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Genomics: New aspect of cancer research

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Abstract - Genomics deals with the study of genes and their function of all organisms. It is that branch of omics that leads to an understanding of the molecular mechanisms of genes, diseases, including the complex interplay of genetic and environmental factors. It is also important in the development of drugs, design of new drugs, vaccines and DNA diagnostics. Genomics-based therapeutics includes traditional small chemical drugs, protein drugs, and gene therapy. It also refers to the large-scale investigation of the structure and function of genes. This field also leads to new drug discovery and development, agricultural sciences and other fields.

Keywords- Genome, Metabolome, Metagenomics, Nitrogenomics, Proteome, Cancer research

1. Introduction

Genomics is that branch of omics that deals with the study of an organism's entire genome. It involves analysis of intragenomic phenomena, viz., heterosis, epistasis and other interactions between loci and alleles within the genome. It also includes various strategies for determining the entire DNA sequence of organisms and fine-scaling the genetic mapping efforts. Also, the aim of this genomic information analysis is to elucidate its effect on and response to the entire genome network. With the vast trove of data about human DNA generated by the Human Genome Project and the HapMap Project, scientists and clinicians have much more powerful tools to study the role that genetic factors play in much more complex diseases, viz., cancer, and cardiovascular disease that constitute the majority of health problems today. Genome-based research is already enabling medical researchers to develop more effective diagnostic tools, to better understand the health needs of people based on their individual genetic make-ups, and to design new treatments for disease. Thus, the role of genomics in health care and medicine is starting to change profoundly. The first examples of this era are the use of personalized medicine. It is important to realize, however, that it often takes considerable time, effort, and funding to move discoveries from the scientific laboratory into the medical clinic. Most new drugs based on genome-based research are estimated to be at least 10 to 15 years away. Screening and diagnostic tests, however, are expected to arrive more quickly. Rapid progress is also anticipated in this field. Clearly, genomics remains just one of several factors that contribute to people's risk of developing most common diseases. Diet, lifestyle, and environmental exposures also come into play for many conditions, including many types of cancer. Still, a deeper understanding of genomics will shed light on more than just hereditary risks by revealing the basic components of cells and, ultimately, explaining how all the various elements work together to affect the human body in both health and disease (Rossi et al, 2007; Busso et al, 2008; Carlson 2008).

2. History of Genomics

This field came into existence in early 1980s. It developed at very fast due to some ongoing genome projects in the 1990s. Previously, this was mainly concerned with sequencing the genomes of various organisms. But with the growth of this science, the knowledge of full genomes has been available for new developments and carries the new field of functional genomics, which came into existence. This mainly concerned with the patterns of gene expression during various conditions. In the year 1972, Walter Fiers and his co-workers at the Molecular Biology unit of the University of Ghent, Belgium, first determined the sequence for bacteriophage MS2 coat protein gene. In 1976, the team determined the complete nucleotide-sequence of bacteriophage MS2-RNA. Frederick Sanger in the year 1977 sequenced the first DNA-based genome of bacteriophage Φ-X174. The first free-living organism to be sequenced was that of *Haemophilus influenza* in 1995. In early 2000, the human genome was completed by the Human Genome Project. The complete sequence was known of about 1879 viruses, 577 bacterial species and roughly 23 eukaryote organisms, of which about half are fungi on 2007. The worm *Caenorhabditis elegans* is an often used simple model for multicellular

organisms. The Japanese pufferfish (*Takifugu rubripes*) and the spotted green pufferfish (*Tetraodon nigroviridis*) are also interesting because of their small and compact genomes, containing very little non-coding DNA compared to most species. Most of the bacteria whose genomes have been completely sequenced are problematic disease-causing agents, such as *Haemophilus influenza*. The mammals, dog (*Canis familiaris*), brown rat (*Rattus norvegicus*), mouse (*Mus musculus*), and chimpanzee (*Pan troglodytes*) are also important model animals in medical research. The zebrafish (*Brachydanio rerio*) is also used for many developmental studies on the molecular level and the flower Arabidopsis thaliana is a model organism for flowering plants (Weckwerth 2008; Bottcher et al, 2008; Dacks et al, 2008).

3. The Genomics Project

The Human Genome Project completed in 2003, which is coordinated by the U.S. Department of Energy and the National Institutes of Health. The goals were a) identifying all the genes in human DNA, b) determining the sequences of the 3 billion chemical base pairs that make up human DNA, c) storing this information in databases, d) improving tools for data analysis; transferring related technologies to the private sector and addressing the ethical, legal, and social issues (ELSI) that may arise from the project. The project began in 1990 initially headed by James D. Watson, who was head of the National Center for Human Genome Research at the National Institutes of Health (NIH) in the United States starting from 1988. But, due to his disagreement with Bernadine Healy over the issue of patenting genes, he was forced to resign in 1992. He was replaced by Francis Collins in April 1993, and the name of the Center was changed to the National Human Genome Research Institute (NHGRI) in 1997. A working draft of the genome was released in 2000 and a complete one in 2003. Most of the sequencing was performed in research institutes and universities from the USA, UK, along with geneticists from China, France, Germany and Japan. The objective of the Human Genome Project was to understand the genetic makeup of the human species; it has also focused on several other nonhuman organisms, i.e. *Escherichia coli*. The roots of the project started from the early work on the inheritance of traits, like those in plants. The genome was broken into smaller pieces; approximately 150,000 base pairs in length. These pieces were termed as bacterial artificial chromosomes (BACs), because it could be inserted into bacteria, where they could be copied by the bacterial DNA replication machinery. Each of these pieces was then sequenced separately as small 'shotgun' project and then assembled. The larger, 150,000 base pairs went together to create chromosomes. This was termed as the hierarchical shotgun approach. This was so because the genome was first broken into relatively large chunks, which were then mapped to chromosomes before being selected for sequencing. The widespread international cooperation and advances in the field of genomics and sequence analysis along with development in computation, the 'rough draft' of the genome was finished in 2000. These drafts covered about 83% of the genome. In February 2001, at the time of the joint publications, press releases announced that the project had been. Improved drafts were announced in 2003 and 2005, filling into ~92% of the sequence currently. The last chromosome was published in the journal Nature, on May 2006. Along with this project, in 1998, a similar, privately funded quest was launched by Craig Venter and his firm Celera Genomics. It was a $300 million project that was intended to proceed at the faster and at fractions of the cost of the roughly $3 billion publicly funded project. The technique known as whole genome shotgun sequencing that had been used to sequence bacterial genomes of up to six million base pairs in length, but not for anything nearly as large as the three thousand million base pair human genome by Celera Genomics. Thus, the Human Genome Project is the most well known of many international genome projects that aimed at sequencing the DNA of a specific organism, which offered the most tangible benefits, important developments in biology and medicine. This are predicted the result of sequencing of model organisms for example, mice, fruit flies, zebrafish, yeast, nematodes and others (Suarez et al, 2007; Cattley et al, 2007; Lyle et al, 2007; Comai 2007).

4. Genomics strategies

In Bacteriophage Genomics Strategies, bacteriophages have been playing a key role in bacterial genetics and molecular biology. These are previously used for defining gene structure and regulation. The first genome sequence of bacteriophage did not lead the genomics revolution, which is further dominated by bacterial genomics. After the prominence of

bacteriophage genomes analysis, researchers started to understand the mechanisms underlying phage evolution. The bacteriophage genome sequences obtained through direct sequencing of isolated bacteriophages. In some case, this can derived as part of microbial genomes, also analysis of bacterial genomes shows the substantial amount of microbial DNA consists of prophage sequences and prophage-like elements (Cheng et al, 2007; Powers 2007). In Cyanobacteria Genomics Strategies having total 24 cyanobacteria for which a total genome sequence are available. Out of this, 15 originated from the marine environment. Study demonstrated that the various sequences used for inferring various physiological and ecological characteristics of marine cyanobacteria and thus, the growing body of genome information also used for addressing global problems by applying a comparative genomics (Ikegawa 2007; Maeda 2007). Computational genomics Strategies deciphering biology from genome sequences using computational analysis. It mainly focuses on understanding the human genome and the principles for DNA control biology of any organisms at the molecular level. Computational simulation is applicable for most important means to biological discovery for the current abundance of massive biological datasets. The various role performed by this techniques including discovering subtle patterns in genomic sequences, proposing cellular signaling networks, proposing mechanisms of genome evolution, predicting precise locations of all human genes using techniques with several mammalian and vertebrate species, predicting conserved genomic regions that are related to early embryonic development, discovering potential links between repeated sequence motifs and tissue-specific gene expression and measuring regions of genomes that have undergone unusually rapid evolution (Legato 2007; Manning et al, 2007). Nitrogenomics Strategies involves the study of genomics pertaining to nitrogen utilization and assimilation in organisms. The genomics of nitrogen assimilation lie at different levels of organisms from microbes to higher organisms, where different genetic controls regulate the actual assimilation (Beyer et al, 2007; Cobourne 2007). Metagenomics Strategies invloves the study of genetic material recovered directly from environmental samples. This enables the study of organisms that are not easily cultured in a laboratory as well as their natural environment (West 2007). Personal genomics Strategies is a field for popularizing the technology to common people. It's main goal to sequence as many people as possible for large scale comparative genomics analysis. Once a great number of 3 billion bases of individuals are collected, human genetic diversity could be completely mapped (Bush 2007).

5. Genomics Technology

5.1. Analytical technologies: Separation techniques

5.1.1 Gas chromatography (GC)

A common problem in the omics field is the consolidation of signal list derived from metabolic profiling of different cell or tissue or fluid states where a number of replicate experiments was collected on each state. It is an approach for the consolidation of peak list based on hierarchical clustering, first within each set of replicate experiments and then between the sets of replicate experiments. The problems of finding the dendrogram tree cutoff, which gave the optimal number of peak clusters and the effect of different clustering methods. This approach is applied to gas chromatography-mass spectrometry metabolic profiling data, which are acquired on *Leishmania mexicana.* Analysis result into robust data matrices, which completely separated the wild-type and two mutant parasite lines based on their metabolic profile (De Souza et al, 2006). Over the past decade, genomics has undergone a rapid development and radiation, diversifying across the biochemical landscape. Targeted approaches, profiling strategies using affinity capture mass spectrometry and solution array represented realistic opportunities to deliver predictive capacity. Many recent applications in genomic and peptide profiling, viz., solid-phase affinity capture mass spectrometry and the targeted approach of antibody arrays have also arose for gene expression analysis (Rice et al, 2006). Predictive metabolite profiling based on resolution of GC-MS data followed by multivariate data analysis applied to three different biofluid data sets. Hierarchical multivariate curve resolution (H-MCR) is used to simultaneously resolve the GC-MS data into pure profiles. Analysis presented an extension of the H-MCR method allowing treatment of independent samples according to processing parameters estimated from a set of training samples. Predictions of the new samples are based on their metabolite profiles, into an existing model, which is the requirement for a working application with clinical diagnosis.

Method also reduced the time for curve resolution process, which only a subset of representative samples, while the remaining samples could be treated according to the obtained processing parameters (Jonsson et al, 2006).

5.1.2 High performance liquid chromatography (HPLC)

Liquid chromatography- mass spectroscopy **(**LC-MS) platform is used in large peptide analysis for combining collision-induced dissociation (CID), electron-transfer dissociation (ETD) and CID of an isolated charge-reduced (CRCID) species derived from ETD, which is determine the sites of phosphorylation and glycosylation modifications. The prediction of large peptide fragments sequence can possible from complex proteins, i.e. beta-casein, tissue plasminogen activator (t-PA) at low femtomol level. It was found that after the incorporation of an additional CID activation step for a charge-reduced species, isolated from ETD fragment ions, improved ETD fragmentation when precursor ions with high > 1000 m/z were automatically selected for fragmentation. Also, the identification of the exact phosphorylation sites is strengthened by the extensive coverage of the peptide sequence with a near-continuous product ion series. This strategy provided good starting survey scan for characterizing enzymatic peptide mixtures over a broad range of masses using LC-MS with data-dependent acquisition. The new LC-MS platform is useful approach for the comprehensive characterization of complex proteins and genomes (Wu et al, 2007). The derivatization of cysteine-containing peptides with benzoquinone compounds is rapid, quantitative and specific in acidic media. During liquid chromatography separation shows the conversion of cysteines into hydrophobic benzoquinone-adducted residues for altering the chromatographic properties of cysteinyl peptides. The benzoquinone derivatization allow the accurate selection of cysteine-containing peptides of bovine serum albumin tryptic digest by diagonal reversed-phase chromatography, which consisted of one primary and a series of secondary identical liquid chromatographic separations, before and after a cysteinyl-targeted modification of the peptides by benzoquinone compounds (Dayon et al, 2007). For identification of phosphoproteins regulated by the phosphoprotein phosphatase (PPP) family of S/T phosphatases, large-scale characterization of changes in protein phosphorylation on extracts from HeLa cells treated with or without calyculin A, a potent PPP enzyme inhibitor. For this, a label-free comparative phosphoproteomics approach using immobilized metal ion affinity chromatography and targeted tandem mass spectrometry was employed to discover and identify signatures based upon distinctive changes in abundance. 232 proteins are identified as either direct or indirect targets for PPP enzyme regulation (Yang et al, 2007).

5.2. Analytical technologies: Detection techniques

5.2.1 Magnetic resonance imaging (MRI)

Genomics, proteomics and metabolomics offers unique ways for probing internal mechanisms of cancer. The study of the global variation of metabolites involved in the development and progression of cancers nuclear magnetic resonance (NMR), which is quite a useful technique. The most fundamental magnetic resonance methodologies with regard to human prostate cancer are magnetic resonance spectroscopy and magnetic resonance spectroscopic imaging. It has been seen that some crucial metabolites could indicate cancerous lesions and have the potential to direct treatment (Jordan et al, 2007). Scientists demonstrated the biological basis of cancer at the molecular level. It is quite possible to model the process of cancer and identify the points at which therapeutics could operate. Genomic analysis also added to conventional pharmacokinetics, pharmacodynamics in preclinical models and at selected points in clinical development; but advancement in functional imaging made this an important tool for assessing response to therapy. Functional analyses of computed tomography (CT) and magnetic resonance imaging (MRI) images also added important information about tumour patho-physiology, positron emission tomography (PET) and single photon emission tomography (SPECT) imaging that made it possible to study the distribution and therapeutic function of drugs (Begent 2007). Genomics, proteomics and metabolomics leased fresh life in new era of biomedical discovery that is already affecting every field of medicine. With their rapid growth there is great interest in applying these technologies not only to diagnose and prevent disorders, but also to enhance brain longevity and mental wellness. Nearly two-thirds of the total genes in the human genome are found to

relate to the brain functions and up to half of the variance in age-related changes in cognition; in which brain volume and neuronal function appeared to be genetically determined (Petrella et al, 2008).

5.2.2 Mass spectrometry (MS)

Advances in genomics technologies in the last decade; mass spectrometry has emerged as the preferred method for in-depth characterization of the various components of biological systems. In-depth understanding of the composition, regulation and function of molecular complexes and pathways has been gained. It is clear that mass-spectrometry-based techniques are vary powerful hypothesis-generating engine, which combined with complementary molecular, cellular and pharmacological techniques, provided a framework for translating large data sets into an understanding of complex biological processes (Cravatt et al, 2007). Genomics and proteomics have grown significantly with the aid of new technologies that were becoming more streamlined. While processing of proteins from a whole cell lysate have typically done in a bottom-up fashion utilizing MS/MS of peptides from enzymatically digested proteins. Top-down proteomics and genomics is becoming a viable alternative that has limited largely to offline analysis by tandem mass spectrometry. Scientists explained a method for high-resolution tandem mass spectrometry of samples on a chromatographic time scale. Single liquid chromatography-tandem mass spectrometry (LC-MS/MS) identified 22 yeast proteins with molecular weights from 14 to 35 kDa. Using anion exchange chromatography to fractionate whole cell lysate detected 231 metabolically labeled (14N/15N) protein pairs from *Saccharomyces cerevisiae*. This is the first demonstration of top-down proteomics and genomics on linear ion trap Fourier transform (LTQ FT) systems using high-resolution MS/MS data obtained on a chromatographic time scale (Parks et al, 2007). Tandem mass spectrometry coupled to liquid chromatography (LC-MS/MS) allowed identification of biological samples in a complex mixture without need for sample purification. Progress in LC-MS/MS-based quantification, phosphoproteomic analysis, and targeted LC-MS/MS using multiple reaction monitoring (MRM) has made LC-MS/MS a powerful tool for studying cell physiology (Pisitkun et al, 2007).

5.4. Genomics in practice

The announcement of the birth of Dolly in late 1990s additional sheep, cows, goats, pigs and mice were cloned. Cloning was found to be attractive, which reduced the effort and time needed for farmers to do what they have been doing for years: selecting and propagating the best of the herd. The significance of the first cloned mammal achieved from an adult cell. One cell, the fertilized egg, contains all of the information needed to multiply and give rise to all of the specialized cells in the body. Cells turn on and off different genes as they become specialized. In cloning differentiated cell reprograms or resets its genetic information so that it acts as a fertilized egg. Cloning has opened many doors, which could lead to remarkable medical advancements but, as with all new technologies, it would be accompanied by ethical and social dilemmas. Today's successes would pave the road to improving efficiencies and help add to the basic understanding of our cells (Seam et al, 2007). In the mid-1980s researchers began to examine the promises of gene-therapy through logical and straightforward solution to genetic disease, i.e. if a gene seemed to be causing a disease, then to cure the disease scientists must remove the bad gene and substitute a good gene. Hundreds of gene therapies protocols exist, one few have been approved for human trials. Gene therapy has yet to fulfill its promise of curing any genetic disease. Human gene therapy experimentation raised many issues and promises to the technology, which is represented as very great and the reality of dangerous. It has been found the for a better gene therapy, some of the given criteria protocol must be followed, i.e. to reappraise the current framework and structure of gene therapy research, to reexamine informed consent procedures and to take public responsibility for their actions (Bottero et al, 2004). Another use of genomics is in the case of transgenic organisms. A transgenic organism is any living creature, such as a bacterium, plant, or animal that received a foreign gene by means of genetic engineering. There are many applications for transgenic organisms in the health and food industries. Scientists developed a variety of transgenic silkworms that spin industrial-strength or glow-in-the-dark fibers, for example, or make silk with human proteins. A mosquito could also be engineered to be unable to carry one type of malaria parasite. Field tests are underway to determine the safety of using transgenic pink bollworms, designed to spread sterility to wild

bollworms, to protect agricultural crops. Most transgenic research are still in the development phase and now is the time to address the impact of transgenomics on the environment, crop production and animal and human health (Hinkelbein et al, 2007).

5.5. Technology development in Genomics and approaches

5.5.1 Data mining

Emerging statistical concepts like data mining techniques can be use for genomic data analysis. A novel concept of statistical significance, called false discovery rate the rate of false-positives among all positive findings that has suggested controlling the error rate of numerous false-positives in large screening biological data analysis. Statistical modeling in genomic data analysis have been presented, viz., analysis of variance and heterogeneous error modeling approaches for analyzing microarray data obtained from multiple experimental or biological conditions. Other machine learning tools such as supervised learning and unsupervised learning have also been used. The former approach included several multivariate statistical methods to investigate co-expression patterns of multiple genes, and the latter were the classification methods to discover genomic biomarker signatures for predicting important subclasses of human diseases (Lee et al, 2008).

5.5.2 Integrative genomics

The partial gain of chromosome arm 17q is the most frequent genetic change in neuroblastoma (NB) and constituted the strongest independent genetic factor for adverse prognosis. Applied chromosome 17 tiling path BAC arrays on a panel of 69 primary tumors and 28 NB cell lines in order to reduce the current smallest region of gain and facilitate identification of candidate dosage sensitive genes. In all tumors and cell lines with 17q gain, large distal segments are consistently present in extra copies and no interstitial gains are observed. Positional gene enrichment analysis for 17q genes over-expressed in NB also showed that dosage sensitive NB oncogenes are most likely located in the gained region immediately distal to the most distal breakpoint of the 2 breakpoint regions. Comparison of gene expression profiles between primary tumors and normal fetal adrenal neuroblasts revealed two gene clusters on chromosome 17q that were over-expressed in NB, i.e. region on 17q21.32 immediately distal to the most distal breakpoint and 17q24.1, a region coinciding with breakpoints leading to superimposed gain (Vandesompele et al, 2008).

5.5.3 Functional Genomics

Sorghum is one of the more allelopathic crop species that produced phytotoxins, viz., benzoquinone sorgoleone and its analogs. Sorgoleone accounted for much of the allelopathy of Sorghum spp., representing the predominant constituent of Sorghum bicolor root exudates. The biosynthetic pathway for this plant growth inhibitor occurred in root hair cells, which involved a polyketide synthase activity utilizing an atypical 16:3 fatty acyl-CoA starter unit, resulting in the formation of a pentadecatrienyl resorcinol intermediate. Analyses is performed by gas chromatography-mass spectrometry with sorghum root extracts identified a 3-methyl ether derivative of the likely pentadecatrienyl resorcinol intermediate, indicating that dihydroxylation of the resorcinol ring is preceded by O-methylation at the 3'-position by a novel 5-n-alk(en)ylresorcinol-utilizing O-methyltransferase activity. Quantitative real time reverse transcription-PCR and recombinant enzyme studies with putative O-methyltransferase sequences obtained from the expressed sequence tag data set is led to the identification of a novel O-methyltransferase highly and predominantly expressed in root hairs, which preferentially utilizes alk(en)ylresorcinols among a panel of benzene-derivative substrates tested (Baerson et al, 2008).

5.5.4 Comparative genomics

DNA microarray hybridization compared the genome content of *Streptomyces avermitilis*, *Streptomyces cattleya, Streptomyces maritimus* and *Kitasatospora aureofaciens* with that of *Streptomyces coelicolor* A3(2), which showed about 93% agreement with the genome sequence data available for *S. avermitilis*. It also showed a number of trends in the genome structure for Streptomyces and closely related Kitasatospora. A core central region is found to be conserved that could be predicted from previous research and is linked to a low degree of gene conservation in the terminal regions of the linear chromosome across all four species. Between these regions there are two areas of intermediate gene conservation by microarray analysis where the gene synteny is still detectable in *S. avermitilis* (Hsiao et al, 2008).

6. Applications of Genomics

Genomics has been applied in many diverse fields. This includes agriculture and drug production, where not only can the best traits be perpetuated but farm animals could also be used as machines for large-scale production of medically important proteins. A transgenic cloned lamb is able to produce milk containing factor IX - the protein that is deficient in haemophiliacs. Genomics has also been applied for maintaining biodiversity. Cloning may be an important tool for preserving endangered species if currently practiced methods fail. Biomedical Research is also an important area where genomics studies are performed. Cloning and other strategies could produce genetically identical laboratory animals which can be used as models for human disease. The most commonly used laboratory animal, the mouse, reproduces rapidly and its genetics is well studied. A mouse was successfully cloned and will likely facilitate the discovery of new treatments for disease. In addition, it provides a model for studying the interaction of nuclear verses mitochondrial genes and for nuclear verses cytoplasmic factors. Some commercial endeavours have been performed too. Researchers got little success in the steps required to make a dog clone, such as development after nuclear transfer and embryo implantation into the womb. Much human disease treated using this area of research. Cells can harvested from early embryos to provide cell and tissue replacement without the hazards of transplantation rejection (Dieterle et al, 2008; Liu et al, 2008).

7. Current Research

The availability of multiple teleost (bony fish) genomes is providing unprecedented opportunities to understand the diversity and function of gene duplication events using comparative genomics (Howarth et al, 2008). Chronic toxicities attributed to botanical dietary supplements may be caused by contamination by heavy metals, pesticides, microbes or by inherent properties of constituents of the botanicals themselves. These chronic toxicity problems may be prevented by implementing good agricultural practices and good manufacturing practices and applying existing toxicity testing similar to those used in drug development or new toxicity assays under development based on proteomics, genomics, or metabolomics (van Breemen et al, 2008). A functional genomics is used for rapid functional identification of putative genes based on the combined in vitro protein synthesis with mass spectrometry. For the rapid identification of functional activity of unknown genes from a sequence database, a new method based on in vitro protein synthesis combined with mass spectrometry was developed (Kim et al, 2008). This comparative genomics study of human vs. insects sheds light on the composition and assembly of protein complexes in the synapse gives the nature of the protein-interaction graphs, their domain composition and the sequence similarity between human and insects differentiate exocytotic from endocytotic proteins and suggest unique evolutionary constraints for each group. The design of proteins of the presynaptic site can be studied from a comparative genomics perspective on human and insects (Yanay et al, 2008). The importance of trehalose metabolism and its role in plants have gone through something of a revolution. Trehalose metabolism and signaling is an area of emerging significance; mutant and transgenic plants of trehalose synthesis display wide-ranging and unprecedented phenotypes for the perturbation of a metabolic pathway. Molecular physiology and genomics have provided a glimpse of trehalose biology that had not been possible with other conventional techniques due to because the products of the synthetic pathway, trehalose 6-phosphate (T6P) and trehalose, are in trace abundance and difficult to measure in most plants (Paul et al, 2008). Perch are promising species for freshwater aquaculture and, differently from other fish and show a wide genetic variability that is undesirable for aquaculture. EST cataloguing and profiling of perch will provide a basis for functional genomic research in this species and also promote studies in comparative and environmental genomics, for identifying polymorphic markers that are useful; the disease resistance of fish and for discovering of new molecular markers of exposure. Using genomic resources of Perch will give immediate and practical benefits in the field of aquaculture, allowing early diagnosis of the fish conditions and helping in the generation of new mechanistic data on the nature of fish responses to different farming conditions (Rossi et al, 2008). Genomics analysis can provide the basis for understanding the evolution of emerging, lethal human pathogens such as *Legionella pneumophila*, the causative agent of Legionnaires' disease. Genomic also revealed that *L. pneumophila* is a genetically diverse

species, in part due to horizontal gene transfer of mobile genetic elements *among L. pneumophila* strains, but also between different Legionella species. The genomic background also plays a role in disease causation as demonstrated by the identification of a globally distributed epidemic strain exhibiting the genotype of the sequenced *L. pneumophila* strain (Cazalet et al, 2008). Diabetic nephropathy occurs in only a few patients with diabetes, it is the major cause of end-stage renal disease in the world. Hyperglycemia and hypertension are important factors predisposing patients to diabetic nephropathy, but accumulating evidence points to critical genetic factors predisposing only a subset of patients with diabetes to nephropathy. Comparative genomics using the robust genetic reagents available in laboratory mice should provide a complementary approach to defining genes that may predispose to diabetic nephropathy in mice and humans. This new studies to identify genetic risk factors for diabetic nephropathy and the unique approaches that may be used to elucidate the genetic pathogenesis of this disorder in mice (Breyer et al, 2007). Genome sequencing of different strains demonstrates enormous interest in the genetic and metabolic diversity of bacteria. Plasmids with an enormous size range are also widespread in the Roseobacter clade indicating an adaptive genomic structure. Comparisons with other highly relevant groups, like the SAR11 clade, have shown drastic differences in genome organization. Physiological characteristics and the different isolation sources indicate that organisms of the Roseobacter clade occupy various ecological niches (Brinkhoff et al, 2008). Genomics technologies are disruptive yet potentially cost-effective because they enable primary prevention, the antidote to runaway costs and declining productivity in health care. Many bioethical and social-policy implications are alarming (Carlson 2005). Genomics study demonstrates the necessity of whole-genome analysis to complement population and gene-based studies, which are of limited utility in uncovering complex events such as recombination that may lead to functional differences in virulence and pathogenicity. The advancement of comparative genomics of human pathogens and emerging disease in wild populations of endangered species are applicable in the analysis of full-length lion lentiviruses (Pecon-Slattery et al, 2008). The ionome is science which can define as the mineral nutrient and trace element composition of an organism and represents the inorganic component of cellular and organismal systems. Ionomics is the study of the ionome, involves the quantitative and simultaneous measurement of the elemental composition of living organisms and changes in this composition in response to physiological stimuli, developmental state, and genetic modifications. Ionomics has the ability to capture information about the functional state of an organism under different conditions, which is driven by biotic and abiotic factors. Ionomics is the potential tool to provide a powerful approach to not only the functional analysis of the genes and gene networks that directly control the ionome, but also to the more extended gene networks that control developmental and physiological processes that affect the ionome indirectly (Salt et al, 2008)**.** Hepatocellular carcinoma (HCC) is a worldwide health issue that has started receiving attention but similar to most types of cancer, hepatocarcinogenesis is a multistep process involving different genetic alterations that ultimately lead to malignant transformation of the hepatocyte. As technology advances and research continues, the genetic changes and influences among these entities will prove essential to improved diagnostic and therapeutic options. It remains a challenge to provide a clear picture of the connection between virus and cancer and providing a direction for future research and treatment (Tan et al, 2008). Phylogenetic and primary sequence characterization of cathepsin B cysteine proteases were studied from the oxymonad flagellate monocercomonoides. Comparative genomics, sequence alignment analysis and phylogenetics are used for cathepsin sequences analysis, which help to study the diversity of eukaryotes demonstrated that absence of the occluding loop is not a feature exclusive to oxymonads, but is relatively common, suggesting that the occluding loop should no longer be used as the defining feature of the cathepsin B subfamily (Dacks et al, 2008)**.** Levels of cytochromes P450 and especially drug transporters due to inflammation in brain, intestine, and placenta have significant implications for the use of many drugs in diverse clinical settings. The development of mouse models of live bacterial infection provides excellent opportunities to explore the impact of infection on drug metabolism beyond the well characterized effects of bacterial endotoxin. Repression of drug clearance pathways by cancer cytokines may result in extreme toxicity

to chemotherapy, compromising treatment of many cancers (Morgan et al, 2008). Induction of drug enzyme activity in the intestine can strongly determine plasma levels of drugs. It is important to predict drug-drug interactions in human intestine in vitro. The study shows that human intestinal precision-cut slices are useful to study induction of drug-metabolizing enzymes and transporters in the human intestine (van de Kerkhof et al, 2008). It's also possible that genes not directly involved in a particular pathway could end up being predictive of clinical outcomes. Although pharmacogenomics has the potential to radically change the way health care is provided, it is only in its infancy. In the future, pharmacogenomics could find uses along the entire drug discovery and development timeline, all the way from target discovery and validation to late-stage clinical trials (Gomase et al, 2008a). Bioinformatics is being increasingly used to support target validation by providing functionally predictive information mined from databases and experimental datasets using a variety of computational tools (Gomase et al, 2008b).

8. New aspect of cancer research

8.1 MicroRNAs (miRNAs)

MicroRNAs are a new class of endogenous, non-coding, small RNAs, which negatively regulate gene expression in a sequence-specific manner. They can act via translational repression or mRNA degradation. MicroRNAs discovery revealed a new and exciting aspect of post-transcriptional gene regulation, which is universally involved in cellular homeostasis. The advent of miRNAs added another level of complication in the already complex regulatory networks of the cell and should be considered gene regulators of equal importance with proteins. Now researchers attention to the miRNA field for an additional reason: an increasing line of evidence indicated that miRNA genes are tightly connected with the process of tumorigenesis. Many miRNAs genes demonstrated to behave as oncogenes or tumor suppressor genes in many types of cancer. The mechanisms by which miRNAs can destabilize the normal cellular processes, promoting cell transformation and tumor progression play a critical role. New technologic use the profiling of the miRNA expression patterns in normal and cancer tissues and discovered unexpected greater reliability of miRNA expression signatures in classifying cancer types than the respective signatures of protein-coding genes. miRNAs play prognostic value in predicting clinical behaviors of cancer patients (Giannakakis et al., 2007; Nervi et al., 2008; Bertucci and Birnbaum 2008; Yang et al., 2008). They are important regulatory molecules in plants and animals. miRNA, by translational repression, mRNA cleavage, and mRNA decay initiated by miRNA-guided rapid deadenylation. Some miRNAs regulate cell proliferation and apoptosis processes that are important in cancer formation. By using multiple molecular techniques, which include miRNA microarray, Northern blot analysis, real-time PCR, up or down-expression of specific miRNAs, it was found that several miRNAs were directly involved in human cancers, including brain, liver, lung, breast, colon cancer and leukemia (Zang, et al., 2007).

MicroRNAs altered in human tumors, both oncogenic and tumor suppressive potential and aslo involvement in the pathophysiology of brain cancer. miRNA germline, somatic mutations and polymorphisms in the protein coding messenger RNA targeted by miRNAs contributing to cancer predisposition, initiation and progression. In somatic cells, miRNA alterations may play a role in tumor initiation, while if present in germ line cells they could constitute a cancer predisposing event. miRNA fingerprinting is the diagnostic and prognostic tools used by medical oncologists. New therapeutic strategies involving miRNA silencing or miRNA mimics could be proposed based on the roles of these small non-coding RNAs as oncogenes and tumor suppressors in brain tumors. The discovery of miRNAs interact with known oncogenes has established further links with molecular pathways implicated in malignant transformation. miRNAs can used as diagnostic markers and their potential as therapeutic molecules has moved miRNAs from the area of basic research to the field of tumor biotechnology. The mechanisms of mRNAs of tumor suppressor- and oncogenes i.e. gross genomic aberrations, epigenetic changes, and minor mutations affecting the expression level, processing and target-interaction potential of the miRNA. Expression profiling of miRNAs has been found to be useful for classification of different tumor types and classified as onco-miRs or tumor suppressor-miRs and may turn out to be potential targets for cancer therapy (Esteller 2008; Negrini et al., 2007; Cowland et al., 2007; Nicoloso and Calin 2007).

8.2 SNP and Genetic association

The development of DNA chip technology has significant impact on the genetic analysis of human disorders. The newly developed single nucleotide polymorphism (SNP) array can use to measure both DNA polymorphism and dosage recomondations. SNP microarray analysis to uncover frequent uniparental disomies and sub-microscopic genomic copy number gains and losses in different cancers. SNP array genotye can determine loss of heterozygosity, genomic copy number changes and DNA methylation alterations of cancerous cells. It can be applied to the identification of cancer predisposition genes, oncogenes and tumor suppressor genes in specific types of tumors. Variations in DNA sequences associated with multiple human disorsers may affect phenotypes in trans via non-protein-coding RNA intermediaries interfering with functions of microRNAs. It defines the nuclear import pathway as a potential major target in many human diseases (Mao et al., 2007; Glinsky 2008a).

A genome-wide association study reveals a structural feature of sncRNA sequences and human microRNAs. These features are useful for multiple seemingly unrelated sncRNA pathways points to a multitude of potential functional and regulatory implications. It involves mechanisms of gene expression regulation, control of biogenesis, stability and bioactivity of microRNAs, sncRNA-guided macromolecular interactions and transcriptional basis of self or non-self discrimination by immune system. Non-protein-coding transcripts are contributing to phenotype-defining regulatory and structural features of a cell. The RNP complexes of sncRNAs of a cell suggesting that informasomes represent the intracellular structures, which provide the increasingly complex structural framework of genomic regulatory functions in higher eukaryotes to facilitate the stochastic, random and probabilistic mode of choices in a sequence of regulatory events defining the phenotype. SNP arrays provide a high-resolution platform for describing several types of genetic changes simultaneously. This array increasing powerful tools for describes the genetic events cancer. The ability to determine allele-specific copy number changes has only recently been described by SNP array and offers a high-throughput platform for large-scale association studies that are likely to lead to the identification of multiple germline variants, which predispose to cancer. SNP arrays are an ideal platform for identifying both somatic and germline genetic variants that lead to cancer. Techniques provide a basis for DNA-based cancer classification and help to define the genes being modulated, improving understanding of cancer genesis and potential therapeutic targets (Glinsky 2008b; Dutt and Beroukhim 2007; Gomase et al., 2008c)

8.3 Transcriptomics in cancer research

A wealth of evidence has pointed to dietary habits as a determinant of premature death, including that associated with heart disease, stroke, diabetes, liver disease, atherosclerosis and cancer. Nutritional genomics refers to the bidirectional interactions between diet and genes. Nutritional genomics encompasses an understanding about how the response to bioactive food components depends on an individual's genetic background i.e. nutrigenetics. Nutrient induced changes in DNA methylation, histone posttranslational modifications, and other chromatin alterations (e.g.- nutritional epigenetics) and nutrient induced changes in gene expression known as nutritional transcriptomics. Nutritional transcriptomics study of nutrition will assist in understanding how genetic variation, epigenetic events and regulation of gene expression alter requirements for, and responses to nutrients. Genes and diet could ultimately help identify modifiable molecular targets for preventing, delaying and reducing the symptoms of cancer and other chronic disorders. High-throughput profiling applications are increasingly used and may now even be considered standard research tools. Transcriptomics technologies for potential biomarkers prediction profiling studies have in turn attracted the attention of basic researchers eager to uncover biological mechanisms underlying clinically useful signatures. In specific transcriptomics are use for gene expression datasets and most current applications in breast cancer research. Use of transcript profiles is to define the molecular signature of diseases e.g. cancer and transcriptomics has used to study intestinal biology (Ross 2007; Culhane and Howlin 2007; Fleet 2007; Schäfer et al., 2007). Interrelationship between the food components and the 'omics techniques' (transcriptomics, proteomics, genomics, epigenomics and metabolomics) have a significant influence on the quality of life as measured by both physical and cognitive performance and modify the risk and severity of a variety of cancer diseases conditions (Milner 2007; He 2006; Puskás et al., 2006; Fan et al., 2006; Miles et al., 2006; Davis and Milner 2004).

8.4 Role of Pharmacogenomics

Applications of Pharmacogenomics to medicine have a long history and the pace of new applications has accelerated in recent decades. Increased investment in science and technology to stimulate a more vigorous and competitive research environment, development of more effective basic and clinical research synergies, recruitment and training of more human resources in genomic medicine, developing mechanisms to stimulate translational research and developing a more modern regulatory framework to ensure, which genomic medicine will successfully contribute to improve healthcare. The treatment of breast cancer with selective estrogen receptor modulators such as tamoxifen and with aromatase inhibitors represents new applications in cancer chemotherapy. The pharmacogenomics ofaromatase inhibitors including the application of a genotype to phenotype research strategy designed to explore the nature and extent of common DNA sequence variation, which encodes aromatase. A genetic variation in the CYP19 gene is important in the activity of aromatase inhibitors and emphasis is on examining multiple genes in pharmacodynamic and pharmacokinetic pathways in women receiving aromatase inhibitors for breast cancer (Weinshilboum 2008; Ingle 2008; Jimenez-Sanchez et al., 2008; Johnson 2008). miRNA molecular diagnostics, pharmacogenomic and clinical laboratory molecular services introduce next-generation miRNA-based diagnostic assays to improve tumor classification, monitor disease progression and potentially allow earlier detection of cancer. These new technologies increased interest of medical practitioners to use molecular biomarkers in early detection, diagnosis and in the prediction of therapeutic treatment efficacy for clinical outcomes, academic and research institutions. Pharmaceuticals have increased their efforts to develop novel molecular biomarkers for several human diseases, including cancer. The identification of molecular biomarkers also enables the development of a new generation of diagnostic products and to integrate diagnostics and therapeutics. Identification and understanding of these carcinogenic gene alterations is the base upon, which we can overcome drug resistance and develop novel treatment approaches understanding of pharmacogenomics of pancreatic cancer treatment (Labourier and Winkler 2008; Manne et al., 2005; Gusev and Brackett 2007; Jain 2005; Kang and Saif 2008).

8.5 Epigenomics a rode of cancer treatment

Epigenetic mechanisms affecting chromatin structure contribute to regulate gene expression and assure the inheritance of information, which are essential for the proper expression of key regulatory genes in healthy cells, tissues and organs. Epigenomics factors such as DNA methylation and histone deacetylation are contribute to the malignant transformation of cells by silencing critical genes. Some drugs inhibit DNA methyltransferases or histone deacetylases are shown to have the potential to reactivate silenced genes and induce differentiation or apoptosis of malignant cells. Histone deacetylase inhibitors are the class of epigenetic modifying agents, which include depsipeptide, butyrate derivatives, suberoylanilide hydroxamic acid and valproic acid. Epigenetic events affect various genes and cellular pathways in a non-random fashion and can predispose to induction and accumulation of genetic changes in the course of tumour initiation and progression. These considerations are critical for a better understanding of tumourigenesis and molecular events underlying the acquisition of drug resistance as well as development of novel strategies for cancer therapy and prevention (Oki and Issa 2006; Leone et al., 2008; Sawan et al., 2008; Baylin and Chen 2005; Rothhammer and Bosserhoff 2007, Sigalotti et al., 2007; D'Alessio and Szyf 2006; Smith et al., 2007; Grønbaek et al., 2007).

8.6 Metabolomics

Integration of novel agents targets chemotherapy for clinical activity in patients with metastatic colorectal cancer. The goal in the future will be to predict which specific chemotherapy and targeted agent combination will most likely benefit individual patients. Personalized therapy for each patient is an important goal for improving the outcome of patients with colorectal adenocarcinoma and includes the intention to maximize efficacy and minimize toxicity of chemotherapeutic agents. Clinical trials driven by molecular targets and agents directed against colorectal adenocarcinoma understand the conflicting data on utility of markers (Hamilton 2008; Iqbal and Lenz 2004). Cytochrome c is primarily known for its function in the mitochondria as a key participant in the life-supporting function of ATP synthesis and the release of cytochrome c and

cytochrome-c-mediated apoptosis are controlled by multiple layers of regulation. Its role in canonical intrinsic apoptosis, cytochrome c amplifies signals that are generated by other apoptotic pathways and participates in certain non-apoptotic functions (Gao et al., 2005b; Shoshan-Barmatz et al., 2006; Ow et al., 2008). E3 ubiquitin ligases are a large family of proteins, which are engaged in the regulation of the turnover and activity of many target proteins. Ubiquitin-proteasomal degradation pathway plays a critical role in protein degradation and regulates a wide variety of cellular functions. This is highly conserved post-translational modification of proteolytic processes is mainly carried out by substrate-specific E3 ligases. The growing understanding of metabolomics in cancer research play important role in cancer development and progression. This lead to the development of a novel class of anticancer drugs targeting specific E3 ubiquitin ligases, as well as the development of sensitive biomarkers for cancer treatment, diagnosis, and prognosis (Lakshmanan et al., 2008; Sun 2006; Newton and Vucic 2007; Pray et al., 2002).

8.7 Bioinformatics approach

Bioinformatics is a rapidly emerging field of biomedical and cancer research. A large-scale genomic and postgenomic data can easily analysed by the help of computational science. Clinical informatics has long developed methodologies to improve biomedical research and clinical care by integrating experimental and clinical information systems (Kim 2002; Kuo 2003; Yang et al., 2008; Molidor et al., 2003). Now days, genome-wide detection of alternative splicing based on Expressed Sequence Tag (EST) sequence alignments with mRNA and genomic sequences has dramatically expanded the understanding of the role of alternative splicing in functional regulation of cancer. Alternative splicing database schema design, it is possible to query genome-wide for alternative splicing patterns that are specific to particular tissues, disease states, gender or developmental stages of cancer. EST alignments can be used to estimate exon inclusion or exclusion level of alternatively spliced exons and evolutionary changes for various species can be inferred from exon inclusion level (Kim and Lee 2008; Hui et al., 2004; Sugnet et al., 2004; Wang et al., 2003). Proteomics technologies are now being advanced for the purpose of identification and validation of new disease biomarkers in cancer. A reliable and useful clinical biomarker must come from a readily attainable source, such as blood or urine and have sufficient sensitivity to correctly identify affected individuals. Also they are sufficient specificity to avoid incorrect labeling of unaffected persons and result in a notable benefit for the patient through intervention, such as survival or life quality improvement. Genomics research have revolutionised cancer research in recent years as high-throughput technologies can now be used to identify sets of genes potentially related with different processes in cancer. Also, managing all genetic data and organising it into useful datasets is still a challenge in the bioinformatics field. Finding relationships between the molecular and genomic information and the clinical information available, within the medical informatics domain and is currently driving the development of translational research in biomedicine (Kohn et al., 2007; Stevens et al., 2003; Boyce and Kohn 2005; Kohn et al., 2003; Simpkins et al., 2005).

8.8 Cancer informatics

Bioinformatics operations are challenged to build data processing and delivery infrastructure, which provides reliable access and enables data integration. Generated data must be processed and stored such that relationships to external data sources can be presented. Consistency and comparability across data sets requires annotation with controlled vocabularies. Metadata standards for data represent are used to access to the processed data should be supported to ensure the maximum possible value is extracted (Covitz et al., 2003; Gao et al., 2006). The development of cancer informatics techniques for oncogenomic analyses such as array comparative genomic hybridization, messenger RNA expression arrays and mutational screens have come to the fore in modern cancer research. These techniques are able to highlight panels of genes that are altered in cancer (Bartlett 2001; Furney et al., 2008; Jiang, et al., 2004). Advances in high-throughput technologies such as DNA microarrays have made it possible to simultaneously measure the expression levels of thousands of genes and proteins. This has resulted in large amounts of biological data requiring analysis and interpretation. The applications of functional genomics, proteomics and informatics to cancer research have yielded a tremendous amount of information, which is growing all the time. This information is available publicly on the internet

and ranges from general information about different cancers from a patient or clinical viewpoint, through to databases suitable for cancer researchers (Devarajan 2008; Mejía-Roa et al., 2008; Brunet et al., 2004; Albertella 2001; Bader and Theofanos 2003).

9. Conclusion

Genomics helped in the evolution of commercial applications of single molecule DNA, RNA and protein analysis. The various technologies extraction of high grade DNA from complex samples, tagging, microfluidics and genomic mapping, addressing high value unmet needs in bio-security, human diagnostics, and food and drug contaminant monitoring. Genomics-mapping technologies are capable of identifying and quantitating individual molecules of DNA, RNA and proteins in a complex sample. The human genome project is the biggest project undertaken to date but there are many research projects around the world trying to map the gene sequences of other organisms. This genomic mapping enables to develop new preventative and therapeutic approaches to the treatment of disease and understand the mechanics of cell biology. Genomics is generating a lot of excitement not only in the scientific research institutes and pharmaceutical companies but also in the financial and insurance worlds. Universal reagent sets are used and no target amplification or culture is required. DNA detection using these technologies provides genomic species identification, while quantitation of RNAs and proteins can be used to track expression, within a highly mutiplexable assay format. Genomics strategies include high-performance DNA sequencing that could dramatically reduce the cost of DNA sequencing for research, drug development, and diagnostic applications.

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