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Bioinformatics up to Date

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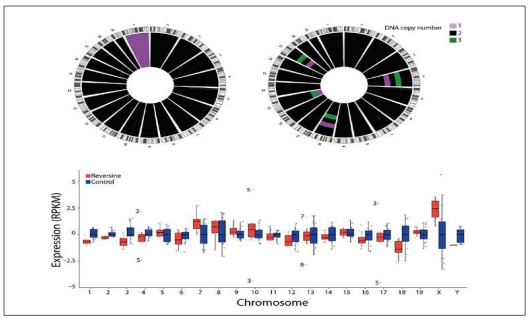
Inside…..

Parallel Sequencing of DNA and RNA Provides Insight into Secret World of Cells

Researchers have developed a large-scale sequencing technique called Genome and Transcriptome Sequencing (G&T-seq) that reveals, simultaneously, the unique genome sequence of a single cell and the activity of genes within that single cell.

The study, published Apr. 27 in Nature Methods, has experimentally established for the first time that when a cell loses or gains a copy of a chromosome during cell division, the genes in that particular region of DNA show decreased or increased expression. While this has long been assumed by genetic researchers, it has not been seen before.



The DNA code that makes up our genome can be found in every cell of our body. This is decoded into a group of molecules in our cells known as RNA, which provide instructions for that particular cell's proteins to perform their particular function. Transcriptome sequencing measures the amount of each RNA molecule in a cell and provides an insight into its function that cannot be gained by looking at the DNA.

Scientists can now see a cell's DNA, including the mutational damage it has sustained on its journey from the fertilized egg, alongside the RNA of the same cell, which enacts all the DNA's instructions, even the errors.G&T-seq is unique in the field as it allows high throughput DNA- and RNA-sequencing from single cells in parallel on a diverse range of sequencers, while previous methods were limited to the interrogation of either the DNA or the RNA of a cell, but not both.

"The potential to scale-up this method is one of the most exciting elements of this research," says Dr. Iain Macaulay, first author and a corresponding author from the Sanger Institute.

"Using this method, we've been able to reveal cellular properties that cannot be seen by DNA or RNA sequencing alone," says Professor Chris Ponting, a corresponding author from the University of Oxford and an Associate Faculty Member at the Sanger Institute. "This kind of integrated analysis, which we hope will soon also include epigenetic data, allows us a more complete understanding of the extent and evolution of cellular heterogeneity in normal development and disease processes."

***[G&T-seq: Parallel sequencing of single-cell genomes and transcriptomes**. Nature Methods (2015)]*

Pain Sensing' Gene Discovered

A gene essential to the production of pain-sensing neurons in humans has been identified by an international team of researchers co-led by the University of Cambridge. The discovery, reported May 25 in the journal Nature Genetics, could have implications for the development of new methods of pain relief.

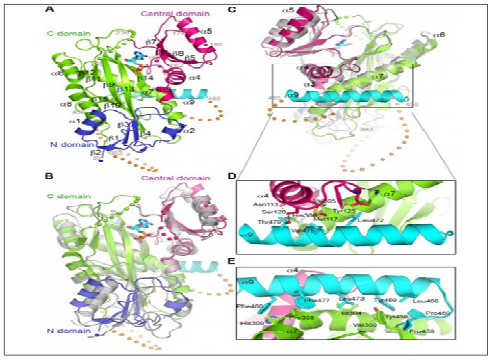
Using detailed genome mapping, two teams of researchers collaborated to analyse the genetic make-up of 11 families across Europe and Asia affected by an inherited condition known as congenital insensitivity to pain (CIP). This enabled them to pinpoint the cause of the condition to variants of the gene PRDM12. Family members affected by CIP carried two copies of the variant; however, if they had only inherited one copy from their parents, they were unaffected.

PRDM12 had previously been implicated in the modification of chromatin, a small molecule that attaches to our DNA and acts like a switch to turn genes on and off (an effect known as epigenetics). The researchers showed that all the genetic variants of PRDM12 in the CIP patients blocked the gene's function. As chromatin is particularly important during formation of particular specialised cell types such as neurons, this provides a possible explanation for why pain-sensing neurons do not form properly in the CIP patients.

[***Transcriptional regulator PRDM12 is essential for human pain perception.*** *Chen, Y-C et al. Nature Genetics; (May 25, 2015)*]

Enzyme Important for Nervous System

Scientists from The Scripps Research Institute (TSRI), working closely with researchers at the National Institutes of Health (NIH), have mapped out the structure of an important protein involved in cellular function and nervous system development.



The new structure provides crucial information for understanding how the protein binds to cellular components. It's also the first structure determined of any ligase in the tubulin tyrosine ligase-like (TTLL) family. Scientists have been especially curious about the role of TTLLs because mutations in these proteins have been linked to a range of neurodegenerative diseases, including retinal dystrophy and the rare Joubert syndrome.

In the new study, the researchers saw for the first time how three positively charged regions of TTLL7 interact with the microtubule substrate. Most importantly, they found that the active site of TTLL7 is ideally positioned to contact the negatively charged "beta-tail" of beta-tubulin, one of the two protein building blocks of the microtubule polymer (alpha- and beta-tubulin). The alpha and beta "tails" that protrude from the microtubule surface are known sites for modification, which in turn, determine which motors and associated protein will bind to the microtubule.

These findings add to the growing understanding of the "tubulin code"—a phenomenon where TTLL7 and similar proteins add amino acids to microtubules and prompt them to fast-track certain proteins for transport.

[***Multivalent Microtubule Recognition by Tubulin Tyrosine Ligase-like Family Glutamylases.*** *Cell (2015)]*

New Tool Significantly Reduces Time of Multiple Genome Analysis

UK research collaboration develops a new bioinformatics pipeline that enables automated primer design for multiple genome species, significantly reducing turnaround time. A key aspect of this is utilising breakthroughs in genomics research to guide the selection of the individuals to incorporate in breeding schemes. Scientists from The Genome Analysis Centre (TGAC) and John Innes Centre have developed a bioinformatics pipeline, PolyMarker that facilitates the design of genomic specific primers for polyploid species. Once identified, these primers can be used to ascertain whether or not an individual organism has the genetic variation associated with a given trait. As an open access tool, researchers and crop breeders can submit their own data to PolyMarker and the online tool will return suggested design primers to identify genetic variations that tag vital traits in their crop samples, with a significantly reduced turnaround time compared to the current manual method.

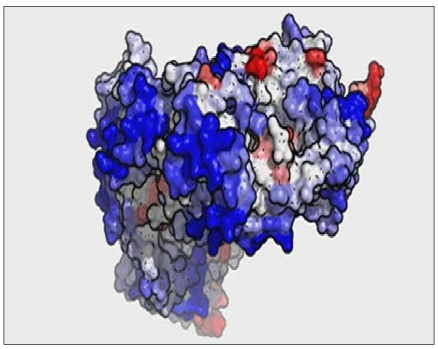
"PolyMarker has already demonstrated its value having been developed and applied in a research project where it identified genetic markers that signal resistance to the wheat yellow rust pathogen (Puccinia striiformis f. sp. tritici). This disease is responsible for devastating bread wheat crops and has developed 'Warrior' strains capable of infecting individuals previously believed to have tolerance."

This innovative online tool has been used to generate putative KASP probes for the 820K markers designed by the CerealsDB project from the BBSRC funded WISP programme (a collaboration between John Innes Centre, the University of Bristol, Rothamsted Research, NIAB and University of Nottingham). Polymarker has also been used to design probes for the 90K iSelect markers set.

[***PolyMarker: A fast polyploid primer design pipeline.***; *Bioinformatics (2015)]*

New 3-D Method to Study of Proteins

Researchers from the Institute of Biotechnology and Biomedicine at the Universitat Autònoma de Barcelona (IBB-UAB) and from the University of Warsaw have developed a new computational method called AGGRESCAN3D which will allow studying in 3D the structure of folded globular proteins and substantially improve the prediction of any propensity for forming toxic protein aggregates. With this new algorithm proteins can also be modelled to study the pathogenic effects of the aggregation or redesign them for therapeutic means.

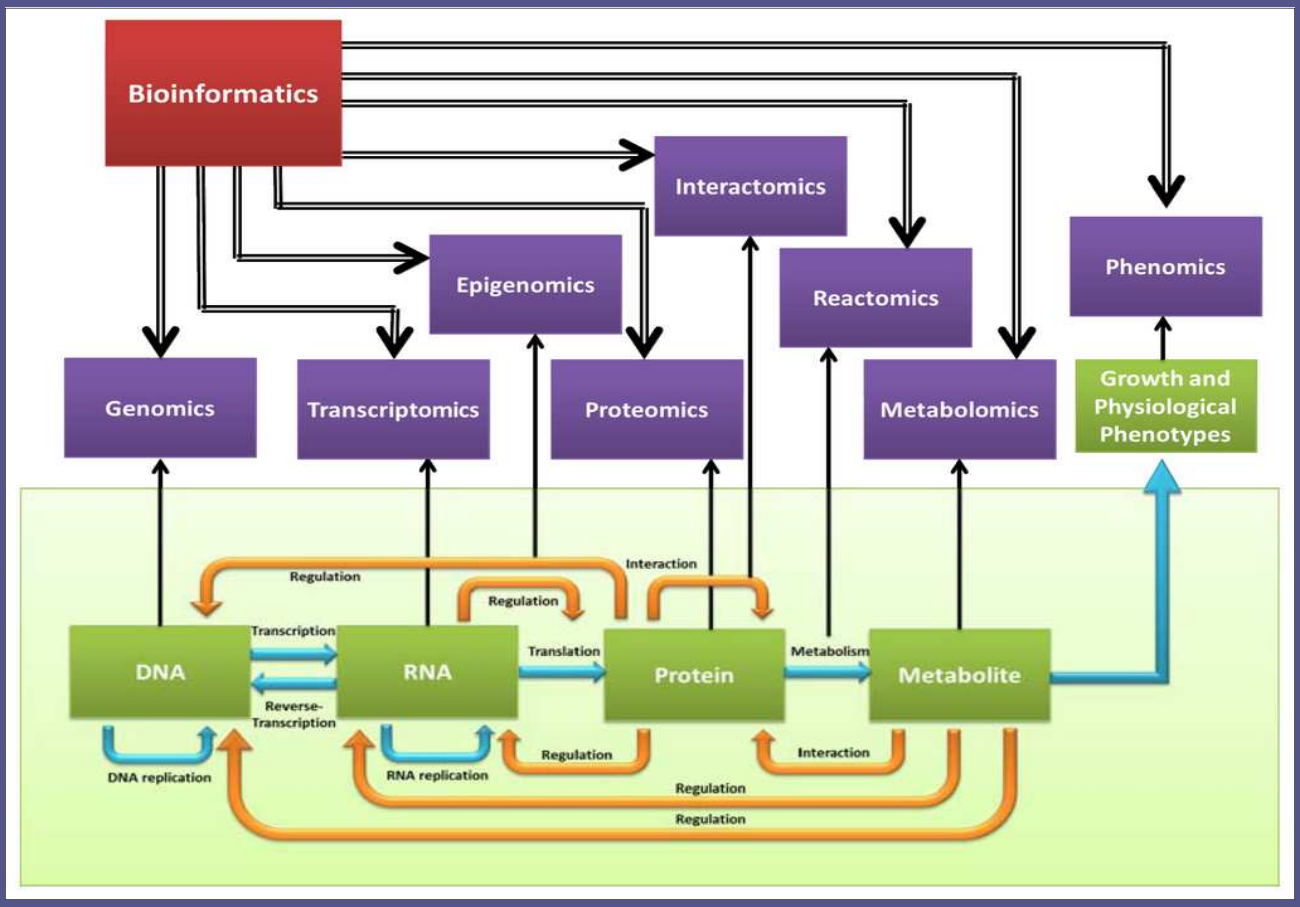


The AGGRESCAN3D (A3D), which was implemented as a web server freely accessible to the academic community, surpasses these limitations with an approach based on the protein structure in folded state. According to the article in which the researchers present the new method, published in Nucleic Acids Research, the new algorithm has a significantly higher precision than others based on linear sequences in predicting the properties of aggregation of globular proteins. It offers new and important features, such as the possibility to facilitate the modelling of pathogenic mutations and the design of proteins for therapeutic means, such as antibodies, with increases solubility.

The new algorithm can be applied to any protein with a known structure or that can be generated by modelling. To validate the new method, researchers used proteins whose aggregation properties had already been characterised experimentally. In the static mode, it is possible to study individual proteins and protein complexes with up to 20,000 atoms and proteins with up to 400 amino acids in dynamic mode

[*Nucleic Acids Research (2015)*]

Bioinfo. Animation



Bioinfo. Patent

Biosensor Remote Collection Packaging System with Bioinformatics Processing

US 20110245648 A1

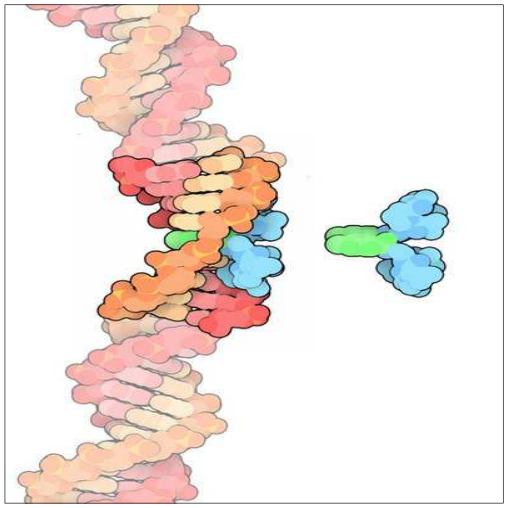
Inventors: Stanford P. Hudson

Abstract

A biosensor kit and method for use thereof for at-home collection of biosensor data having one or more biosensors with a top patch-shaped layer affixed to a bottom patch-shaped layer, the layers being made of cushioning sheet material, such as medical foam tape, and having a biosensor circuit disposed between the layers such that the top layer and bottom layer form a protective, dual-mode encapsulation of the biosensor circuit for cushioning against the skin or a garment of a wearer, and for protection of the biosensor circuit during shipment and handling. The kit further includes a carrier card of suitable size to receive and carry the biosensors in a substantially flat, co-planar arrangement in a substantially flat envelope or pouch for shipment through flat piece mail or postal service. The cushioning sheet material of the biosensor layers is sufficient packing material to avoid requiring additional protective packing material.

Actinomycin

Actinomycin is the first natural antibiotic discovered that has anti-cancer activity. It was discovered in the bacterium Streptomyces antibioticus in 1940. Unfortunately, it is too toxic for general use, killing cancer cells but also poisoning the patient, but related molecules have subsequently been discovered, and are now widely used for cancer chemotherapy. Early studies of actinomycin revealed that it intercalates into the DNA double helix. Actinomycin is composed of two parts: a flat ring (shown here in green) that resembles the DNA bases, and two cyclic peptides composed of unusual amino acids (shown here in blue). The flat ring intercalates between bases in the DNA double helix, and the cyclic peptides fit perfectly into the major groove of the DNA (PDB entry 173d). The result is a stable, but lethal, complex with the cell's genome.



Many different intercalating molecules have been discovered, either in living organisms or designed by scientists. Based on their different sizes and shapes, they target different topoisomerases. Actinomycin blocks type II topoisomerases, which are involved with detangling DNA.

Kindly send us your feedback to

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