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Review Article

THE ERA OF GENOMICS IN MEDICINE: AN OVERVIEW

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ABSTRACT

Genomics has become a cornerstone of modern biomedical research, transforming our understanding of the genetic basis of health and disease. The completion of the Human Genome Project marked the beginning of a transformative era in biomedical science, ushering in genomics as a central pillar of modern medicine. Over the past two decades, rapid advances in next-generation sequencing, bioinformatics, and systems biology have reshaped our understanding of disease pathogenesis, risk prediction, diagnosis, and therapeutic development. Advances in high-throughput sequencing technologies, bioinformatics, and data integration have enabled comprehensive analysis of genomes at unprecedented scale and resolution. This review provides an overview of the fundamental concepts, methodologies, and applications of genomics in clinical practice and biomedical research. We summarize key genomic technologies, including next-generation sequencing, genome-wide association studies, and functional genomics approaches, and discuss their roles in elucidating disease mechanisms, identifying genetic risk factors, and enabling precision medicine. The review also highlights emerging areas such as single-cell genomics, epigenomics, and multi-omics integration, which are further refining biological insights across diverse systems. In addition, we address current challenges related to data interpretation, ethical considerations, and clinical translation. By synthesizing recent developments and future directions, this article aims to provide a comprehensive resource for researchers and clinicians seeking to understand the impact of genomics on biomedical science and healthcare.

Keywords: *Genome wide association study, Human genome project, Single cell genomics, Transcriptome*

INTRODUCTION

The genome is an organism's complete DNA blueprint, while the transcriptome is the set of all RNA molecules, the proteome is the entire collection of proteins, and the metabolome is all the small-molecule metabolites in a cell or organism. Genome is the complete set of genetic instructions in an organism's DNA, including both genes and non-coding sequences. Its main function is to provide the blueprint for building, running, and maintaining an organism and for passing on hereditary information. While "expressosome" isn't a standard term, the related field of transcriptomics focuses on the transcriptome, which is the complete set of RNA molecules transcribed from the genome. It indicates which genes are being actively expressed, providing information on gene expression patterns [1].

Proteome is the entire set of proteins within a cell or organism. It is responsible for the physical structure and the catalytic machinery (like enzymes) of the cell, which are crucial for many biological processes. Metabolome is the complete set of all

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small-molecule metabolites in a cell, tissue, or organism. Metabolites are the products and intermediates of metabolic processes; their study provides insights into the organism's metabolism and cellular state [1]. These layers are interconnected and essential for understanding a biological system holistically:

- **Information flow**: The genome provides the instructions for creating RNA (transcriptome), which then directs protein synthesis (proteome). Proteins, in turn, are responsible for catalyzing the metabolic reactions that produce the metabolites of the metabolome [1,2].
- **Complex interactions**: Information doesn't just flow one way; there are complex, bidirectional flows of information and regulation between these levels [1,2].
- **Systems biology**: By studying these different 'omic' layers together, systems biology provides a comprehensive understanding of how their complex interactions lead to the emergent properties of a cell or organism, contributing to diseases and other biological phenomena [1,2].

Genomics is the sub-discipline of genetics devoted to the mapping, sequencing and functional and comparative analyses of genomes. The word genomics appears to have been coined by Thomas Roderick in 1986 to refer to genetics subdiscipline of mapping, sequencing and analysing the function of entire genomes and to serve as the name of a new journal genomics dedicated to the communication of new information in this sub-discipline [3].

Table 1: Genome size comparision [4]

Species	Chromo-some	Genes	Base pairs
Human (Homo sapiens)	46 (23 pairs)	28,000 to 35,000	3.1 billion
Mouse (Mus musculus)	40	22,500 to 30,000	2.7 billion
Puffer fish (Takifugu rubripes)	44	31,000	365 billion
Malaria mosquito (Anophles gambiae)	6	14,000	289 million
Fruit fly (Drosphila melanogaster)	8	14,000	137 million
Round worm (Caenorhabditis elegans)	12	19,000	9.7 million
Bacterium (E.coli)	1	5,000	4.1 million

Genomics is the study of genomes, including sequencing genomes and determining the complete set of proteins and genes in an organism. The first genomes sequenced included *Haemophilus influenzae* in 1995 and the human genome was completed in 2003, taking 13 years. Genomics provides information on genes, metabolic pathways, and the functioning of organisms through approaches like genome sequencing, structural genomics, functional genomics, comparative genomics, and proteomics [3,4].

DATABASES FOR GENOMIC DATA

Genomic databases store, organize, and provide access to DNA, RNA, and protein sequence information along with functional annotations. They are essential for bioinformatics, comparative genomics, and biomedical research. Commonly used major genomic databases [5,6]:

1. GenBank (NCBI, USA): One of the largest nucleotide sequence repositories and includes DNA, RNA, and ESTs.
2. Ensembl (EMBL-EBI and Wellcome Trust Sanger Institute, UK): Provides annotated eukaryotic genomes. Offers genome browsing, comparative genomics, and visualization tools.
3. UCSC Genome Browser (University of California, Santa Cruz): Interactive genome browser for visualizing genomic sequences and annotations. Widely used for human and model organism genomes.
4. DDBJ (DNA Data Bank of Japan): International nucleotide sequence database, collaborating with GenBank and EMBL.
5. 1000 Genomes Project Database: Resource of human genetic variation. Useful for population genetics and disease association studies.
6. RefSeq (NCBI): Curated, non-redundant reference sequences for DNA, RNA, and proteins.

Applications of genomic data include gene identification and annotation, comparative genomics across species, variant analysis in disease studies, and evolutionary and population genetics.

GENOME SEQUENCING

Whole genome sequencing is the process of determining the complete DNA sequence of an organism's genome in a single analysis, covering both coding (genes) and non-coding regions. The most comprehensive form is Whole Genome Sequencing (WGS), which provides a base-by-base view of the entire genome. Types of genome sequencing include [7]:

- Whole genome sequencing (WGS) covers the entire genome.
- Whole exome sequencing (WES) targets only protein-coding regions (~1–2% of genome).
- Targeted sequencing focuses on specific genes or regions.

Techniques of genome sequencing include [7]:

- Sanger sequencing (first-generation, low throughput).
- Next-Generation Sequencing (NGS): High-throughput, rapid, and cost-effective.

- Third-generation sequencing (e.g., PacBio, Nanopore): Long-read technologies.

Applications of genome sequencing include [7,8]:

1. Medical diagnostics: Detection of genetic disorders, cancer mutations, rare diseases.
2. Pharmacogenomics: Tailoring drug therapy based on genetic makeup.
3. Microbial genomics: Identification of pathogens and antimicrobial resistance genes.
4. Evolutionary biology: Understanding genetic diversity and evolutionary relationships.
5. Personalized medicine: Predicting disease risk and guiding preventive healthcare.
6. Agriculture: Crop improvement and livestock breeding.

Structural genomics is about the study of genome structure. Structural genomics is quite advanced with the complex nucleotide sequences available for many organisms. Structural genomics seeks to describe the three dimensional structure of every protein encoded by a given genome. Structural genomics emphasizes high throughput determination of protein structures. This is performed in dedicated centers of structural genomics [9].

Functional genomics is about the study of genome function. Functional genomics includes analyses of transcriptome, the complete set of RNAs transcribed from a genome and proteome. Indeed functional genomics has spawned an entirely new discipline, proteomics, which has its goal the determination of the structures and functions of all proteins in an organism [10].

Comparative genomics is about the study of genome evolution. Comparative genomics is a field of biological research in which the genomic features of different organisms are compared. Genomic features encompass the structural and functional components of an organism's genetic material. This includes raw DNA sequences, protein coding genes, gene order and regulatory regions. Together, these elements form the core of structural genomics, which maps, sequences, and analyzes the physocal architecture of the genome. Comparative genomics comparing the nucleotide sequences of genomes has provided new information about the realtionships between various taxonomic groups. Bioinformatics is the science of storing, comparing and extracting information from biological systems especially DNA and protein sequences [11].

Pharmacogenomics

Pharmacogenomics reflects combination of pharmacology and genomics, and the role of genome in drug response. Genetic makeup of an individual affects his response to drugs. Genomics and epigenetics dealing with effects of multiple genes on drug response [12].

CORRELATED GENETIC, CYTOLOGICAL AND PHYSICAL MAPS OF CHROMOSOMES

The choromosomal locations of genes and other molecular markers can be mapped based on recombination frequencies, positions relative to cytological features, positions relative, or physical distances (Figure 1). Correlating genetic, cytological, and physical maps of chromosomes provides a complete framework for understanding genome structure and function, bridging the gap between recombination data, visible chromosomal landmarks, and exact DNA sequences. Chromosome mapping provides information about the location of genes and DNA sequences. Different types of maps are used, and correlating them gives a comprehensive understanding of genome organization [13].

1. Genetic map: Based on the frequency of recombination (crossing over) between genes, measured in centiMorgans (cM). It provides a relative order of genes but not exact physical distances [14].

2. Cytological map: Based on microscopic visualization of chromosomes, uses staining techniques (e.g., G-banding, FISH) to identify chromosomal bands. Genes or markers are located relative to visible landmarks on chromosomes [15].

3. Physical map: Based on the actual DNA sequence or the number of base pairs between markers, and constructed using restriction mapping, contigs, sequencing, and bioinformatics tools. It provides the most precise information in terms of base pairs [16].

Correlating all three maps allows accurate localization of genes, from their recombination behavior to cytological position and physical DNA sequence [13-16].

- Genetic maps show the *order of genes* based on recombination.
- Cytological maps anchor these positions to *visible chromosomal regions*.
- Physical maps provide the *exact nucleotide position*.

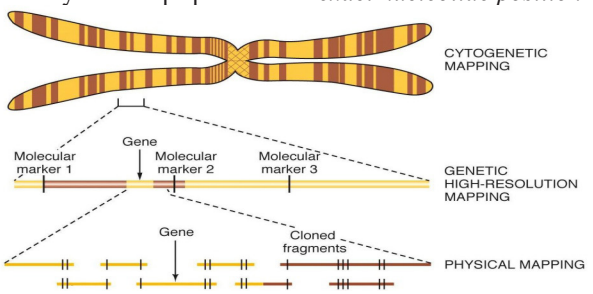

Figure 1: Large scale genome mapping [17]

POSITIONAL CLONING

Positional cloning is a genetic technique for finding the specific gene responsible for a trait or disease, even without knowing the gene's function or protein product. It involves mapping the gene's location on a chromosome using genetic markers and then systematically narrowing down the region through a process that can include chromosomal walking until the target gene is isolated. It can be used to identify and clone any gene with a known phenotypic effect in any species. Positional cloning has been extensively used in many species, including humans. This positional cloning depends on the availability of detailed map of regions of choromosomes where genes of interest reside. Major efforts focused on developing detailed maps of human genome and genomes of important model organisms such as Drosophila, Caenorhabditis elegans (round worm, a nematode) and Arabidopsis thaliana plant. In case of human and Drosophila genomes, the genetic and physical maps can be correlated with cytological maps of the choromosomes. Physical maps of a chromosome can be correlated with the genetic and cytological maps in various ways: 1.PCR, 2. Southern blotting, and 3.In situ hybridization [18].

MAP POSITION BASED CLONING OF GENES

Map-based (or positional) cloning is a genetic technique used to locate and isolate a specific gene responsible for a known phenotype, even if the gene's function is unknown. It involves identifying a molecular marker linked to the gene of interest through genetic linkage analysis, and then using this marker to physically map and "walk" along the chromosome to identify and isolate overlapping DNA segments until the gene is found. This iterative process, often requiring large populations and advanced techniques like chromosome walking, allows researchers to pinpoint the gene's exact location and sequence. The first eukaryotic genes to be cloned were genes that are expressed at very high level in specialized cells and tissues. About 90% of protein synthesized is hemoglobin in mammalian reticulocytes. Detailed genetic, cytogenetic, physical maps of chromosomes allow scientists to isolate genes from the chromosome [19].

CHROMOSOME WALKS AND JUMPS

Chromosome walking and jumping are molecular biology techniques for characterizing and mapping large segments of DNA or whole chromosomes. Chromosome walking involves a gradual, step-by-step process of using a known DNA fragment to identify and clone overlapping neighboring fragments. In contrast, chromosome jumping uses rare-cutting restriction enzymes and DNA circularization to bypass repetitive DNA regions, allowing researchers to jump over large distances along the chromosome more quickly. Choromosome walks are initiated by the selection of the molecular marker close to the gene of interest and use this clone as a hybridization probe to screen a genomic library for the overlapping clones identified in library screen. Repeat the procedure of isolating overlapping genomic clones allow a researcher to walk along chromosome to gene of interest. It is easier in organisms such as *A. thaliana, C. elegans* which have small genome and less repetitive DNA [20].

CHROMOSOME JUMPS

Chromosome jumping is a molecular biology technique for physical genome mapping, allowing researchers to bridge large, distant segments of DNA simultaneously without cloning the intermediate sequences. It works by using rare cutting restriction enzymes to cut genomic DNA into large fragments, which are then circularized and further digested with frequent cutting enzymes to isolate the ends of these large fragments, enabling a "jump" across hundreds of kilobases to a distant point on the chromosome. When the distance from the closest molecular marker to gene of interest a large technique called chromosome jumping can be used to speed up an otherwise long walk. Each jump covers 100 kb or more. It has proven especially useful in work with large genomes such a human genome. If molecular marker such as RFLP, VNTR, STR map close to gene, the gene can be usually isolated by chromosome walks or chromosome jumps [21,22].

RNA AND PROTEIN ASSAYS OF GENOME FUNCTION

RNA and protein assays for genome function analyze how these molecules interact to regulate genetic processes by examining the RNA molecules transcribed from DNA and the proteins that interact with them. Techniques like ChIP-seq and RNA-protein pull-down assays identify which proteins bind to specific RNA molecules, while methods such as in situ hybridization (ISH) and RNA-seq quantify RNA levels and their spatial distribution within the cell, revealing the functional roles of these RNA-protein complexes in gene expression, structure, and cellular processes. The availability of nucleotide sequence for entire genomes had led to the development of microarray, Gene chip and reporter gene technologies

that permit researchers to study the expression of all genes of an organism simultaneously [23].

MICROARRAY

A microarray is a "lab-on-a-chip" technology that allows scientists to simultaneously analyze the expression of thousands of genes or detect variations in a DNA sample by hybridizing it with known sequences (probes) immobilized on a solid surface. The process involves labeling a biological sample's nucleic acids, often with fluorescent dyes, and then allowing them to bind to the specific probes on the array. A specialized scanner then detects the signal, such as fluorescence, to measure gene expression levels or identify genetic variations like single nucleotide polymorphisms (SNPs). Microarray contains thousands of hybridization probes on a single membrane or other solid support [24].

GENE CHIPS

A gene chip, also known as a DNA microarray, is a laboratory tool that analyzes the activity of thousands of genes simultaneously by attaching known DNA sequences (probes) to a solid surface, typically a glass slide, in an ordered grid. Researchers use gene chips to study gene expression, detect DNA mutations, and identify gene polymorphisms by measuring how fluorescently labeled target DNA or RNA molecules from a sample bind to the specific probes on the chip. This technology enables a comprehensive view of gene networks, providing insights into disease, drug response, and various biological processes that would be impossible with traditional single-gene analysis. The thousands of probes are synthesized on silicon wafers 1-2 sq cms in size. These microarray and gene chips help to study transcription of thousand of genes simultaneously. Chimeric genes contain the coding region of green fluroscent protein of jelly fish fused with the coding regions of genes of experimental organisms can be used to study the localization of proteins in living cell [25,26].

Among prokaryotic genomes, *Haemophilus influenzae* was the first cellular organism to have its entire genome sequence in 1995. By Feb 2011 complete sequences of the genomes of 1412 Archea and bacteria were available in data bases.As eukaryotic organisms have increased their complexity the proportion of their genomes that encode proteins have decreased. Comparative genomics has revealed remarkable conservation of synteny related eukaryotic species such as mammals and the cereal grasses [27].

Mitochondrial and chloroplast genomes are usually circular and range in size from 6 kb to 2500 kb whereas chloroplast genomes also are usually circular and are typically 120 to 292 kb in size with more than 100 genes [28].

HUMAN GENOME PROJECT

The human genome project was an **international collaborative research program** aimed at mapping and sequencing the entire human genome. It was officially launched in **1990** and completed in **2003** (ahead of schedule). The amount of information in this first draft of human genome was overwhelming including the sequence of over 2650 Mb pairs of DNA. It is coordinated mainly by the **U.S. Department of Energy (DOE)** and the **National Institutes of Health (NIH),** with contributions from many countries [29].

The main objectives of human genome project [29,30]:

- To determine the complete sequence of the 3 billion base pairs of human DNA.
- To identify and map all human genes (~20,000–25,000).
- To construct a detailed physical map of the entire human genome
- To determine the nucleotide sequences of all 24 human choromosomes by the year 2005.
- To store the information in databases and make it publicly accessible.
- To develop new technologies for sequencing and data analysis.
- To address the ethical, legal, and social implications (ELSI) of genome research.

Major achievements of human genome project

- Produced the first complete draft of the human genome (2001).
- Identified the approximate number of human genes.
- Revealed that much of the genome consists of non-coding DNA.
- Advanced sequencing technologies, paving the way for modern genomics.

The human genome is more than 25 times the size of the previously sequenced *Drosophila* and *Arabidopsis* genomes and more than 8 times the sum of all genomes sequenced before it. The sequence of human genome provided one surprise there appeared to be only about 25,000 to 30,000 genes. Exons make up 1.1% of genome and introns 24% with 75% of the genome being intergeneric DNA. Nearly complete sequence of euchromatic DNA in the human genome was released in Oct 2004 [30,31].

Applications of human genome project [32]:

1. Medicine: Identification of disease-causing genes, personalized medicine, pharmacogenomics.
2. Biotechnology: Development of diagnostic tools and targeted therapies.
3. Forensics: DNA fingerprinting and identity testing.
4. Anthropology and evolution: Understanding human evolution and genetic diversity.
5. Agriculture: Improvement of crops and livestock using comparative genomics.

CONCLUSIONS

The advent of large-scale genomic initiatives, beginning with the human genome project, catalyzed a profound transformation in biomedical research and clinical practice. What was once an aspirational vision of personalized medicine has steadily evolved into a tangible reality, driven by advances in sequencing technologies, computational analytics, and integrative multi-omics. Genomics now informs disease classification, refines diagnostic precision, guides targeted therapeutics, and enables more accurate risk stratification across a broad spectrum of conditions.

Despite these achievements, the integration of genomics into routine healthcare remains a work in progress. Persistent challenges including variant interpretation, data standardization, equitable representation of diverse populations, ethical governance, and clinician preparedness must be systematically addressed to ensure responsible and effective implementation.

As we move further into the genomic era, the future of medicine will increasingly depend on interdisciplinary collaboration among clinicians, researchers, bioinformaticians, policymakers, and patient communities. The era of genomics in medicine is not merely a technological milestone; it represents a paradigm shift toward more precise, predictive, preventive, and participatory healthcare.

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