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Use of Multiomics Technology in Genomic Study and Role of DNA Adductomes in Identifying Cause of Certain Diseases and Environmental Pollutions

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Abstract

With the advancement of –omic research in biological sciences , new vistas have opened in different disciplines of Genetics and health sciences. Again this revolution in these disciplines is possible with technological improvement of DNA sequencing technology. This modern technology is known as Next Generation Sequencing. Now-a-days biological analysis is done using multiple –omes such as Genome, Proteome, Transcriptome, Epigenome, Metabolome etc. Recently another Biological technique known as DNA Adductome is used to detect the cause of DNA damage done by many chemical agents, drugs, pollutants etc. Details of Next Generation Technology and Alignment technology have been discussed in the article. The application of Next Generation Sequence (NGS) technology has been applied for the improvement of crop plants.

Another-omic technology is the study of DNA Adductomes. When DNA is bound to any chemical it is called DNA Adduct. The adduct formation is leading to DNA damage resulting into mutation. The origin of many human diseases like cancer and others have been found to be due to the formation of DNA adducts. The way of adduct formation in DNA has been discussed with special reference to human health. The measurement and identification of environmental pollutants can be monitored through the study of DNA Adduct. Thus this multiomic technology including DNA Adductomes may bring revolution in medicine and toxicological studies.

Keywords: Multiomics; Next Generation Sequening; Alignment Technology; Plant Genomics; Crop Plants; DNA Adductomes; Environmental Pollution; Human Diseases

Abbreviations: SAGE: Serial Analysis of Gene Expression; PAH: Pollycyclic Aromatic Hydrocarbons; WBC: White Blood Cell; HRMS: High Resolution Mass Spectrometry; MS: Mass Spectrometry; NGS: Next Generation Sequence; BLAST: Basic Local Alignment Search Tool; GWAS: Genome Wide Association Study; NGST: Next Generation Sequencing Technology; SAGE: Serial Analysis of Gene Expression.

Introduction

With the progress of research in genomic studies and advancement of technology, a new subject MULTIOMICS has been developed with the fusion of technology and biological science in making an integrated approach to analyse Proteome, Transcriptome, Epigenome, Metabolome

Microbiome and DNA –adductome using complex biological processes particularly through data analysis. In this system biological analysis is done using multiple –omes such as Genome, this integrated or combined analysis of data of different-omes, scientists can made a new and definite approach in understanding different problems in plant science, microbiology, human disease, environment and others. In future this new technology may revolutionize the field of medicine and biology. Several complicated diseases may be understood and analyzed through multiomic studies. Single –omic studies cannot give the detailed correct ideas of biological processes but integrated analysis of multiomic data at a time can give scientists an extra power to understand the mechanism of many complicated processes in living organisms including human. These biological processes are multilayered and complex as it is seen even if the central dogma is visualised where it has been noted that there is an intertwined relationship between DNA, RNA and Protein meaning thereby that there are multiple layers of information to connect genotype and phenotype.

With the use of multiomic data, the phenotypic expression from genotype or any alteration in the gene expression can be correctly identified through information from multiple layers (Genomics, Epigenomics, Transcriptomics and Proteomics) leading to open a new vistas in biological and medical science.

Multiomics or Integrative omics is a technique of biological analysis in which the data are taken from many –omes to study in a concerted way to find associations between biological entities in facilitating the identification of markers of severe diseases and other phenotypic or metabolic disorders as well as the interaction of all biological functions within a cell and body. The multiomic analysis use many softwares related to multiomic analysis and applications of Machine learning.

Different–Omic Strategies

Genomics

Genomics is a new subject after Genetics dealing with the study of all genes (genomes) in an organism including interactions of genes with each other and with the environment. With the advancement of technology and the discovery of DNA sequencing and high performance Computational biology like Bioinformatics this new subject Genomics has been developed first in the Jackson Laboratory of USA in 1986 by Dr. Tom Roderick.

While Genetics is dealing with the study of genes and their inheritance meaning thereby the way certain characters or traits carried by genes are transmitted from one generation to another including the expression and effect of genes in the organism. Both Genetics and Genomics are used for detailed genetical studies.

With the advancement of technology and computer science, the new subject Genomics has gained its importance and wide application in deciphering complex diseases of human like heart disease, asthma, diabetes, cancer and others. In plant science and agriculture also this new subject Genomics has opened a revolution in plant breeding after the discovery of whole genome sequencing of many economically important plants leading to the isolation of desired genes, their cloning and even transfer to the target plants through Gene Transfer technology (Genetic Engineering) and thus avoiding long procedure of plant breeding process.

Actually the work of genomics started with the initiation and completion of Human Genome Project. This project started in 1990 and was completed in 2003. The objective of the project was to find out all the base pairs present in the human DNA for the mapping and sequencing all genes present in the human genome. These complete sequencing of human genome has wide application in identifying mutations, genes, diseases, Cancer cells, Forensic work , genotyping of bacteria and viruses , drug design, in the study of evolution and many others. The success of Human Genome Project has initiated this type of Whole Genome Sequencing work in other organisms like in both plant and animal breeding programme for making revolution in food production in agriculture and animal husbandry. Genomic research is now very precise and easier with the advancement of sequencing technology.

So the latest sequencing technology should be discussed first. Recently Sequencing Technologies have been developed using many softwares to make whole genome sequencing in a very short time at low cost. All these techniques have been discussed below.

Next Generation Sequencing

The earlier sequencing methods used were the method of i)Sanger and ii) Gilbert. Of these two methods, the method of Sanger (dideoxy chain termination method) was widely used for its easy protocol, less time consuming and less harmful reagents. With the use of Sanger`s method the whole genome sequencing was done in bacteriophage φ X174 of 5386 bp, genome of Haemophilus influenza 1,830,140 bp, Saccharomyces cerevisae (Yeast) of 12,156,177 bp. Then Human genome (14.8 billion bp) was sequenced after random fragmentation of genome using Shotgun technique in 2001 [1]. But the limitation of Sanger`s method is i)

not cost effective and ii) cannot sequence large number of samples in one run. For these reasons Next Generation Sequencing technique is developed in having ultra-high throughput, stability and speed. It helps to identify the order of nucleotides in whole genome sequence of DNA or RNA with wide applications in biology including medical sciences.

Till 2015, Sanger`s method of Sequencing was widely used as no new technique was developed at that time even though there was limitations in Sanger`s method with capability of sequencing less number of bases in one turn. Large genome of complex organism takes much time. So, high throughput sequencing technologies were developed that is known as Next Generation Sequencing Technology (NGT). It can generate enormous data in short time at minimum cost. The Next Generation Sequencing Technology has been advanced to fourth generation technology starting from first generation Next Generation Technology.

The First Generation of Sequencing starts with the use of Sanger`s method from 1972. Then comes the Maxam and Gilbert`s method in 1977. However the method of Sanger is widely used in the First generation of Sequencing. With the help of this method , the sequencing of whole genome has been done first in bacteria Haemophilus influenza (1995), then eukaryotic genome of Saccharomyces cerevisiae (1996) and Human genome Draft in 2001.

The Second Generation of Sequencing was started with the initiation of platform for Next Generation of Sequencing (NGS) by Roche, Solexa Genome Analyzer and Illumina in 2006, 2007 and 2008 respectively.

The first commercial platform of Third Generation technology was started by Helicose Biosciences in 2008 followed by Personal Genome Machine by Ion Torrent in 2010 and different techniques developed by Pac Bio RS Sequencer till 2016.

The Fourth Generation Technology was developed by Oxford Nanopore Technologies in 2014 and was commercialised in 2018 [1].

The most used advanced technology is the Semiconductor sequencing by Ion Torrent and Nanopore sequencing by Oxford Nanopore Technologies and NABsys [2]. The first commercial sequencing device was developed by Oxford Nanopore Technologies in 2012. This was then more commercialised by different companies like Roche with IBM, Electronic Biosciences and NABsys [3]. With the development of the techniques of Next Generation Sequencing, the work of sequencing can be done in a short period with rapid pace at a very economic cost. The sequencing of whole genome of small organism can be done in one day.

The use of NGS technology in plants has played a very important role in enriching the knowledge of Crop genomes leading to its utilization in plant breeding as well as in getting new information in Gene regulation both at the cellular and whole plant level. It can also be used in Clinical medicine for the diagnosis of human diseases caused by genetic disorder, epigenetics, and forensic studies and in the analysis of gene expression.

Plant genomes are very complex with high repetitive element of high copy number and transposable element with segmental and tandem duplication. In addition to this, autopolyploids and allopolyploids are present. All these characters are causing many difficulties in making genome assembly or sequencing library. For this reason Genome Alignment technologies or Read Alignment technology have been developed to compare related DNA or Protein sequences. So these can also be called as Reference Genomes or Whole Genome Alignment.

Alignment Technology in Genomes

With the development of Next Generation Sequencing technology, the whole genome sequences have been done in large number of organisms. Now the Comparative Genomics have been developed to know the similar sequences at the interspecific and intraspecific level which has an important role in selecting conserved and desired sequences (genes) and evolutionary relationships between species. Comparison of genomes of several thousand sequences of higher organisms can be easily done with high performance by using Alignment Technologies that can generate Reference genome sequences for the species of interest [2].

In the study of comparative genomics the use of alignment technology is needed to find out homologous regions in another organism by comparing the whole genome sequences of two or more organisms through study of Whole Genome Alignments. It is the method for the prediction of evolutionary relationships or homology at the nucleotide level between two or more genomes as well as to estimate the frequency and location of rearrangement and duplication of sequences or common structural function. Another alignment method commonly used in genetics is Read Alignment.

Read Mapping or Read Alignment

In the Next Generation Sequencing a read refers to the DNA sequence from small section of DNA sequences (fragments) from Whole genome sequencing data or the sequence obtained from a single sequencing experiment can be used.

This study can also be done from small fragments or sequences of RNA through Real Time PCR followed by the conversion of RNA sequences to cDNA through Reverse Transcription. Then these sequences are aligned to small sequences (fragments) of the Whole Genome sequences which is called Read Alignment or Mapping. These data can be used as a Reference Genome. These high quality genomes can be differentiated from Whole Genome Sequences in having low number of gaps, less errors and high percentage of sequence assembled into chromosomes. It is known that genomes of viruses and some prokaryotes have complete end to end sequence. But in case of eukaryotic genomes this is different with many gaps as for example in the position of centromeres, telomeres etc. Vertebrate Genome Project first released reference genomes of four mammals (three birds, one reptile, one amphibian and five fishes [4]. All these studies fall under Functional Genomics.

With the improvement of Next Generation Sequencing technology it has been found that the normally used software BLAST (Basic Local Alignment Search Tool) is not sufficient to analyze large number of sequence data using advanced technology. Then the method of Read Alignment has been developed to tackle large number of sequence data. Only reading of sequence data does not throw any light on the origin and order of the sequence or it cannot give a correct idea on genome. So the reconstruction of the whole genome of an organism is needed. Generally the method used for analysis of data is called Brute Force Approach or algorithm to find all solutions in solving the problem. This process is simple but very slow. The technique of Read Alignment can be thousands of orders of magnitude faster than the Brute Force Approach. It can find out the difference between the read and reference genome leading to the detection of genetic variants. The study of genome can be done either by comparing mapping data with a reference genome or by de novo assembling the reads. Recently the analysis of genomic data is done by comparing alignment of sequence reads with reference sequence of the genome to find out variants. The Reference genome of any organism can be obtained from NCBI Database or from dedicated browsers such as Emsemb or UCSC Genome Browser or can be downloaded from NCBI using GenBank, Ref Seq.

Plant Genomics

Plant genomes are very complex with variations in chromosome number, size and in ploidy levels. There is a wide variation in nuclear genomes of plants from less than 100 million base pairs to more than 100 billion base pairs containing large number of repeats, transposable element etc. It has been estimated that nearly 100,000 genes are expressed in tobacco plant while only 25,000 genes are expressed in Arabidiopsis [5]. But all genes do not encode proteins showing that small percentage of genes are functional that is encoding proteins. These genes are called i) Low Copy Number DNA as these are present as single copy or small number of copies. So there are many non-coding genes not only in plants but also in higher organisms. There are some ii) Medium Copy Number DNA that encodes ribosomal RNA and these rRNA genes are repeated to several thousand times in plants. In case of animal the number of ribosomal genes is generally 100 to 200.The rest of DNA in plants are of highly repetitive sequences called iii) High Copy Number DNA. It has been noted that half of the genome in Maize consists of repetitive sequences which is like Retroviral like DNA.

With the advancement of techniques of DNA mapping and DNA sequences, Plant genomic studies have done a great deal in selecting desired genes from the whole genome sequences of crop plants to achieve increased yield in crop plants and to select disease resistant plants etc. It is known that plant chromosomes ate very complex with multiple copies of repetitive sequences and genes. With the innovation of sequencing methods in molecular biology, the process now becomes easy to bring the improvement in economically important plants particularly crop and medicinal plants. The advancement of Bioinformatics has played a great role in the development of Comparative Genomic analysis, evolutionary analysis and Genome wide Association Study (GWAS) in plant.

Advance researches in Plant Genomics are possible due to the development of new technology in DNA sequencing method which is called Next Generation Sequencing Technology.

With the development of Whole Genome sequencing Project, the sequences of large number of economic important and crop plants are available that has been utilized for the understanding of complex genomes of plants through next generation sequencing technology (NGST) to generate reference genome sequences of interest. This complexity of genomes of plant was a problem to scientists for long time prior to the advent of NGST. Previously time-consuming clone by clone method and method of physical genetic map, molecular mapping techniques were used. Recently NGS platforms like GS-FLX , llumina HiSeq and Roche Technology are being used for whole genome shot gun strategy for sequencing various organisms including crop plants as large number of data are available in a short period of time [6]. The rapid development of NGS technology is possible with the advancement of the subject Bioinformatics. The sequencing of many crop genomes is possible with the help of advanced Sequencing Technology leading to its application in crop improvement [6].

Genome Assembly or Sequence Assembly

The genome assembly is done by putting a large number of short sequences of DNA together to recreate the original DNA sequences or chromosomes. So this genome assembly or sequence assembly is one of the important step after performing Next Generation Sequencing.

Generally the identification of marker or specific genes from the whole genome sequences are being done through two methods such as i) *de novo* Assembly and ii) Reference Genome sequencing.

The former method refers to the genome assembly of a novel genome data without using any reference data. The second method is also sequence data base but acting as a representative example of a species set of genes. Once the reference genome is available the genome assembly of any organism will be easier and accurate.

Use of Reference Genomes/NGS Technologies in Plants

Thus the Reference Based Alignment or Reference Genome has an important role in identifying genetic variations, genomic structure and function, genetic assembly of closely related species, molecular markers and candidate genes. In plants. Genome Sequencing has been done in many crop plants using NGS technology to understand the complexity of genomes leading to the identification of many new genes with new functions, genetic variations (SNPs) particularly to note insertions/deletions, translocations, Copy number variations, new linkage characters and others. All these studies may definitely help in the crop improvement programme through plant breeding, in the study of evolutionary history of crop species, adaptation to environmental conditions etc [6]. With the availability of Reference genome, marker genes, SNPs can be identified easily in the target regions of any genome for increasing the selection efficiency. Another advantage of modern technology is that the time of selection is very short in perennial crops where phenotypic expression of a trait may require several years. Again the NGS –based marker discovery techniques have an important role in getting SNPs and genotyping simultaneously as well as there are many transcript sequence and gene data present in public domain [7].

Crop Plants

The use of NGS technologies has acquired large number of genomic data of many important crops at a rapid pace leading to do linkage mapping, gene expression studies, Marker-assisted breeding easily which has accelerated the crop improvement programme. With the advancement of modern technology advances were made in crop and other plants are due to the introduction of many disciplines like Transcriptomics, Proteomics, Genomics, Metabolomics, Epigenomics etc along with different Bioinformatic softwares. The third generation sequencing technology the cost of whole genome sequencing of crop plants is reduced to minimum while the speed, quality and throughput increase exponentially [8]. Using third generation device made by Applied Biosystems and was called SOLID (for sequencing by Oligo Ligation and Detection) the crop improvement programme has made the process very quick and precise as the sequencing of single DNA molecule can be done without any amplification. This third generation sequencing method can generate 10,000 bp reads in a short time followed by the production of highly accurate *de novo* assemblies that can generate contiguous reconstruction of genomes with repetitive elements [2]. Again Gene expression studies can be done with the help of next Generation Sequencing Technology and RNA-seq data. For example, the RNA-seq studies of Puccinia striiformis f.sp. tritici may be used to find genes encoding effector proteins for the development of wheat varieties resistant to this pathogen through plant breeding [9,2].

It is known that Africa has high percentage of hunger and malnourishment with insufficient food , deteriorating natural resources with vast population. So Next Generation Sequencing Technologies were used to increase sustainable productivity in crops. Most of the crops used in Africa was clonally propagated such as Cassava, Yams, Bananas and Plantains and seed crops like Cowpea, Sorghum and Millet. Agriculture in Africa has been carried out with innovative breeding strategies by smallholder farmers growing locally adapted crops which are known as Orphan Crops. Generally there is no High yielding nutritional varieties that respond to biotic and abiotic stresses [8].

Solanaceae

Plants of this family are the most important economically as well as medicinally after crop plants. These important plants are Potato (Solanum tuberosum), Eggplant (S. melongena), Tomato, Capsicum etc. that are used worldwide [3]. For this reason, NGS technologies are being used in this family to identify genes for high yielding, disease resistant varieties as well as large number of sequence data to identify relationship with genotype and phenotype. All members of these edible species have high nutritional value and beneficial effects on human health due to the presence of antioxidants and Carotenoids, Vitamin C, A and E, Flavonoids and Capsicin (anti cancer chemicals), anthocyanin and many secondary metabolites used in medicine.

With the advancement of Nest Generation Sequencing technologies, the whole genome sequencing of many important members have been done in getting average read length of 200bp in Solanaceae. Again the development of HeliScope method by Helicos Biosciences was able to obtain read length of 30 to 35 bp. This technique is based on fluorescence detection system using fluorescent dye as marker. Another technology known as PacBio Rs is a single molecule real time sequencing technology that is able to detect long DNA sequence like 5500 -8500 bp as well as the DNA methylation site having 4-methylcytosine and 6-methyladenine [3]. Another modified Oxford Nanopore Technologies is able to done long reads up to the sequencing of 10kb sequences of DNA in a short time. With the help of these advanced technologies, complete decoding of genome of different species of the family, Gene expression studies, Whole genome association studies, Genome assisted breeding can be done which has a wide application in plant improvement programme.

The gene expression studies can be done through Transcriptome sequencing studies through Next generation sequencing technologies. This study has a vast potential in noting sequence variations in different species or varieties and in the mapping of candidate genes/QTL for identifying traits. In Potato, fourth largest crop in the world, 4, 20, 074 ESTS are recorded and is kept in NCBI database as a valuable resource in potato germplasm for future research. Through transcriptome sequence studies, 22,704 transcripts were identified in potato with 83% of known function [10,11,3].

Transcriptome analysis using NGS technology (RNA-Seq) has made easier and successful to make expression profiling of many plants. Previously Microarray and SAGE (Serial analysis of gene expression) methods were used. This transcriptome analysis may give a complete picture of gene exptrssion under different environmental conditions [6]. Thus different NGS technologies are very useful particularly in increasing the speed in sequencing and other studies for the plant improvement programme.

DNA Adductomes

When DNA is covalently bound to any chemical, it is called DNA adduct. When any toxic chemical is bound to a piece of DNA, it may cause cancer in human as DNA is damaged resulting in mutation. With the increase of pollutants and many toxic chemicals in air, food containing preservatives, pesticides etc. many diseases and disorders are found in the human population throughout the world. For this reason this new field of DNA adductomes has been developed.

Covalent modification of DNA by toxic chemicals leads to genomic instability leading to mutations and altered gene expression causing abnormal cell division, cell growth and function [12]. Thus the study of DNA adduct has a great potential in noting the carcinogenic effects of toxic chemicals, their mode of action and the damage caused by these chemicals as well as to identify the marker.

DNA Adducts and their Formation

Many toxic chemicals present throughout the world are found not only in the environment but also in food, diet and also originated as electrophilic metabolites in human during metabolism. These hazardous chemicals may covalently bind to DNA then it is called DNA Adduct causing damage to DNA leading to mutation and their abnormalities even to cancer by interfering DNA transcription, replication as well as by inducing mutations (Figure 1).

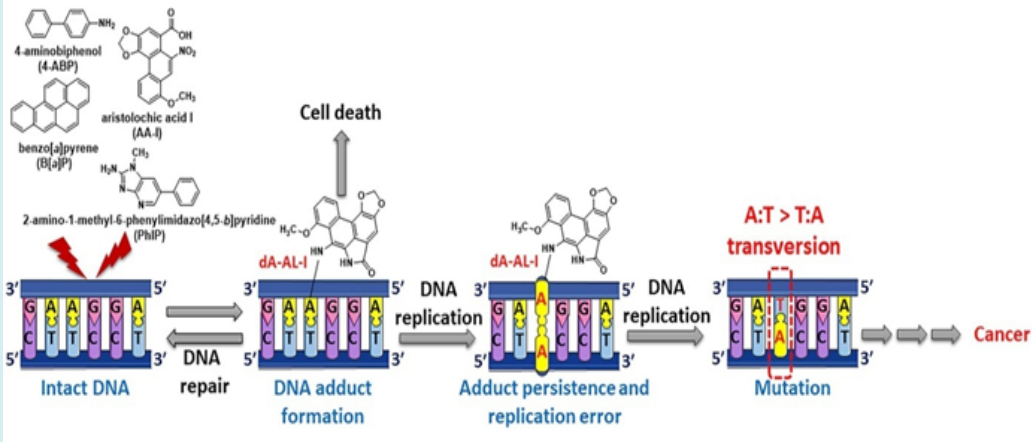

Figure 1: Showing DNA Adduct formation and its effect [14].

The toxic chemicals generally enter the human body from the environment such as air pollutants, radiation, water contaminants, food, drugs and also toxic chemicals derived from metabolisms etc [13]. If DNA adduct is not entered much in the body , then it can be eliminated or repaired through using normal enzyme systems. When DNA adducts (chemicals bund to DNA) are not repaired then these chemicals generally induce cancer by inducing mutations in oncogenes like H-ras , K-ras and p53 tumour suppressor genes [14]. Tobacco used by persons cause a serious health problem by inducing cancers leading to millions of deaths annually. Tobacco contains nicotine and carcinogens. The mode of action of main carcinogenic chemicals present in tobacco NNK (4-(methylnitrosamine)-1-(3-pyridyl)-1-butanone) and NNN (N′- nitrosonornicotine) cause cancer in forming mutation through DNA adducts [15].

DNA Adductomes in Health and Environmental Pollution

There are some common chemicals that generally bind to DNA to form DNA adduct. These are:

- Acetaldehyde.
- Cisplatin: a chemotherapy drug.
- DMBA 7: 12 –Dimethyl benz anthracene - an immunosuppressor and a powerful carcinogen.
- Malondialdehyde: a product of lipid oxidation.
- Polycyclic aromatic hydrocarbon (PAH): a carcinogen resulting from burning coal, oil, gas, wood, garbage and tobacco.

Pollycyclic aromatic hydrocarbons (PAH) are very carcinogenic in human by forming PAH-DNA adducts causing mutations showing the importance of identification of DNA adducts to identify and prevent cancer in human. The formation of DNA adduct with PAH is done after metabolic activation to hazardous chemical Benzopyrene as shown in (Figure 2).

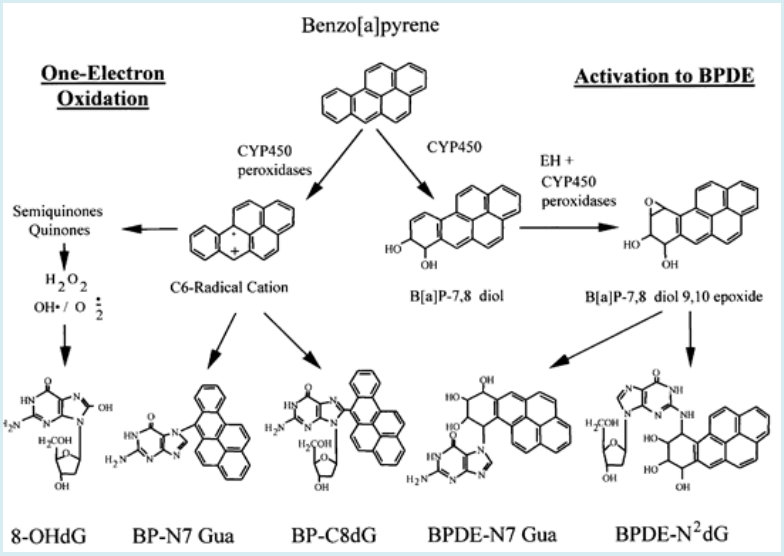

Figure 2: Showing the method of changes in one of the PAH, Benzo[a]pyrene, through some metabolic pathways for causing DNA damage through two methods [16].

For this reason researches are going on to develop the biological markers for the measurement of DNA- adducts. Biological monitoring of DNA adducts can be done in WBC (White Blood Cell) counts in human. But from data analysis it has been found that high resolution techniques like capillary electrophoresis and mass spectrometry are needed [16]. So the most promising marker will be the measurement of DNA adducts after exposure to any aromatic compounds. The aromatic compounds are not directly bound to DNA but different metabolites are adducted to DNA following different metabolic pathways (Figure 2) either through one electron oxidation or two electron oxidation [16]. It has been noted that there is a direct link of DNA adduct with cancer. Toxic chemicals and their metabolites can bind to DNA (DNA adduct) causing mutations leading to cancer in human. Different methods like Immunoassays, Gas chromatography, Mass spectrometry and Liquid Chromatography/Mass spectrometry are used to measure DNA adducts [14]. DNA adducts may also bound to RNA and Protein besides DNA to cause many diseases in human (Figure 3).

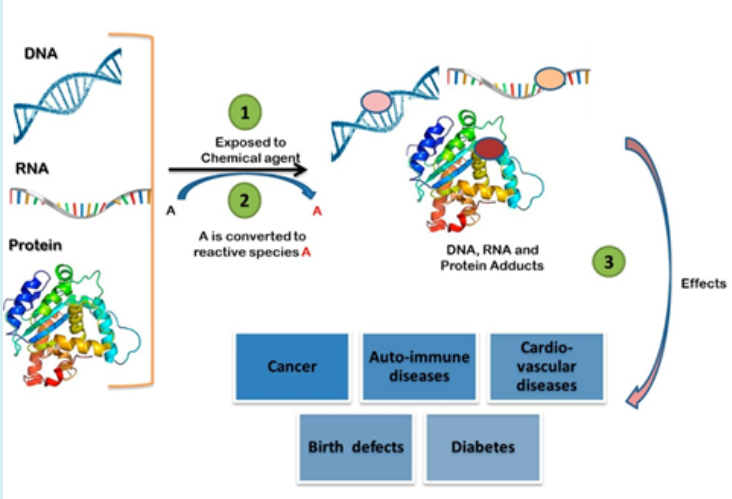

Figure 3: Showing how adduct is formed from exposure to various chemical agents in DNA, RNA and Protein in causing diseases in human [17].

The damage in DNA caused by DNA adducts are generally repaired by enzymes normally, otherwise it can make disturbances in DNA replication and transcription causing single or multiple mutations. When DNA adduct is formed by some alkylating agents at the O^6 position of the Guanine and O_2 (2 will be superscript) and O^4 positions of the thymine then it will induce CG to AT, AT to GC and AT to TA multiple mutations [14]. It has also been found that the exposure of hazardous chemicals due to anthropogenic effect may also cause developmental and reproductive disorder in wild populations through covalent modifications of the genome, all these disorders in animals may abruptly affect their survival through loss of their populations in nature [18].

Chemical mutagens (carcinogens) cause cancer by causing mutations in oncogene like H-ras , K-ras and tumour suppressor genes p53 in inducing DC to AT mutation leading to lung cancer particularly in smokers with exposure to PAH. The most common PAH causing cancer are Chrysene, 5-methylchrysene, 6-methylchrysene, Benzo[c] phenanthrene, etc. These chemicals are very prone to form DNA adduct in oncogenes. In China people who are using traditional Chinese herbal medicine with plant Aistolochia causes exposure to AA (Acrylamide) inducing cancer. It has been noted that exposure to AA also occurs in rural areas of Croatia and other Balkan countries by taking home-baked bread contaminated with Aristolochia seeds [14].

Again researches are going on to use –omic technologies to understand the multiple factors that may be responsible for male fertility in human through the study of changes in gene expression with the help of epigenomics and Proteomics to identify the fault. Previously most treatments were the use of the same therapy repeatedly hoping for a better result. With the use of new –omic technology it is possible to identify the faulty genes or proteins as these techniques may help to evaluate the genetic blueprint such as the gene sequences and their expression, information encoded and translated into protein which again is changed to active form through protein folding. The study of all these steps critically it will be possible to detect the correct reason for male infertility. With the advancement of technology the whole genome sequencing becomes easy and cost effective [19].

Environmental Pollution

Anthropogenic activities are responsible for different types of changes in the global climate causing either excessive heat in the climate, rain and landslides etc throughout the world or ecological disturbances causing environmental pressure in nature. These activities are also causing increase in pollution of toxicological chemicals in air, water and in the environment and human health. The adductomics technique is used in toxicological research to identify the polluted chemicals to animal and human causing many harmful effects. This omic approach or adductomes may be used as a biological marker to detect specific covalent adduct binding to DNA that may cause DNA damage.

Generally chemical agents do not directly bound to DNA forming adduct unless these compounds are transformed to reactive metabolites by some metabolic enzymes like Cytochrome P450 [17]. Reactive compounds react with DNA, Protein, RNA, Lipids and other macromolecules to form adducts (Figure 2). The techniques used to identify or detect adducts are as follows:

- P32 -Post labelling.
- Immuno-assay.

- Electro chemical detection.
- Mass Spectrometry (MS).
- Liquid Chromatography-MS.
- Gas chromatography-MS.
- High Resolution Mass Spectrometry (HRMS) etc.

The exposure to hazardous chemical agents occurred through diet, environmental pollutants, pesticides, preservatives, Polycyclic aromatic hydrocarbons (PAH), Aquatic pollutants causing many diseases to human like neurological disorders, auto-immune diseases, lung diseases, cardiovascular disorders, cancer with the formation of adducts [17]. Anticancer drugs are used to kill cancer cells by forming Drug-DNA adduct. The environmental assessment in the aquatic system of Baltic sea showed that there are many contaminants in the sediments of the sea like PAH, PCB and heavy metals etc. Research from the department of Environmental Science and Analytical Chemistry of Stockholm University showed that these contaminants are causing reproductive disorders and aberrations in embryo. The experiment was done in wild aquatic Amphipod, Monoperia affinis, using DNA adductomics with High Resolution Mass Spectrometry (HRMS) methods employing Orbitrap MS instrumentation [18]. These aberrations emphasised the manifestation of toxicity related DNA modifications.

Conclusions

Thus Multiomic studies have opened a new vista in genomic studies of plant and animals in many disciplines including their improvement in yield and production as well as in pathology and toxicological research. This has made a tremendous development in human health particularly in many deadly diseases like cancer, cardiovascular diseases with the development of Adductome studies. All these improvements are possible with the development of technological advances such as Next Generation Sequencing methods. This Omic technology has made a great revolution in understanding the diseases, health and developing the monitoring the progress of action of drugs in controlling diseases through studies of DNA adductome and Drug adductomes. DNA adductomic is the most recent –omic discipline that has now been used in the measurement of DNA adducts both in medicine and toxicology to control diseases in human and to identify and eradicate environmental hazardous toxic chemicals.

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