



BioBits

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*Quarterly E-Newsletter from Bioinformatics Centre (Dic)
Kerala Agricultural University, Thrissur*

About Us

The Bioinformatics Centre (DIC) at KAU runs under the Biotechnology Information System Network (BTISnet) programme of DBT, Ministry of Science & Technology, and Government of India. The Centre was upgraded to Distributed Information Centre during 2004 to promote Bioinformatics research and education. The Centre enhances access to global information in life sciences especially plant sciences and plant biotechnology involving scientists and students of the University and other S&T institutions and acts as a support centre to the Centre for Plant Biotechnology & Molecular Biology. The Centre is involved in a wide range of research work on plant responses to biotic and abiotic stresses, plant metabolomics using systems biology approaches, plant-pathogen interaction studies and study of active compounds in anti cancer medicinal plants. In addition to this, the Centre offers a credit course in Bioinformatics to post graduate Plant Biotechnology students conducts routine training programmes in Bioinformatics and maintains various databases relevant to agriculture.

Cover Story

Bioinformatics is not only the hub of all life sciences but also the cutting edge knowledge for those who would like to make a breakthrough... Bioinformatics and computational biology involve the use of techniques including applied mathematics, informatics, statistics, computer science, chemistry and biochemistry to solve biological problems usually on the molecular level. Major research efforts in the field include sequence alignment, gene finding, genome assembly, protein structure alignment, protein structure prediction, prediction of gene expression and protein-ligand interactions etc.

Complex computational and biological problems are now being addressed and this has led to significant advances in our understanding of biology. No biological discipline will be unaffected by these technological breakthroughs. Bioinformatics can revolutionize not only the research sector but its judicious application can do wonders in transferring knowledge to millions of marginal farmers of the country. This issue of 'Biobits' present before you the recent, most relevant developments/Research outcomes in Plant Biotechnology/ Bioinformatics.

Cover Story

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Evidence of plant climate adaptation using supercomputers

Using supercomputers, scientists found genes sensitive to cold and drought in the plant *Arabidopsis* that helps it to survive climate change. These findings increase basic understanding of plant adaptation and can be applied to improve crops. The iPlant Collaborative and the supercomputers Stampede, Lonestar and Ranger of the Texas Advanced Computing Center aided in the research.

Instead of knocking out or ramping up genes with genetic engineering, the researchers studied natural variation in genes. They wanted to understand how the genes have evolved in response to the processes of natural selection through gene flow and mutation in the field. Genes or snippets of the four-letter DNA molecule carry not only the code for which proteins make for its survival but also the instructions for how many to make or express.

As a plant starts to sense dropping temperatures, a cascade of gene expression can allow the plant to acclimatize to cold temperatures, and in effect prepare itself for the coming freezing conditions. So the science team used prior lab work that exposed seedlings of *Arabidopsis* to artificial cold and drought stress to measure changes in gene expression across the entire genome.



The team sought was what's called a SNP polymorphism, a single letter difference in over 100 million DNA base pairs for finding the right gene. The scientists took the genes found and compared them with genomic data from previous studies that sampled *Arabidopsis* from populations throughout Europe and Asia. They narrowed that reference data to 1,003 strains of the flowering mustard weed. The result suggested that there are changes in the DNA sequence that are adapted to those local conditions and that are associated with changes in gene expression.

The research team statistically tested for associations between climate and SNP polymorphism by making the hypothesis null or assuming no association. They randomized climatic variation with respect to SNP polymorphism variation.

The computational challenges were daunting, involving thousands of individual strains of *Arabidopsis* with numerous markers across the genome and testing for a dozen environmental variables. As it is impossible to do it on a standard computer, they used cluster like Stampede or Lonestar, the most powerful and significant current supercomputers in U.S. The computational time on the clusters helped them to evaluate the hypothesis that generated from the SNP data. The researchers developed R statistical programming language code to divide large computing jobs into smaller ones in order to run in parallel on the nodes of a cluster. It is a helpful, timely program impacting plant biologists in individual labs around the world.

Mapping the maize genome

The researchers at Brigham Young University and Rutgers University have developed a protocol that highlights the utility of positional cloning technique in plant taxa with much larger genomes, such as maize. They have applied this mapping technique to the maize genome and have published their protocol - the first detailed step-by-step protocol on positional cloning - in a new article in the January issue of *Applications in Plant Sciences*.



Positional cloning is a laboratory technique used to locate the position of a disease-associated gene along the chromosome. This approach works even when little or no information is available about the biochemical basis of the disease. Positional cloning is used in conjunction with linkage analysis. Maize is one of the most important cereal crops in the world. The complete genome of maize has been sequenced, but its size

and complexity presents a challenge to researchers seeking to identify specific genes responsible for traits. In plants, the positional cloning method has been traditionally used in studies of model organisms such as rice and *Arabidopsis*; with smaller genomes providing important insights into plant genetics. This approach has contributed to the successful mapping of genes involved in numerous human diseases such as Huntington's disease and cystic fibrosis, an important first step in understanding these conditions.

The research group successfully utilized this technique with populations similar in size to *Arabidopsis* and rice. This helped them to carry out their work in an easy manner. The availability of complete sequence of the maize genome has now made positional cloning to be used to identify genes responsible for traits caused by mutations as well as by natural genetic variation. This study proposes their work to be applied on any plant species that is genetically tractable and has a sequenced genome including emerging models important for evolutionary and ecological questions that could benefit from the functional insights due to positional cloning.

Source: <http://www.sciencedaily.com/releases/2015/01/150120142702.htm>

Origins of agriculture shape future of food

Agricultural decisions made by our ancestors more than 10,000 years ago could hold the key to food security in the future, according to new research by scientists at the University of Sheffield. Scientists, looking at why the first arable farmers chose to domesticate some cereal crops and not others, studied those that originated in the Fertile Crescent, an arc of land in western Asia from the Mediterranean Sea to the Persian Gulf. They grew wild versions of what are now staple foods like wheat and barley along with other grasses from the region to identify the traits that make some plants suitable for agriculture, including how much edible seed the grasses produced and their architecture.

Dr. Catherine Preece, who headed the study with colleagues from the University's Department of Animal and Plant Sciences and Department of Archaeology, indicated amazing results surprised them because numerous other grasses that our ancestors ate, but we do not; is because they produce just as much seed as wild wheat and barley. It is only when these plants are grown at high densities, similar to what we would find in fields, that the advantage of wild wheat and barley is



The study identified two key characteristics shared by the wild relatives of current crop plants. Firstly they have bigger seeds, which means they grow into bigger seedlings and are able to get more than their fair share of light and nutrients, and secondly, as adult plants they are less bushy than other grasses and package their big seeds onto fewer stems. This indicated that crop wild relatives perform better than the other wild grasses, they are competing with and are better at high density in fields, making them ideal for using in agriculture. The results are important because our expanding human population is putting increasing demands on food production.

Scientists are trying to understand the traits that have made some grasses into good crops so that those characteristics can be identified in other plants that can be useful for future domestication. So far the researchers have been conducting their experiments in greenhouses and their results indicate that the traits affecting how plants compete with each other are crucial factors in determining the success of a crop. The team of scientists now plans to observe how the plants interact in their natural environment; by growing them in experimental fields in Turkey, the heart of the Fertile Crescent. Cereal breeders are taking an increasing interest in the wild relatives as a source of useful traits that may help to increase yields or increase resilience to climate change.

Source: <http://www.sciencedaily.com/releases/2014/12/141210204517.htm>

Plant derived JHAN's kill Yellow fever Mosquito Larvae

Insects are responsible for major economic losses worth billions of dollars by damaging crops, stored agricultural products and causing infectious diseases leading to millions of deaths. Most of the currently available insecticides present environmental and health risks and further, insects develop resistance complicating pest-control strategies. Hence, there is an urgent need to develop novel effective insecticides with little environmental risks.

'Insect-specific growth regulators' are compounds that regulate the growth of insects. They represent attractive pest-control agents since they pose no health risk to humans and are also environmentally safe. One hormone in insects, called juvenile hormone, is a particularly attractive target for insect growth regulators as it exists only in insects and it plays a key role in insect development, reproduction and other physiological functions.



An international team of scientists, including an entomologist at the University of California, Riverside, has investigated in detail how juvenile hormone acts and has devised a method to prevent its working.

The researchers led by Dr. Alexander Raikhel, a distinguished professor of entomology at Riverside, discovered potent compounds in plants that counteract the action of juvenile hormone. These compounds, called juvenile hormone antagonists (JHANs), make up plants' innate resistance mechanism against insect herbivores.

In collaboration with Korean scientists, the research team screened 1,651 plant species and identified five JHANs from two plants that are effective in causing mortality of yellow fever mosquito larvae, specifically by retarding the development of ovaries.

They isolated five diterpene secondary metabolites with JH activity from two plants: *Lindera erythrocarpa* and *Solidago serotina*. The Korean Scientists are testing the effect of these five molecules on other agricultural pests. These newly discovered natural molecules could lead to the development of a new class of safe and effective pesticides to control mosquitoes and may be other agricultural pests.

Source: <http://www.sciencedaily.com/releases/2015/01/150127165030.htm>

GRP78: Single target for many diseases

A protein called GRP78 could be a universal therapeutic target for treating human diseases like Brain cancer, Ebola, Influenza, Hepatitis and superbug bacteria such as MRSE and MRSA. A pre-clinical study led by Dr. Paul Dent and colleagues from Virginia Commonwealth University published in the December issue of *Journal of Cellular Physiology* (2014).

GRP78 is part of a family of proteins called chaperones. The chaperone GRP78/Dna K is conserved throughout evolution down to prokaryotes. A chaperone helps to shape chains of amino acids into proteins and keep them active in the correct 3D shape.

A drug combination of the clinically tested OSU-03012 (AR-12) and FDA approved Phosphodiesterase 5 Inhibitors (Viagra, Cialis) were used to target GRP78 and related proteins. It could prevent the replication of a variety of major viruses in infected cells;

made antibiotic-resistant bacteria vulnerable to common antibiotics and found evidence that brain cancer stem cells were killed. Data were obtained in multiple brain cancer stem cell types, Influenza, Mumps, Measles, Rubella, RSV, CMV, Adenovirus, Coxsackie virus, Chikungunya, Ebola, Hepatitis, *E. coli*, MRSA, MRSE and *N. gonorrhoeae*, among others.

The chaperone proteins are very important as they make extra protein compared to normal / uninfected cells. The team found that the OSU/Viagra drug combination reduced infectivity via reduced viral receptor expression on the surface of target cells and the prevention of virus replication in infected cells. Similarly, the OSU/Viagra drug combination reduced expression of viral receptors for Ebola, Marburg, Hepatitis A, B and C, and Lassa fever viruses and in cancer cells; expression of oncogene receptors was reduced by the drug combination. Likewise in bacteria, expression of the equivalent GRP78 protein called Dna K was reduced and induced cell death in pan-antibiotic resistant forms of *E. coli*, MRSE, MRSA and *N. gonorrhoeae*.

Dr. Dent and his group have also discovered that OSU/Viagra treatment can kill tumor cells but doesn't harm normal tissues like the liver and the heart. It can reduce the levels of proteins called "pumps" in the mouse brain which make tumor cells resistant to chemotherapy and stops brain cancer chemotherapy from entering into the brain.

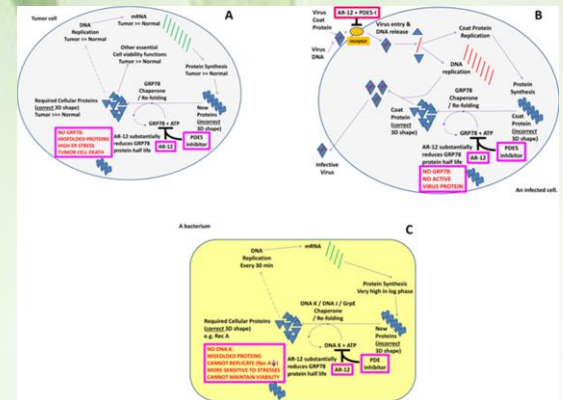


Fig.: Molecular mechanisms by which OSU-03012 (AR-12) and PDE inhibitors. (A) kill tumor cells; (B) prevent production of new infective virions. (C) prevent bacterial growth

The Centre is involved in a wide range of research work like plant-pathogen interaction studies, study of active compounds in medicinal plants, *in-silico* analysis of phytochemicals against various diseases and creation of databases and their maintenance. *In silico* docking studies on phyto compounds are carried out to predict the preferred orientation of one molecule to a second when bound to each other to form a stable complex. The binding efficiency, interaction and dock score would help a long way in identifying novel phytochemicals against serious diseases.

This particular column is especially for readers and those who are interested in the field of Bioinformatics. Here we are creating a new opportunity to share your valuable ideas with senior scientists. So post your comments and suggestions to mail bic@kau.in or kaubioinfo@gmail.com.

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