish, a vulnerable and overfished species.

"We have pretty limited information on yelloweye rockfish because they live in these rugged habitats that are really hard to get to," Clarke said. "So this new footage should give us a better understanding of where these fish are and how they utilize these rocky habitats."

As of now, the researchers still aren't sure why corals would occupy one rocky habitat and not another one nearby. But Pacific Coast cruises through the summer from Washington down to Southern California should provide some answers.

"Deep-sea corals are really incredible habitats," said Kacky Andrews, program manager for NOAA's coral-reef conservation program. "We have species that can live up to 4,000 years of age, making them some of the most long-lived species on the planet." The corals face tremendous threats, such as damage from fishing gear and ocean acidification, Andrews said. Researchers will look for damage from fishing gear, while taking water samples to address changes in pH.

They will also take coral samples to determine what species they are and to better understand how fast they grow, all of which will help managers design conservation measures.

"This is a very underappreciated habitat, which we know surprisingly little about," Andrews said.

## **Headline 2: Botanical Garden braces for blooming corpse plant**

**Published by:** PhysOrg

**Date of Publication:** June 21, 2010

**Source:** <http://www.physorg.com>

The University of California Botanical Garden at Berkeley, nestled in Strawberry Canyon just above the central campus, features a mind-boggling 12,000 kinds of plants and breathtaking views of the Bay Area. The term breathtaking soon will describe the rotten flesh-like stench of the garden's about-to-blossom Titan Arum, also known as the corpse plant.

This will be the sixth Titan Arum flower to fascinate visitors to the garden's Tropical House since 2005. But the still rare event, a plant world equivalent of a gasp-inducing car wreck, always draws crowds.

"I've been watching this plant for the past week, but just got the final confirmation that it will be a bloom," Paul Licht, director of the UC Botanical Garden and a professor emeritus of integrative biology, said Wednesday. "We expect it to start growing quite quickly now, and it can easily grow up four inches a day."

This particular corpse plant has grown four inches, to about 25 inches, since Sunday and is expected to continue at a rapid pace until it reaches an exceptionally stinky and spectacular crescendo - in the form of a bright green and deep maroon flower - probably around July 1. The powerful odor is at its peak for about 24 hours and attracts insects to pollinate it. Then the stink can come and go for several days.

The Botanical Garden is using its website, Facebook page and Twitter to update the stinky plant's progress and to solicit suggestions for names until early Monday (June 21). The winner will receive a young *Amorphophallus titanum* plant, a family membership or a one-year extension of a current membership. The garden's previous blooms included Trudy (2005), Titania (2007), Odora and Odorado (2008) and Tiny (2009).

This Titan Arum is from the garden's original collection that arrived from Sumatra as seeds 15 years ago, and its brothers and sisters are on display alongside it at the garden.

"We will have 'babies' for sale from our earlier bloom by Titania for anyone wanting to impress their neighbors," said Licht. "The titans make nice house plants, except perhaps during the one night they bloom."

The garden is open from 9 a.m. to 5 p.m. daily, and is closed the first Tuesday of each month. When the latest bloom occurs, the garden will be opening after hours to members, and memberships will be sold at the gate.

The Titan Arum, or *Amorphophallus titanum*, is the largest flowering structure in the plant world. Discovered in Sumatra in 1878 by Italian botanist Odoardo Bocconi, the plant's swollen underground

stem - or corm - needs to weigh around 30 pounds or more before blooming. That typically takes at least seven years, but it can obviously take longer.

The flowering structure is not really a single flower, but a stalk of tiny male and female flowers that are kept from sight at the base of the central phallus-like structure called the spadix, which heats up to human body temperature. It is surrounded by a pleated skirt-like covering, the spathe, which is bright green on the outside and deep maroon inside when it opens. The flower bud is open for a day or two before it starts to collapse.

### **Headline 3: Fern's Evolution Gives Arsenic Tolerance That May Clean Toxic Land**

**Published by:** Science Daily

**Date of Publication:** June 14, 2010

**Source:** <http://www.sciencedaily.com>

Isolating a gene that allows a type of fern to tolerate high levels of arsenic, Purdue University researchers hope to use the finding to create plants that can clean up soils and waters contaminated by the toxic metal.

The fern *Pteris vittata* can tolerate 100 to 1,000 times more arsenic than other plants. Jody Banks, a professor of botany and plant pathology, and David Salt, a professor of horticulture, uncovered what may have been an evolutionary genetic event that creates an arsenic pump of sorts in the fern.

"It actually sucks the arsenic out of the soil and puts it in the fronds," Banks said. "It's the only multi-cellular organism that can do this."

Without a genome sequenced for *Pteris vittata*, Banks and Salt used a method of gene identification called yeast functional complementation. They combined thousands of different *Pteris vittata* genes into thousands of yeast cells that were missing a gene that makes them tolerant to arsenic.

The yeast was exposed to arsenic, with most of it dying. The yeast strains that lived had picked up the genes from *Pteris vittata* that convey arsenic resistance.

To confirm that this was the correct gene, its function was knocked down and the plant was exposed to arsenic. Without the gene functioning properly, the plant could not tolerate arsenic.

"It tells us that this gene is necessary for the plant to function on arsenic," said Banks, whose findings were published in the early online version of the journal *Plant Cell*. "We looked for a similar gene in the plant *Arabidopsis*. We couldn't find it. It can't be found in any flowering plant."

Banks and Salt found that the protein encoded by this gene ends up in the membrane of the plant cell's vacuole. Salt said the protein acts as a pump, moving arsenic into the cell's equivalent of a trashcan.

"It stores it away from the cytoplasm so that it can't have an effect on the plant," Salt said.

Banks said understanding how the *Pteris vittata* functions with arsenic could lead to ways to clean up arsenic-contaminated land.

"Potentially you could take these genes and put them in any organism that could suck the arsenic out of the soil," Banks said.

Salt said rice plants could be modified with the gene to store arsenic in the roots of plants -- instead of rice grains -- in contaminated paddies.

Banks and Salt found another gene in *Pteris vittata* that looks almost exactly the same as the one that controls arsenic tolerance. When the fern was exposed to arsenic, the confirmed arsenic-tolerance gene increased its expression while the similar gene did not.

Salt said the gene that regulates arsenic tolerance could be a duplicate of the other that has changed slightly to give itself a new function.

"The fact that it has these two genes could be a sign of evolution," Salt said. "One of the thoughts of gene evolution is that one copy could continue to do what it has always done, while the duplicate can develop another function."

The plant might have evolved to accumulate arsenic, Banks and Salt theorized, as a defense against animals or insects eating them.

Banks hopes findings such as this will lead to more research emphasis on non-flowering plants. She said there are characteristics in plants such as *Pteris vittata* that cannot be found in other organisms.

The next step in their research is to put the arsenic-tolerance gene from *Pteris vittata* into *Arabidopsis* to see whether it gives the new plant the same characteristics.

The National Science Foundation funded the research.

#### **Headline 4: Climate Change Complicates Plant Diseases of the Future**

**Published by:** Science Daily

**Date of Publication:** June 24, 2010

**Source:** <http://www.sciencedaily.com>

Human-driven changes in the earth's atmospheric composition are likely to alter plant diseases of the future. Researchers predict carbon dioxide will reach levels double those of the preindustrial era by the year 2050, complicating agriculture's need to produce enough food for a rapidly growing population.

University of Illinois researchers are studying the impact of elevated carbon dioxide, elevated ozone and higher atmospheric temperatures on plant diseases that could challenge crops in these changing conditions.

Darin Eastburn, U of I associate professor of crop sciences, evaluated the effects of elevated carbon dioxide and ozone on three economically important soybean diseases under natural field conditions at the soybean-free air-concentrating enrichment (SoyFACE) facility in Urbana.

The diseases downy mildew, Septoria brown spot, and sudden death syndrome were observed from 2005 to 2007 using visual surveys and digital image analysis. While changes in atmospheric composition altered disease expression, the responses of the three pathosystems varied considerably, Eastburn said.

Elevated carbon dioxide levels are more likely to have a direct effect on plant diseases through changes to the plant hosts rather than the plant pathogens.

"Plants growing in a high carbon dioxide environment tend to grow faster and larger, and they have denser canopies," Eastburn said. "These dense plant canopies favor the development of some diseases because the low light levels and reduced air circulation allow higher relative humidity levels to develop, and this promotes the growth and sporulation of many plant pathogens."

At the same time, plants grown in high carbon dioxide environments also close their stomata, pores in the leaves that allow the plant to take in carbon dioxide and release oxygen, more often. Because plant pathogens often enter the plant through the stomata, the more frequent closing of the stomata may help prevent some pathogens from getting into the plant.

In elevated ozone, plant growth is inhibited and results in shorter plants with less dense canopies. This can slow the growth and reproduction of certain pathogens. However, ozone also damages plant tissues that can help pathogens infect the plant more easily.

"Elevated levels of carbon dioxide and ozone can make a plant more susceptible to some diseases, but less susceptible to others," Eastburn said. "This is exactly what we've observed in our climate change experiments."

U of I's SoyFACE was the first facility to expose plants to elevated ozone under completely open-air conditions within an agricultural field.

"The SoyFACE facility allowed us to evaluate the influence of natural variability of meteorological factors such as drought and temperature in conjunction with imposed atmospheric composition (elevated carbon dioxide and ozone) on naturally occurring soybean diseases across several growing seasons," Eastburn said.

He believes rising temperatures and changes in rainfall patterns will also affect development of plant disease epidemics.

"In some cases, changes of only a few degrees have allowed plant diseases to become established earlier in the season, resulting in more severe disease epidemics," Eastburn said. "The ranges of some diseases are expanding as rising temperatures are allowing pathogens to overwinter in regions that were previously too cold for them."

For example, warmer winters may allow kudzu to expand its range northward. Because kudzu is an alternate host for the soybean rust pathogen, one result of rising temperatures may be that soybean rust arrives in Illinois earlier in the soybean growing season, Eastburn said.

"Information derived from climate change studies will help us prepare for the changes ahead by knowing which diseases are most likely to become more problematic," he said. "Now is the time for plant pathologists, plant breeders, agronomists and horticulturalists to adapt disease management strategies to the changing environment."

Eastburn's soybean research was recently published in *Global Change Biology*. Researchers also included Melissa DeGennaro and Evan DeLucia of the U of I, Orla Dermody of Pioneer Hi-Bred Switzerland, and Andrew McElrone of the University of California -- Davis.

This research was funded by the National Science Foundation, an SJU Sigma Xi grant, the Illinois Council on Food and Agricultural Research, the Soybean Disease Biotechnology Center, the Illinois Soybean Association, USDA Hatch funds, and the Office of Science, Department of Energy Grant.

Eastburn will share his latest research on global climate change and the implications for future plant disease epidemics at the 2010 U of I Agronomy Day on Thursday, Aug. 19. For more information on Agronomy Day, go to <http://agronomyday.cropsci.illinois.edu/>.

### **Headline 5: Super-Yeast Generates Ethanol from Energy Crops and Agricultural Residues**

**Published by:** Science Daily

**Date of Publication:** June 15, 2010

**Source:** <http://www.sciencedaily.com>

A new type of baker's yeast (*Saccharomyces cerevisiae*) has been developed which can efficiently ferment pentose sugars, as found in agricultural waste and hardwoods.

Researchers writing in BioMed Central's open access journal *Biotechnology for Biofuels* describe the creation of the new *S. cerevisiae* strain, TMB3130, which demonstrated significantly improved aerobic growth rate and final biomass concentration on sugar media composed of two pentoses, xylose and arabinose.

Marie Gorwa-Grauslund, from Lund University, Sweden, worked with an international team of researchers to generate the novel micro-organism. She said, "To the best of our knowledge, this is the first report that characterizes molecular mechanisms for improved mixed-pentose utilization obtained by evolutionary engineering of a recombinant *S. cerevisiae* strain."

Normal baker's yeast cannot ferment pentose sugars at all. By inserting the required genes from other fungi and bacteria it is possible to make a relatively inefficient transgenic strain that can ferment pentose sugars. Gorwa-Grauslund and her colleagues took one of these recombinant strains, TMB3061, and grew it on a mixture of xylose and arabinose sugars in order to select a stable population most capable of metabolising the pentose feedstock.

She said, "There is considerable interest in developing 'second-generation' biofuels to refine and upgrade non-food material, especially dedicated energy crops and agricultural residues such as straw, bagasse, stover and corn hulls. Our yeast demonstrates a significant step towards this goal."

### **Headline 6: An IPCC for biodiversity?**

**Published by:** SciDev

**Date of Publication:** June 07, 2010

**Source:** <http://www.scidev.net>

An independent, international science panel would improve standards and infrastructure for biodiversity science, says an editorial in *Nature*.

This week, in South Korea, government representatives from across the world will decide whether to create a panel, reminiscent of the Intergovernmental Panel on Climate Change (IPCC), to review the science and anticipated effects of changes in biodiversity.

The proposed panel, the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES), will conduct regional as well as global assessments — in part to address the fact that biodiversity change is a more local affair than climate change.

It will likely allocate part of its budget to building scientific capacity in developing countries, predicts the editorial. And by working with groups such as the Group on Earth Observations Biodiversity Observation Network, it could improve predictive models of global change and allow biodiversity science to flourish, it adds.

But the panel must work with other organisations that influence biodiversity. For example, if the UN Food and Agriculture Organization were involved, farmers and fishermen would be more likely to stand behind its conclusions.

Despite recent hiccups, the IPCC "remains the gold standard for independent scientific assessment", says the editorial. More importantly, its reports on the economic impacts of climate change have made the issue much harder for policymakers to ignore.

"If the IPBES can do the same for biodiversity and ecosystem change, it will be very much worth its proposed annual budget of around US\$12 million", concludes the editorial.

## **Headline 7: [Between Shoot and Root, Researcher Unlocks New Tool for Biofuel Industry](#)**

**Published by:** Science Daily

**Date of Publication:** May 19, 2010

**Source:** <http://www.sciencedaily.com>

Plant geneticists are on a determined quest -- to control auxin, a powerful plant growth hormone. Auxin tells plants how to grow, where to lay down roots, how to make tissues, and how to respond to light and gravity. Knowing how to manipulate auxin could thus have enormous implications for the production of biofuel, making plants grow faster and better.

A recent publication in the journal *PLoS Biology* from the laboratory of Prof. Shaul Yalovsky of Tel Aviv University's Molecular Biology and Ecology of Plants Department describes a special protein, the ICR1, found to control the way auxin moves throughout a plant affecting its development. When this protein is genetically engineered into valuable biofuel crops such as corn, sugarcane or experimental like switchgrass, farmers can expect to get a far larger yield than what they harvest today, Prof. Yalovsky has found.

In short, much more biofuel for the buck.

"We've found a mechanism that helps the shoot and root talk to each other," says Prof. Yalovsky. "Somehow both parts of the plant need to speak to each other to say: 'Hey down there, I'm up here and there's lots of sun,' or 'I'm down here in the roots and it's too dry.'" The plant's shoots need to respond to its environment. We've discovered the mechanism that helps auxin do its job."

### **Putting energy into sugar**

Auxin is considered the most important plant hormone for plant growth and root growth. Prof. Yalovsky explains that knowing how to manipulate it can lead to much bigger yields of non-food crops, like those needed for biofuel. Efficiency is now a limiting factor in biofuel production, and

scientists are looking for anything that can produce biofuel in the same amounts as the production of traditional fossil-based fuels.

The ICR1 protein that Prof. Yalovsky has isolated works together with a group of proteins called ROPs, which his lab also isolated in previous research. Together, this system of work in harmony to manipulate the composition and vascular tissues of plant cell walls. The researchers found specifically that ICR1 can be manipulated and, as a consequence, influence auxin distribution in plants. Plant scientists now have a tool that allows breeders to grow certain plant organs of choice, with the possibility of manipulating plant cell wall composition -- the kinds of tissues needed in making biofuel. In the *PLoS Biology* report published recently, the researchers spell out the links between the mechanisms that regulate cell structure and the development of the whole plant. The ICR1, they explain, influences the way the hormone auxin moves around the plant.

### **Breaking down the walls**

Plant tissue is made of cells engulfed in a tough cell wall that helps it retain shape and rigidity. It's composed of cellulose, a polysaccharide, and lignin, which is the woody material in a plant. Current methods for removing the unwanted lignin in the cell wall -- which must be removed to produce biofuel -- amounts to about a 50% loss cellulosic material which could be used for biofuel.

Ideally crop growers want to maximize the amount of cellulose in the plant, which can be broken down to make sugar for ethanol. The new system found in proteins and developed at Tel Aviv University has the potential to increase crop yield and make fuel production more cost-effective. His approach could mean less lignin, more cellulose and ultimately more biofuel, says Prof. Yalovsky.