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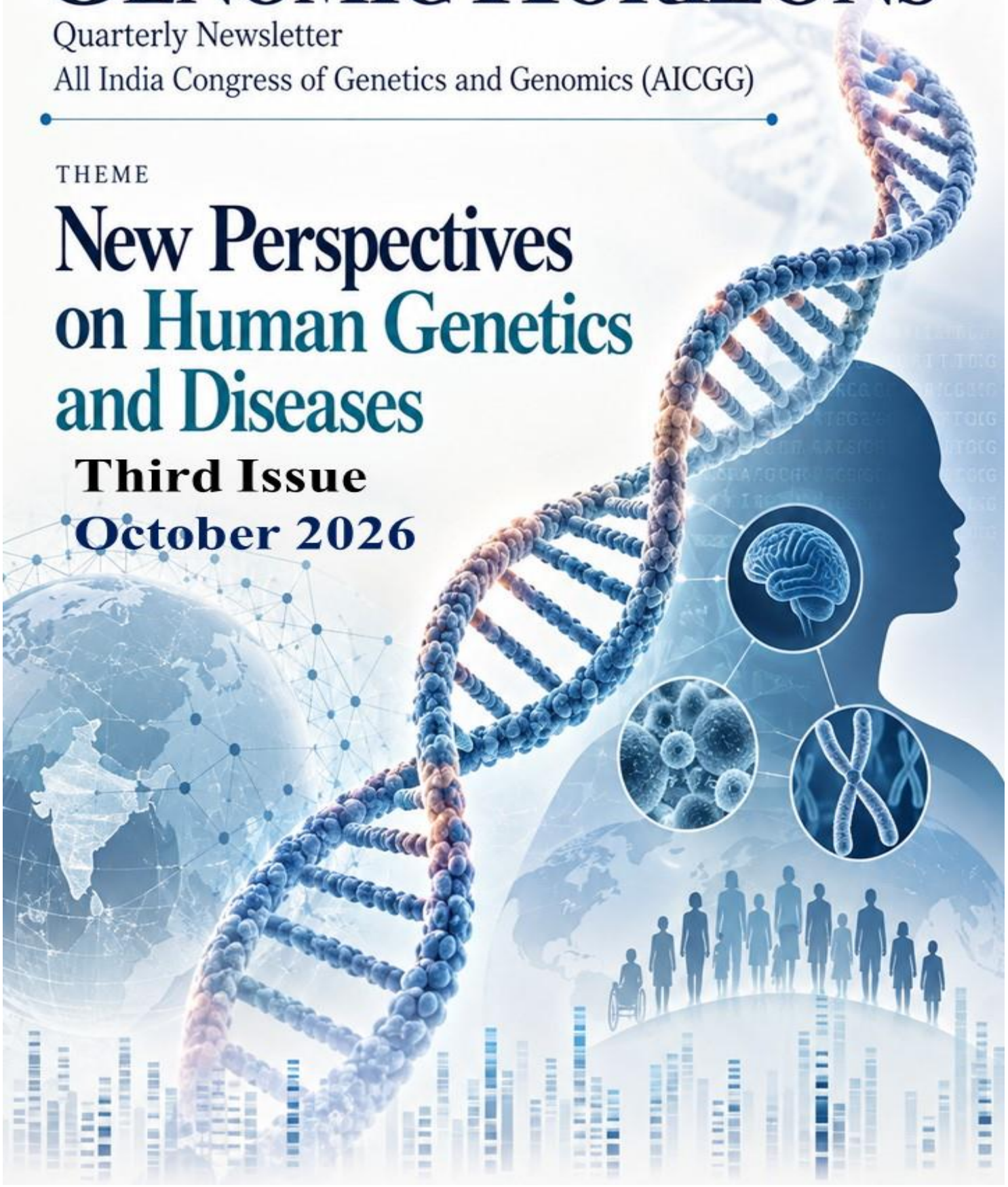
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Third Issue
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New Perspectives on Human Genetics and Diseases

Third issue

October 2026

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Editorial

From Chromatin to the Clinic: Genetics and Genomics Across Scales

Genetics has always worked at more than one scale at once. A genome is, at the same time, a molecule that must be folded and packaged inside a nucleus, a sequence whose variants must be read and interpreted, and a record that, layer by layer – transcriptome, proteome, metabolome – is translated into the biology of health and disease. This issue's contributions trace exactly that arc: from the physical architecture of chromatin, through the integration of multiple molecular layers in precision medicine, to the genomic dissection of two very different human diseases – oral cancer and chronic kidney disease.

The Architecture of the Genome

Long before a gene is transcribed, its fate is shaped by how tightly it is packaged. Differential condensation of chromatin, first distinguished by Heitz in 1928 as the contrast between transcriptionally silent, late-replicating heterochromatin and transcriptionally active, early-replicating euchromatin, remains one of the oldest and most enduring organizing principles in genetics. Constitutive heterochromatin – concentrated in centromeres, telomeric knobs and chromomeric bands – was once regarded as genetically inert, a repetitive filler protecting active genes. That view has been substantially revised: heterochromatic genes, though generally quiescent, are called into service at specific developmental moments – sex determination through the Y-linked SRY gene being a well-known example – and the amount and distribution of heterochromatin itself is under genetic control, correlating with recombination frequency, flowering time and gamete viability in classical cytogenetic studies of radish and Brassica. Facultative heterochromatin, exemplified by X-inactivation, shows that the same packaging can be reversible, adding a layer of developmental plasticity on top of sequence. These findings are a reminder that genome function cannot be inferred from sequence alone; structure is regulation.

Multi-Omics and the Future of Precision Medicine

If chromatin architecture is one axis of complexity, the sheer number of molecular layers between genotype and phenotype is another. Genome and exome sequencing have transformed the diagnosis of inherited disease, yet a substantial fraction of patients with suspected genetic disorders still leave the clinic without a molecular answer, in part because structural variants and repetitive regions elude short-read technology, and in part because a detected variant is not automatically a causal one. Multi-omics integration – layering transcriptomic, proteomic and metabolomic data onto a genomic backbone – is emerging as the response to both problems, while single-cell and spatial technologies reveal cellular and anatomical heterogeneity that bulk profiling obscures. Functional genomics is closing the interpretive gap directly: a recent high-throughput screen of 2,832 JAG1 variants reclassified 26 variants of uncertain significance as likely pathogenic, illustrating how experimental evidence, not computation alone, resolves ambiguity. Artificial intelligence now sits atop these datasets, but its value is bounded by the diversity of the data it is trained on – a caution that applies with particular force to genomic medicine in populations that remain underrepresented in reference datasets, India included.

Cancer Genomics and the Path to Precision Immunotherapy

That last caution is borne out directly in this issue's work on gingivo-buccal oral squamous cell carcinoma (OSCC-GB), the most common cancer among Indian men and one driven substantially by smokeless tobacco and areca-nut use. Bulk transcriptomic profiling of 72 treatment-naïve patients, together with matched leukoplakia and normal tissue, resolved OSCC-GB into two molecular subtypes: an immune-quiescent GB1 and an immune-active GB2, the latter comprising roughly three-quarters of the cohort and marked by elevated checkpoint ligands (PD-L1, CD80, CD86, HVEM) and coordinated receptor expression on infiltrating T cells. Checkpoint ligand expression rose progressively from normal mucosa to leukoplakia to tumour, suggesting that immune remodeling begins before overt malignancy. A three-gene classifier (CD226, CD38, KBTBD8)

separated the subtypes with 86% accuracy, and comparison against 471 TCGA-HNSC cases showed partial but incomplete concordance – fewer than six patients in the entire TCGA cohort met conventional tumour-mutational-burden thresholds for checkpoint responsiveness, hinting that in HNSCC, immune activity may be driven more by microenvironment and epigenetic regulation than by mutation count. The authors are appropriately cautious: these are transcriptomic signatures, not treatment outcomes, and experimental validation in independent, geographically diverse Indian cohorts is the necessary next step before any translational claim can be made.

Genetic Variants and Kidney Disease

A parallel logic – using computation to prioritize what merits further biological scrutiny – runs through this issue's analysis of NPHS1, the gene encoding nephrin, the transmembrane protein that maintains the glomerular slit diaphragm and, with it, the selective permeability of the kidney's filtration barrier. Chronic kidney disease affects an estimated 11–13% of the global population, and NPHS1 mutations are an established cause of nephrotic syndrome ranging from congenital to adult-onset disease. Working from 7,917 annotated SNPs, a stepwise in silico pipeline – conservation filtering, regulatory prediction, pathogenicity scoring and structural modelling – narrowed the field to 33 evolutionarily conserved variants and two non-synonymous substitutions, E117K and N1077S. The two told different stories: E117K was consistently flagged as damaging across PolyPhen-2 and PANTHER, produced steric clashes with a neighbouring residue in the modelled three-dimensional structure, and reduced predicted protein stability, whereas N1077S was largely tolerated by the same algorithms despite its own modest destabilizing effect. The exercise is a useful demonstration of how far sequence-to-structure prediction has come – and an equally useful reminder that, as with the OSCC-GB checkpoint signature, computational prioritization identifies candidates for functional validation rather than a finished answer.

A Common Thread

Read together, this issue's contributions describe a single pipeline stretched across four very different systems: how a genome is packaged determines what can be expressed; how gene expression is captured across omic layers determines what can be diagnosed; and how computational prediction – whether applied to a transcriptomic immune signature or a single amino-acid substitution – determines what is worth validating experimentally next. The recurring caveat across all four contributions is the same one raised for genomic medicine generally: predictions built on reference datasets and computational models carry the biases of the data and populations they were built on, and their clinical value is realized only once independent, adequately powered validation – ideally in the same population the prediction is meant to serve – has been done.

In this Issue

This issue brings together 6 different contributions spanning classical cytogenetics to computational structural biology. **Dr Ashok K Giri** highlights the importance of genomics,telomere biology, and nanotechnology in arsenic susceptibility and toxicity. **Prof Nandjee Kumar** revisits the genetics of heterochromatin, tracing the discovery, classification and functional significance of constitutive and facultative heterochromatin from classical cytogenetic studies to modern chromatin biology. **Anuradha Sharma and Minakshi Vashist** survey how multi-omics integration, single-cell and spatial technologies, CRISPR-based functional genomics and artificial intelligence are together redefining precision medicine, while cautioning that equitable representation must remain central to that effort. **Debodipta Das** reports transcriptomic profiling of gingivo-buccal oral cancer that resolves two immune subtypes and a three-gene classifier with implications for precision immunotherapy in Indian patients. **Sonali Chhabra and Gursatej Gandhi** present an *in silico* structural and functional analysis of NPHS1/nephrin variants, identifying E117K as a stronger candidate for pathogenicity than N1077S. **Sunandini Ghosh** highlights how **obesity in Indian urban professionals** is driven by lifestyle. It shows that visceral fat is a key biomarker of metabolic syndrome risk**,** and suggests that natural compounds like curcumin and quercetin could serve as safer, effective alternatives to drugs like Ozempic for obesity management.

Together, these contributions illustrate the breadth of contemporary genetics – from the physical structure of chromatin to the computational dissection of disease-associated variants – and the shared discipline of validation that connects them.

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Editor-duo

Dr. Nilanjana Banerjee & Dr. Vikas Srivastava

Article 1

Genomics and Arsenic Toxicity: Molecular Insights into Human Susceptibility

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Genetics and genomics, once propelled by the transformative impact of the Human Genome Project, have now matured into powerful technologies—whole genome sequencing, single-cell transcriptomics, CRISPR-based genome editing, and AI-driven bioinformatics [1]—that are reshaping both research and medicine.

One of the pressing challenges we face is chronic arsenic toxicity**,** a global health issue affecting millions. Arsenic is a potent human carcinogen, and its hallmark manifestations include pre-cancerous and cancerous skin lesions. Interestingly, only 15%–20% of exposed individuals develop these lesions, while the majority do not—an observation that points to underlying genetic and molecular differences. Beyond dermatological effects, arsenic exposure also leads to conjunctival irritation, peripheral neuropathy, respiratory distress, and cancers of internal organs. Our studies in West Bengal have shown significantly higher chromosomal aberrations and micronucleus formation in individuals with skin lesions compared to those without, underscoring the biological complexity of arsenic susceptibility [2].

Recent research highlights the role of genetic polymorphisms **in** determining inter-individual vulnerability. Multidrug resistance proteins (MRPs), encoded by the ABCC gene family, are known to efflux arsenic metabolites. In particular, MRP4 (ABCC4) acts as a high-affinity transporter of toxic arsenic compounds. However, the association of ABCC4 polymorphisms with arsenic-induced disease remains poorly understood. Our study examined five non-synonymous ABCC4 SNPs for their possible link to premalignant hyperkeratosis, opening new avenues for understanding arsenic susceptibility [3].

Another frontier lies in telomere biology. Telomere integrity is essential for genome stability and cancer prevention. Emerging evidence suggests that epigenetic modifications—DNA methylation and post-translational changes—play a critical role in regulating telomere length 4]. Recent studies in West Bengal, show that chronic arsenic exposure from drinking water alters telomere length, accelerates cellular senescence, and increases the risk of precancerous and cancerous conditions [5].

Very recently, innovative approaches such as a simplified theranostic nanoparticle system for targeted drug delivery and ROS detection in inflammatory bowel disease [6] have shown promise, exemplifying how genomics and nanotechnology can converge for precision medicine. Recent Indian research highlights that nanoparticle-based systems are being developed to improve arsenic detoxification and targeted drug delivery, especially using arsenic trioxide (ATO) nano-carriers for cancer therapy and ceria nanoparticles for water purification. These approaches aim to reduce toxicity, enhance bioavailability, and provide site-specific treatment [7].

In summary, the integration of genomics, telomere biology, and nanotechnology offers a promising path to address the complex challenge of arsenic toxicity. By uncovering genetic susceptibility factors, clarifying telomere regulation under exposure, and advancing nanoparticle-based detoxification and drug delivery systems, these approaches together point toward precision medicine solutions that can reduce disease burden and improve outcomes in affected populations.

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Article 2

Genetics of Heterochromatin

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In eukaryotes, the chromatin is a highly complex structure with DNA and basic proteins in a ratio 1:1. The basic proteins are usually called histones and have high content of basic amino acids such as arginine, lysine and histidine. The degree of compaction of DNA of metaphase chromosomes is as high as 5,000-10,000 times and the dimension of human metaphase chromosomes measures up to 10 µm with a compaction value of about 7,000-fold.
The chromatin has the unique property of condensation and de-condensation throughout the cell cycle. The chromatin is highly condensed at prophase/metaphase and de-condensed at telophase/interphase. Such differential condensation has been called heteropycnosis. The over-condensation of chromatin is called positive heteropycnosis and under condensation of chromatin is called negative heteropycnosis.

The differential stainability of chromosomes with basic dyes led to the discovery of euchromatin and heterochromatin. distinguished heterochromatin as darkly stained regions of the chromosome which are transcriptionally inactive and replicate late during cell cycle while euchromatin as poorly stained regions of the chromosome which are transcriptionally active and early replicating during cell cycle. In fact, euchromatin and heterochromatin are two states of the same substance (DNA) and are interchangeable. This variation of stainability is correlated with the changes of condensation and de-condensation of chromatin at various stages of cell division. [1] defined heterochromatin as a dynamic, functional component regulating chromosome structure and gene expression during development that highlighted its role in genome organization and species-specific evolution.

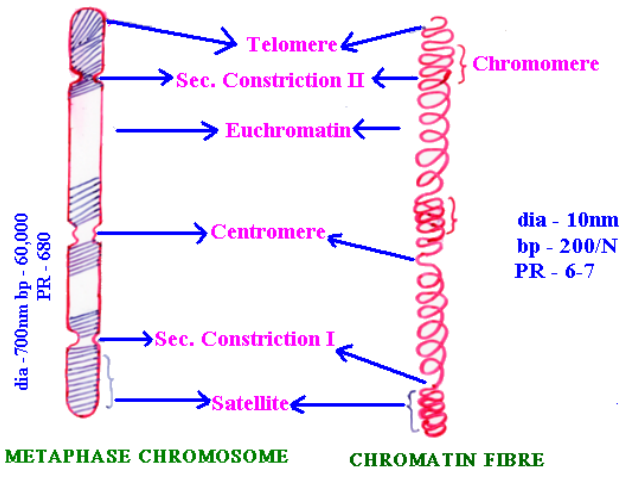


Fig: Structure of a metaphase chromosome and chromatin fibre.

Characteristics of heterochromatin

1. Heterochromatin shows the phenomenon of positive heteropycnosis i.e. deeply stained

regions of chromosomes due to heavy condensation of DNA.
2. Heterochromatin actually represents the tight coiling and packaging of the chromatin material.
3. Heterochromatin replicates late at the end of S phase of cell cycle.
4. The crossover frequency is almost negligible in hetero-chromatin due to over condensation of DNA. When a heterochromatic region is translocated to the euchromatic segment, the activity of euchromatic genes is heterochromatinised.
5. Generally the heterochromatic region contains highly repetitive DNA sequences (satellite DNA), hence any loss/gain of heterochromatic segments imparts no phenotypic effect. The repetitive DNA acts as spacer between the active genes and also protects them during gene regulation.
6. Heterochromatinisation may involve a segment of a chromosome (e.g. telomeres, pericentric regions) or the whole chromosome (e.g. one X chromosome of female human, Y chromosome of male human and B- chromosomes of plants and animals or the whole haploid set of chromosomes in male mealy bugs).
7. Heterochromatin contains more DNA and genes (74%) in contrast to euchromatin (13%), though the genes in the heterochromatic regions are repressed .

Genetic nature of heterochromatin

The earlier thought that heterochromatic regions are devoid of active genes, genetically inert and unable to transcribe RNAs, has now been contradicted by recent research with an explanation that genes are also present in the heterochromatic regions. The genes of heterochromatin behave a special status because they are not always metabolically active rather expressed at specific occasions in the life cycle e.g. bobbed eye gene in drosophila, hairy earlobe gene in man, ZFY & SRY genes in animals and plants that are located in Y chromosome which is completely heterochromatinized.
It is a fact that the most of the active genes are located in loosely packed euchromatin but the heterochromatic genes are active for a short period for specific purposes. The heterochromatic genes play a significant role in chromosome pairing, gene recombination, sex determination, gene regulation and evolution.

Types of heterochromatin

Heterochromatin may be classified into two major types (i) Constitutive heterochromatin and (ii) Facultative heterochromatin

1. *Constitutive heterochromatin:*

The constitutive heterochromatin is always heteropycnotic throughout the cell cycle in all types of cells and is never reversed back to euchromatic state. It tends to have a constant position on the homologous chromosomes. It is highly repetitive and inactive during protein synthesis. Within a chromosome the constitutive heterochromatin has been found to occur in certain regions of the chromosome that constitute specific structures such as (a) Chromocentres in centromeric regions (b) Knobs/satellites in telomeric regions (c) Chromomeres/bands in intercalary regions.
1. Chromocentres:
The chromocentres are dark staining heteropycnotic bodies in the interphase nuclei and represent the pericentric constitutive heterochromatin located in the centromeric region of chromosomes.
The term chromocentre was first coined by Baccarine in 1908 to denote the central mass to which chromosomes of Drosophila are attached in the nuclear region. Eiechorn (1934) believed that the chromocentres are probably the prophasic chromosomes with minor modifications. Delay (1948) confirmed that the chromocentres actually represent the regions of the chromosomes on the side of the centromere. Nagl (1979) interpreted that chromocentres are centromeric constitutive heterochromatin which shows variation in shape and size with differential DNA replication.

Dayal et al.[2-6], Kumar (1995), Kumar et al. [7] , Sikka, Singh and Dayal (1988) and Yadav and Kumar (1991) made extensive studies on the structure and behavior of chromocentres in radishes and brassicas) and demonstrated that the number and distribution pattern of chromocentres are related with homo and heterozygosity of the material. The homozygotes have higher frequency of chromocentres and wider distribution patterns than the heterozygotes (hybrids). This means that the hybrids are less heterochromatinised with reduced number and narrow distribution of chromocentres. Conclusively, the number and distribution of chromocentres are genotypically controlled.

Heitz (1934) identified two types of constitutive heterochromatin α constitutive and β constitutive heterochromatin. The former is compact and resistant to de-staining while the latter is relatively less compact and less resistant to de-staining.

2. Knobs:

The knobs are spherical bodies in the telomeric regions of chromosomes and contain constitutive heterochromatin that help in protecting the active genes of euchromatin. The chromosome knobs are very distinct at the pachytene stage of meiosis. They may vary in size but their number and position are constant on the chromosomes. The knobs have been studied in maize and found out that chromosome 9 contains a large terminal knob which is a valuable genetic marker for distinguishing chromosomes of related species and races.

The distal region of a chromosome consists of a secondary constriction usually called satellite chromosome which is composed of constitutive heterochromatin. The number of satellite chromosomes varies from species to species e.g. 2 pairs in barley, 5 pairs in humans.

3. Chromomeres and bands:

The chromomeres are bead-like deep staining compact structures observed at early prophase I of meiosis. The chromomeres proximal to the centromere are large and become progressively smaller towards the chromosomal ends, however their number and position are specific for a particular species at a particular stage of development. The larger chromomeres are generally heterochromatic whereas smaller chromomeres are euchromatic containing active genes to specify 10-100 proteins per chromomere. The heterochromatic chromomeres serve as markers to identify specific chromosome segments at pachytene stage as seen in maize and tomato. The distance between the two chromomeres is remarkably constant in the same species during different stages of development. For example at the pachytene stage the interchromomeric distance is 0.83 μm in tomato, which is considered as a marker for a species.

The pachytene chromosomes have peculiar feulgen positive bands which are deeply stained due to supercoiling of DNA. These dark bands actually represent heterochromatic chromomeres and the lightly stained inter-bands represent euchromatic regions. The heterochromatic bands glow very sharply under fluorescent microscope. Each heterochromatin band consists of about 3000 bp and is specific for a particular chromosome.

Pardue and Gall (1969) discovered the differential staining pattern of constitutive heterochromatin that led to the discovery of chromosome banding technique and C-banding was identified by using Giemsa solution, however later on Caspersson et al. (1970) recognised Q- banding by using quinacrine mustard stain, Sumner et al.(1971) recognised G- banding by using Giemsa stain followed by trypsin solution, Hsue and Arrighi (1971) recognised R banding by using reverse Giemsa staining, Singh and Tsuchiya (1982) developed N-banding by using Giemsa stain with nHCl to locate non-histone proteins specifically linked to nucleolar organiser region (NOR) of eukaryotic chromosomes and Yamamoto and Mukai (1989) developed advance fluorescence in situ hybridisation (FISH) for staining specific sequences within a chromosome.

2. *Facultative heterochromatin:*

The facultative heterochromatin remains heteropycnotic at certain stage of cell cycle and generally appears by conversion of euchromatin to heterochromatin which may again be reverted back to euchromatin by losing the over-condensation of chromatic material. This phenomenon is called position effect.

The facultative heterochromatin is characterised to have inactive genes which are repressed due to

heavy condensation of the chromatin and replicating late in the S-phase of cell cycle. The share of facultative heterochromatin is about 2.5% of the genome e.g. one of the X chromosome in females and Y chromosome in males.

Genetic control of heterochromatin:

Cytogenetical studies of the inbred lines of an allogamous population and their hybrids have been utilized as one of the tools for understanding the genetics of heterochromatin in rye (Rees, 1961),maize (Zecevic,1961), radish [2-6], turnip [9] and cultivated brassicas [7].

The varietal populations exhibit a balanced buffer system in which an optimum level of heterozygosity is maintained by cross pollination and regulated by natural selection. Forced breeding breaks up the genetic balance of the allogamous population into a large number of inbred lines with increased homozygosity. In F1 hybrids of the inbred lines, the lost heterozygosity is not only restored but excelled to the level of heterosis. This showed that the homozygous inbred lines have higher numbers with wider distribution of chromocentres than their hybrids and the varietal populations.

The mode of inheritance of constitutive heterochromatin has extensively been studied in radishes and has been confirmed that populations with narrow distribution of chromocentres show dominance over those having wider distribution pattern. Evidently the F1 hybrids have narrow distribution of chromocentres, however the F2 hybrids displayed a wider range of distribution of chromocentres than the F1 hybrids and showed a continuous nature of variation from which a polygenic control of chromocentres frequency can be inferred.

Correlations of constitutive heterochromatin:

It is interesting to note that constitutive heterochromatin (chromocentres) is correlated with cytological characters such as chiasma frequency, physiological characters such as days to flower, chlorophyll contents and embryological characters such as micro/mega-sporogenesis and micro/mega-gametogenesis.

1. Chiasma frequency: A concomitant study of chromocentres in varietal populations of radish [4] and cultivated crucifers [7] revealed a significant negative correlation between chromocentres and chiasma frequency. The higher is the amount of constitutive heterochromatin as inferred from chromocentres count; the lower is the chiasma frequency and consequently the genetic recombination and vice-versa.
2. Days to flower: The frequency of chromocentres has also been found to be negatively correlated with the number of days to flower in radish [6] and in brassicas (Kumar and Kushwaha, 1996).This means that an increase of constitutive heterochromatin can reduce the number of days to flower.
3. Chlorophyll contents: Kumar et al. (1995) confirmed in the species of Brassica that the frequency of chromocentres is inversely related to the chlorophyll contents.
4. Micro/mega-gametogenesis: Kumar (1984) reported higher rate of degeneration of tapetum in the inbred lines of radish with increased number of chromocentres representing pericentric constitutive heterochromatin. Further, Kumar (1985) and Dayal (1989) demonstrated that the ovules of highly heterochromatinised inbred lines of radish are functionally less efficient than their hybrids and original varietal populations. The frequency of embryo sac abortion is much higher in the inbred lines with reduced fertility.

Factors affecting constitutive heterochromatin

Recent studies have revealed that the amount of constitutive heterochromatin is significantly reduced by specific doses of Parthenium extracts (Mehta et al.1994), chemical mutagens such as ethyl methane sulphonate, hydrate hydrazine (Kumar, 1995). Functions of heterochromatin

Once thought to be genetically inert and metabolically inactive, heterochromatin plays a very important role on specific occasions. It is a fact that the most of the active genes are located in the euchromatic regions of the chromosome but this does not mean that the heterochromatic regions are useless and devoid of any active gene.In fact, there are several specific active genes which are tightly packed up in the condensed DNA of heterochromatin that regulate many vital functions mentioned as below:

1. Chromosome pairing: Lacour and Well (1970) revealed that the process of chromosomal pairing during zygotene stage of meiosis is regulated by the genes located in the heterochromatic regions of chromosomes.
2. Gene regulation: Hsu (1975), Nagl (1979), Davidson and Britten (1979), Lavania and Sharma (1982) confirmed that the constitutive heterochromatin plays a key role in gene expression in eukaryotes.
3. Genetic recombination: Muntzing (1974), Rees and Jones (1977) argued that since crossover frequency is always lower in the heterochromatic regions of the chromosome, the probability of genetic recombination is greatly reduced.
4. Sex determination: Badge and Goodfellow (1991) of Cancer Research Institute, London discovered that the SRY gene of Y chromosome in mammals is responsible for differentiation of embryos into males. Since the Y chromosome is completely heterochromatinised, the heterochromatin plays a significant role in sex determination.

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Article 3

From Genome to Disease: How Multi-Omics Is Redefining Precision Medicine

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Introduction

Human disease is rarely the consequence of a single genetic alteration. Although the identification of disease associated variants has transformed our understanding of inherited and acquired disorders, the biological effects of these variants can depend on gene regulation, cellular context, environmental influences and interactions among multiple molecular pathways [1]. This complexity has created a need for approaches that can examine human disease beyond the DNA sequence alone.

Advances in high throughput molecular technologies have made it possible to study several biological layers simultaneously. Genomics provides information about DNA variation, whereas transcriptomics, epigenomics, proteomics and metabolomics provide complementary information about gene activity, regulatory mechanisms, protein function and cellular metabolism [2]. The integration of these datasets, commonly referred to as multi-omics, is therefore emerging as an important strategy for understanding disease biology and improving precision medicine.

From genetic variation to biological function

Genomic sequencing has substantially improved the diagnosis of inherited disorders. Exome and genome sequencing can identify pathogenic variants across large portions of the genome and have become important components of modern genetic diagnosis [1]. However, a considerable proportion of patients with suspected rare genetic disorders remain without a definitive molecular diagnosis even after genomic testing [1].

One important reason is that not all disease-causing variation can be adequately detected or interpreted using conventional approaches. Structural variants, repetitive sequences and other complex genomic alterations may require additional technologies for accurate characterization [3]. Long read genome sequencing is therefore gaining increasing attention because it can provide improved resolution of complex genomic regions and structural variation [3].

Variant interpretation represents another major challenge. The identification of a genetic alteration does not automatically establish that the alteration is responsible for disease. Variants of uncertain significance remain particularly difficult because their clinical relevance cannot be determined from sequence information alone [4]. Functional studies and additional molecular evidence are consequently becoming increasingly important for transforming genomic observations into clinically meaningful information.

Connecting genotype with phenotype through multi-omics

A major strength of multi-omics lies in its ability to connect different stages of biological regulation. A DNA variant may influence gene expression, alter RNA splicing or affect protein abundance, ultimately producing a cellular or clinical phenotype [1,2]. Examining only one molecular layer may therefore provide an incomplete picture of disease.

For example, transcriptomic analysis can identify changes in gene expression associated with a disease state, while proteomic analysis can determine whether those transcriptional changes are reflected at the protein level. Metabolomic analysis can provide additional information about the biochemical consequences of altered cellular pathways [2]. Integrating these measurements can therefore help identify molecular relationships that may not be apparent from genomic analysis alone.

This approach is particularly relevant to complex diseases, in which multiple pathways contribute to disease susceptibility and progression. Multi-omics integration is increasingly being investigated for disease mechanism studies, biomarker discovery, diagnosis, prognosis and therapeutic development

[2,5].

Importantly, the value of multi-omics does not simply lie in collecting larger quantities of data. Its major contribution is the possibility of connecting molecular information across biological levels and generating a more coherent explanation of how genetic variation contributes to disease.

Single cell and spatial genomics

Traditional molecular studies frequently analyse tissue as a bulk sample. Such analysis combines signals from multiple cell populations and can conceal important differences between individual cells. Single cell technologies have addressed this limitation by enabling molecular characteristics to be investigated at the level of individual cells [6].Single cell profiling has demonstrated that tissues previously considered relatively uniform can contain diverse cellular populations with distinct molecular states. These differences can be particularly important in cancer, immune mediated disorders and other diseases in which specific cell populations may contribute disproportionately to disease progression [6].Spatial transcriptomics provides an additional dimension by retaining information about the location of molecular signals within tissues. It allows gene expression patterns to be mapped to specific tissue regions and cellular neighbourhoods, providing information about cell to cell interactions that cannot be obtained from conventional bulk analysis [7].The integration of spatial transcriptomics with other molecular approaches, including spatial proteomics and epigenomic profiling, could ultimately facilitate the development of comprehensive molecular maps of healthy and diseased tissues [7]. Such approaches may be particularly valuable for understanding tumour microenvironments, inflammatory processes and tissue responses to injury.

Functional genomics and genome editing

Another important development in human genetics is the increasing ability to experimentally investigate the consequences of individual genetic variants. Genome wide association studies have identified numerous variants associated with human traits and diseases, but statistical association alone does not demonstrate biological causality [8].

CRISPR based functional genomics provides an important experimental framework for addressing this limitation. Disease associated variants can be introduced or modified in cellular models, allowing their effects on gene regulation and cellular phenotypes to be examined directly [8]. CRISPR based approaches can also be applied to noncoding genomic regions, including promoters, enhancers and regulatory elements, which are increasingly recognized as important contributors to human disease [8].

These technologies are particularly relevant for variants of uncertain significance. For example, a high-throughput functional study of 2,832 JAG1 variants identified 486 variants with abnormal functional effects, including 439 missense variants. Among 144 uncertain variants reported in patients, functional evidence contributed to the reclassification of 26 variants as likely pathogenic [4]. Such studies demonstrate how experimental evidence can complement computational predictions and clinical observations, reducing uncertainty in genomic variant interpretation [4,8].

Artificial intelligence and genomic medicine

The expansion of genomic and multi-omics datasets has created a parallel challenge in data analysis. Modern experiments can generate extremely high dimensional datasets in which biologically meaningful relationships may be difficult to identify using conventional analytical methods.

Artificial intelligence and machine learning are increasingly being applied to genomic and omics data to identify complex patterns, support variant interpretation and develop predictive models [9]. AI based approaches can potentially integrate genomic, clinical and molecular information at a scale that would be difficult to achieve through manual analysis alone [9].

However, computational prediction should not be considered equivalent to biological validation. The performance of an AI model depends on the quality, diversity and representativeness of the data used for development. Issues related to reproducibility, interpretability, data quality and algorithmic bias therefore remain important considerations in the translation of AI into genomic medicine [10].

Equity must remain central to genomic medicine

The future of precision medicine will also depend on whether genomic advances benefit diverse populations. Human genomic research has historically included disproportionate representation of certain ancestral groups, creating potential consequences for variant interpretation and clinical applicability [10].

Insufficient representation can make some genetic variants more difficult to interpret and may

contribute to disparities in the clinical application of genomic medicine [10]. Expanding genomic research across diverse populations is therefore not simply a matter of increasing sample size. It is essential for ensuring that genetic discoveries and precision medicine approaches are scientifically robust and clinically relevant across populations.

The road ahead

Human genetics is moving from a primarily sequence centred discipline towards an integrated view of biological systems. Genomic sequencing remains fundamental, but its interpretation is increasingly strengthened by transcriptomics, epigenomics, proteomics, metabolomics, single cell technologies and spatial profiling [1,2,6,7].

At the same time, functional genomics is helping establish the biological consequences of disease associated variants, while artificial intelligence is providing new approaches for interpreting increasingly complex datasets [8,9]. Together, these developments are creating an opportunity to move from simply identifying genetic alterations towards understanding how those alterations contribute to disease.

The ultimate objective of precision medicine is not to generate more molecular data, but to convert molecular information into clinically meaningful knowledge. The central question in modern human genetics is therefore evolving from **"Which genetic variant is present?"** to **"How does an individual's molecular profile contribute to disease, and how can that knowledge improve diagnosis, prevention and treatment?"**

This transition from genome centred analysis to integrated molecular understanding represents one of the most promising directions in human genetics. If genomic, molecular, computational and clinical information can be integrated responsibly, precision medicine may increasingly become a practical framework for understanding disease at the level of the individual.

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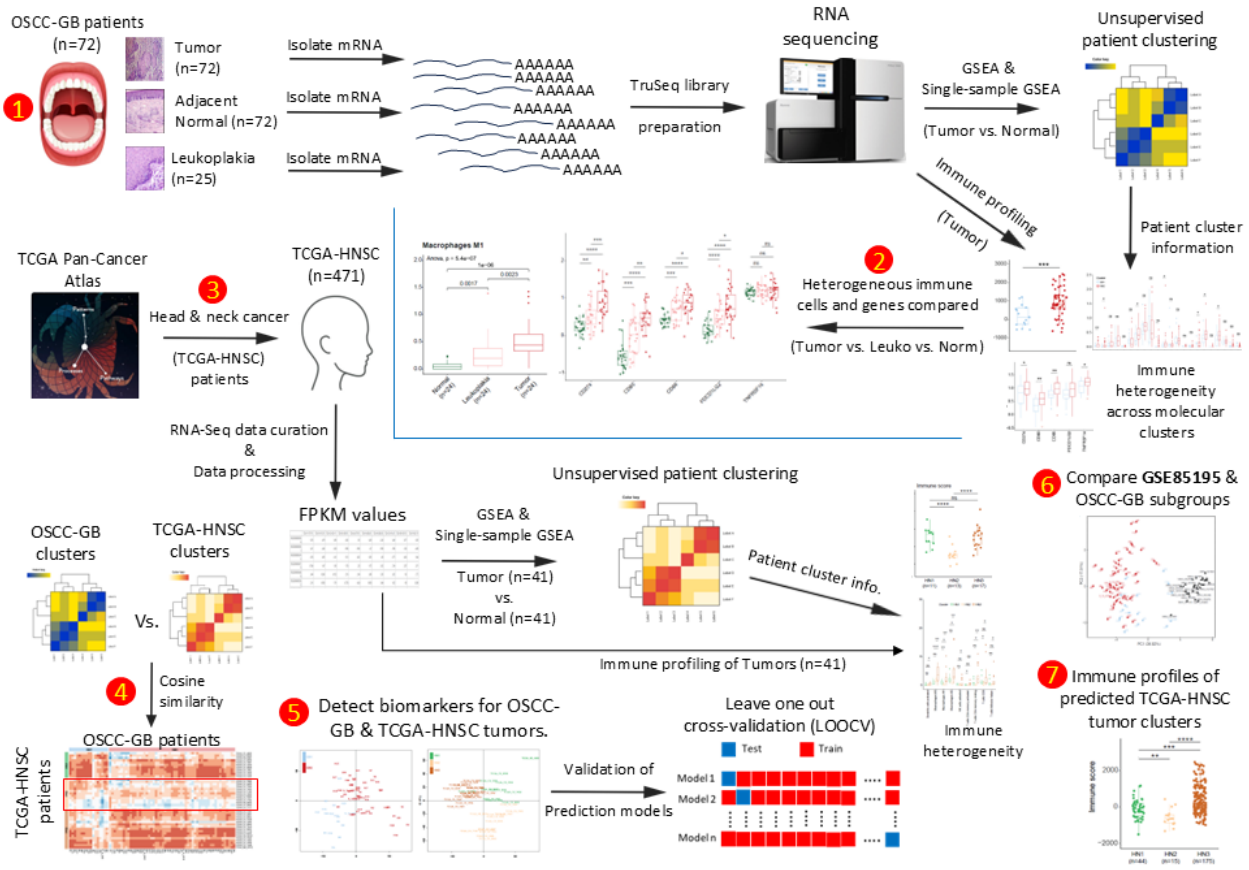
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Article 4

New Genomic Perspectives on Gingivo-buccal Oral Cancer: Towards Precision Immunotherapy

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Cancer of the oral cavity without involvement of the tongue – called, oral squamous cell carcinoma of the gingivo-buccal region (OSCC-GB) – is the most common cancer among men in India. It is driven largely by smokeless tobacco (*gutkha*, *khaini*) and areca-nut use. It is usually studied as part of the broader, etiologically heterogeneous, category called head and neck squamous cell carcinoma (HNSCC). Studying HNSCC may possibly not reveal specific alterations responsible for tumours in specific subsites, such as the gingivo-buccal region. In our recent study we focused on OSCC-GB; the results have been published in *Molecular Medicine*. We performed transcriptomic profiling of OSCC-GB patients to characterize the tumour immune microenvironment and explore its potential implications for precision immunotherapy.

We performed bulk RNA sequencing of tumour and matched normal tissues collected from the oral cavities of 72 treatment-naïve OSCC-GB patients. In 25 patients, a premalignant lesion called

lukoplakia was also present in the oral cavity; from these patients we additionally collected a

leukoplakia tissue. This allowed us to excavate molecular changes spanning normal mucosa, premalignant tissue and frank cancer. Compared with normal tissues, tumours displayed characteristic hallmarks of malignant transformation, including activation of immune signaling *(enhanced inflammatory and cytokine activity)*, angiogenesis (*increased blood-vessel formation to support tumour growth*), and cell-cycle programmes (*increased DNA replication and cell division*), accompanied by suppression of oxidative phosphorylation (*reduced mitochondrial energy production*) and fatty acid metabolism (*altered lipid utilization*), consistent with metabolic reprogramming associated with the Warburg effect (*preferential use of glycolysis and lactate production despite oxygen availability, supporting rapid growth and proliferation*). However, more precise inferences could be drawn only when we analysed data on each patient separately, as opposed to analysis of characteristics in a pool of patients.

Using single-sample gene-set enrichment analysis of 50 hallmark biological programmes, we performed unsupervised clustering that separated OSCC-GB into two molecular subtypes, GB1 and GB2. GB2, comprising approximately three-quarters of the cohort, showed greater infiltration of $CD4^+$ and $CD8^+$ T cells, M1 macrophages, and memory B cells, together with higher expression of the immune checkpoint ligands *PD-L1*, *CD80*, *CD86*, and *HVEM* in tumours compared with paired normal tissues. The expression of these ligands also correlated strongly with their corresponding receptors on infiltrating T cells, suggesting an active immune checkpoint regulatory landscape. Such immune infiltration coupled with checkpoint activation is a feature associated with response to checkpoint blockade in cancers. However, none of the patients in our OSCC-GB cohort received immune checkpoint inhibitor therapy; these findings should, therefore, be regarded as a transcriptomic signature of immune activation. The implication of this finding on treatment is unclear.

A parallel analysis of the normal-leukoplakia-tumour trajectory indicated that immune engagement begins early: leukoplakia tissue showed elevated M1 macrophage and memory $CD4^+$ T cell infiltration relative to normal mucosa, and checkpoint ligand expression rose monotonically from normal to leukoplakia to tumour. This raises the possibility that the tumour immune microenvironment starts to shift before overt malignancy, with potential relevance for risk stratification.

We identified a three-gene classifier comprising *CD226*, *CD38*, and *KBTBD8* that distinguished GB1 from GB2 with 86.1% cross-validated accuracy. Each gene has an independent association with immune regulation or immune checkpoint biology.

Comparison with 471 TCGA-HNSC patients showed both overlap and divergence: two of three TCGA subtypes resembled the immune-active GB2 profile, while one remained distinct. Notably, none of the 41 TCGA-HNSC patients with paired tumour-normal data, and only six of the full 471-patient cohort, had a tumour mutational burden above the threshold typically used as a proxy for checkpoint-inhibitor responsiveness. Consistent with our findings in OSCC-GB, this analysis suggests that immune activity in HNSCC may be influenced more strongly by the tumour microenvironment and epigenetic regulation than by mutational burden. More broadly, these findings highlight an important consideration for genomic medicine in India: population, geography, environmental exposures, and anatomical subsite can shape cancer risk and biology, and therefore biomarkers and reference datasets derived from geographically or biologically distinct populations may not be directly transferable to Indian patients.

Since the immune-related inferences of this study were based on computational deconvolution of transcriptomic data, direct experimental validation in an independent patient cohort is required. We hope that our study will precipitate collaborative efforts for validation of our inferences and also to undertake prospective immunotherapy studies among OSCC-GB patients of multiple regions of India so that translational benefits based on generalizable inferences can be derived.

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Article 5

Nephrin and Kidney Disease: Exploring Nphs1 Genetic Variants

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Introduction

Chronic Kidney Disease (CKD) is defined as abnormalities of kidney structure or function, manifested by glomerular filtration rate less than 60 ml/min/1.73 m^2 or markers of kidney damage, including albuminuria, tubular disorders, urinary sediment abnormality, histological or structural abnormality, or both, persisting for at least three months. CKD is a progressive, heterogeneous disorder which in a small proportion of cases can lead to End Stage Renal Disease (ESRD), necessitating dialysis or renal transplantation for survival [1]. A meta-analysis estimated a global CKD prevalence of 11-13% [2]. Diabetes and hypertension are major risk factors and cause up to two-thirds of CKD cases worldwide. Genetic susceptibility and gene-environment interactions are also implicated in irreversible nephron damage [3].

The primary site of damage is the glomerular filtration barrier. Nephrin, coded by the *NPHS1* gene, is crucial for maintaining the structural and functional integrity of the slit diaphragm and, together with the foot process actin cytoskeleton, contributes to the selective permeability of the glomerular filtration barrier [4]. Injury to podocytes can result in massive proteinuria and a decline in renal function. Mutations in *NPHS1* have been identified as a cause of nephrotic syndrome ranging from congenital to adult-onset disease, characterized by massive proteinuria, hypoalbuminaemia and edema, and may result in ESRD [5].

Nphs1 And Nephrin

The *NPHS1* gene is located on chromosome 19q13.1 and is approximately 26 kb in size with 29 exons. The protein product, nephrin, belongs to the immunoglobulin superfamily and is an integral transmembrane protein comprising an extracellular domain with eight immunoglobulin-like modules and one fibronectin type-III-like motif, a single transmembrane domain and a short intracellular domain. Nephrin is a crucial component of podocytes in the glomerular filtration barrier and is required for maintaining its integrity. More than 200 mutations have been identified in *NPHS1*, and the complete three-dimensional structure of nephrin has not yet been experimentally determined.

In Silico Analysis of *NPHS1*

The present analysis used a step-wise approach comprising sequence retrieval, selection and identification of conserved SNPs, SNP analysis, structure modelling, structure validation, modelling of SNPs on the protein structure and prediction of protein stability. SNPs were retrieved from dbSNP and the related protein sequence was obtained from UniProt (UniProt ID: P060500). SNPs with putative functions were prioritized on the basis of functional significance, evolutionary conservation, validation and minor allele frequency (MAF). Of 7917 SNPs present in *NPHS1*, 46 had MAF ≥0.10 and validation and were used for further computational analysis. Using Ensembl genome browser release 92 and manual verification of SNPs in evolutionary conserved regions of 26 eutherian mammals, 33 conserved SNPs were identified. RegulomeDB, SNPinfo (FuncPred) and PolymiRTS were used for functional prediction of regulatory SNPs; PANTHER, MutPred2, SIFT and PolyPhen-2 for analysis of non-synonymous SNPs; RaptorX, I-TASSER and Phyre2 for protein structure modelling; RAMPAGE for validation of the three-dimensional structure; Chimera

for modelling variants on the protein structure; and I-Mutant 2.0 for predicting the effect of mutations on protein stability.

Results

Identification and Analysis of *NPHS1* Variants

Thirty-three SNPs of a total of 7917 SNPs in the *NPHS1* gene were validated with MAF ≥0.1 and showed evolutionary conservation. These included 31 non-coding SNPs, including one in the 3′ UTR region, 27 in the intronic region and three in the 5′ region of the gene, and two non-synonymous SNPs (rs3914995 and rs4806213). These 33 SNPs were further analyzed using different algorithms.

Analysis of Regulatory Variants

The non-coding SNPs were submitted to SNPinfo (FuncPred) and RegulomeDB. Based on the information obtained from SNPinfo, four SNPs, one intronic (rs412175) and three in the 5′ region (rs401824, rs1137844 and rs619833), were observed to have an effect on transcription factor binding sites (TFBS). RegulomeDB classifies regulatory SNPs according to the likelihood of affecting transcription factor binding. For *NPHS1*, two SNPs (rs412175 and rs28489596) were classified as category 2b, indicating that they were likely to affect binding. One SNP (rs5827941) was classified as category 3a, indicating that it was less likely to affect binding. Eighteen SNPs fell into categories 4-6, representing minimal binding evidence, while the remaining SNPs were classified as category 7, with no annotation data available. The regulatory analysis therefore identified specific non-coding variants with potential regulatory relevance.

Predicted Effects of Non-synonymous Variants

SIFT, PolyPhen-2, MutPred2 and PANTHER algorithms were used to predict the effects of non-synonymous SNPs on protein structure and function. The rs4806213 (N1077S) variant was predicted as benign by MutPred2 (score = 0.200;
≥0.5 is pathogenic) and PolyPhen-2 (score = 0.010; values nearer to 1.0 are damaging), and as tolerated by SIFT (score
= 0.617; values nearer to 0.05 are damaging). PANTHER predicted this variant to be probably damaging, with a preservation time of 455 million years; greater preservation time implies greater likelihood of functional impact on the protein.

The rs3914995 (E117K) variant was predicted to be probably damaging by PolyPhen-2 (score = 0.999) and PANTHER (preservation time = 455 million years). MutPred2 indicated that this SNP may be pathogenic (score = 0.535), with a probability of 0.27 of altering the transmembrane property and a probability of 0.22 of causing a gain of ADP-ribosylation at the neighbouring arginine at position 115. SIFT predicted E117K to be tolerated (score = 0.675).

Structural Analysis of Nephrin Variants

Protein structure modelling was performed using two template-based methods, RaptorX and Phyre2, and one template-free ab initio method, I-TASSER. The Phyre2 model covered 967 (78%) of 1241 amino acid residues of nephrin, while the I-TASSER model, assessed using Ramachandran plots with RAMPAGE, showed 716 (57.8%) of 1241 residues in the energetically favored region. The RaptorX structure, with 92% of residues in the favored region, 6.1% in the allowed region and 1.9% in the outlier region, was selected as the most probable structure of nephrin (Fig. 1a).

The two selected variants were modelled on the nephrin three-dimensional structure using Chimera. On visualization of the three-dimensional structure, no apparent clashes occurred when asparagine was substituted with serine at position 1077 (N1077S). In contrast, substitution of glutamic acid at position 117 by lysine (E117K) led to steric clashes between lysine at position 117 and arginine at position 115 (Fig. 1b). Using I-Mutant2.0, the E117K amino acid substitution had a DDG of -0.67 kcal/mol, while N1077S had a DDG of -0.14 kcal/mol. A DDG value less than zero indicates a decrease in protein stability.

Conclusion

The *in silico* analysis identified conserved *NPHS1* variants with potential regulatory and functional

effects. E117K showed stronger evidence of a potentially damaging effect, with predicted structural clashes and reduced protein stability, whereas N1077S showed largely benign or tolerated predictions but was also associated with decreased stability. These findings provide a basis for further investigation of *NPHS1* variants and their potential effects on nephrin structure, stability, and glomerular function.

a) b)

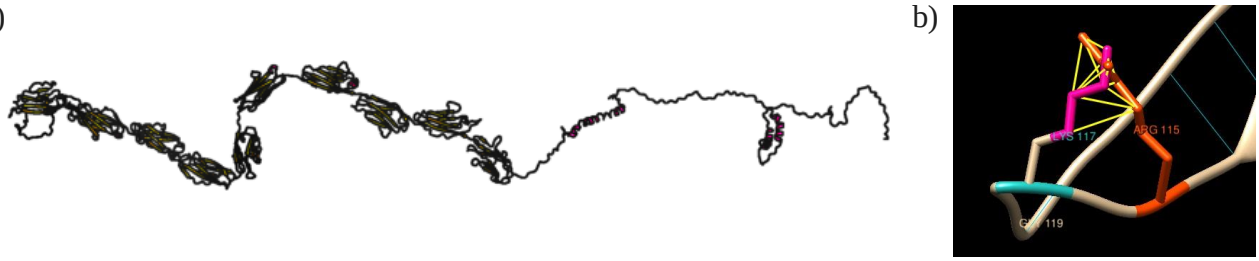


Fig. 1: a) 3D structure of Nephrin predicted by RaptorX; b) Variant residue Lysine at position 117. Yellow lines represent network of clashes; blue lines represent hydrogen bonds.

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Article 6

Nature, Nurture and Chromatin: A Preventive Approach to Obesity

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It was a scorching, sunny morning in June, and Koyel was quite late for work. Hurriedly, she passed through the office entrance. Amidst the rush, the elevator was out of service. She started climbing the stairs, but paused midway, catching her breath. At only thirty-four years of age, she felt much older. Koyel knew the concept of 'eat less, and move more', yet her sedentary work culture didn't let her attain the promised weight-loss journey. What she didn't know was that her struggle was shared by more than a billion people worldwide, contributing to an annual economic burden of $23.2 billion (approx. 1.7% of the GDP) in India, ranking third globally after China and the USA [1]. Obesity is not simply the concept of an increase in body weight; rather, it is a complex metabolic dysregulation associated with varied comorbidities, including cardiovascular disease risk, type 2 diabetes mellitus, polycystic ovarian syndrome, hypothyroidism, osteoarthritis, and even cancer. The cumulative effects of obesity are popularly termed obesity and related metabolic syndrome (OMS) [2] (Genetic-epigenetic crosstalk is a significant determinant of the disease manifestation. Genetic inheritance and environmental factors contribute to the modifications of epigenetic markers, resulting in genotypic and/or phenotypic changes in human health [3]. DNA methylation and chromatin protein modifications are two significant epigenetic mechanisms influencing gene expression. Lifestyle factors largely regulate the disease predisposition, onset, and progression. Diet, mental health, and physical activities are the most discussed and reliable lifestyle factors [4]. These factors have been widely reported, arousing our interest in studying the reversible epigenetic changes in Indian urban academic professionals with sedentary lifestyles.

Adult volunteers aged 18-60 years from different campuses of the University of Calcutta, Kolkata, India, participated in our anthropometric analysis. Bioelectric impedance was used to monitor approximately 15 physiological parameters, including body weight, body fat percentage, body mass index, visceral fat percentage (the ectopic fat largely responsible for cardiovascular disease risk), subcutaneous fat percentage, resting metabolism, etc. The biostatistical analysis of the data collected from 650 participants inferred the significance of visceral fat percentage as a biomarker of OMS risk. Cardiovascular disease risk was highlighted in the overweight and obese young female participants (age<35 years). Altered liver function, elevated triglycerides, and abnormalities in red blood cells were positively correlated with obesity in our study population [5]. The observations provided an opportunity to get mechanistic insights.

Complex interconnected pathways are associated with the pathogenesis. *In silico* and clinical exome sequencing approaches were employed in our study to investigate the significant and associated pathways involved in disease manifestation. Enrichment analysis and protein-protein interaction network analysis, as observed in obese probands (demography-matched representatives of the study population), indicated the predominance of adipocytic functions and energy homeostasis. STRING network analysis was followed by pathogenicity prediction and associated protein functions utilizing bioinformatic tools, including SIFT, PANTHER, MetaSNP, DYNAMUT, iMUTANT, MutPred, etc. The leptin-melanocortin and adiponectin-PPAR pathways were identified as the prominent target pathways. The identified pathogenic variants of the studied genes (rs28954113, rs28932472, rs149540566, and rs150343979) linked with inherited obesity, although reported in European and African populations, were not recorded in any South Asian countries, including the Indian subcontinent [6]. This ruled out the probability of obesity inheritance in our study population. Rather, lifestyle

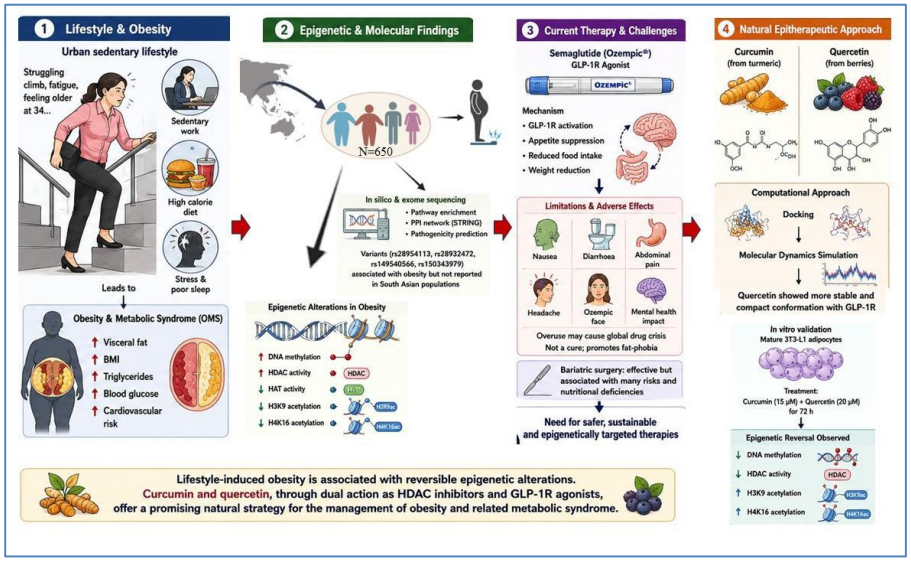
practices that influence the epigenetic alterations could be a possible contributing factor for OMS in the study participants.

Lifestyle and environmental effects mostly induce inter-individual variations in epigenetic modifications. The question here arises: how can these epigenetic alterations be reversed? To understand the underlying mechanism, we investigated variations in DNA methylation, histone acetyltransferase (HAT)-histone deacetylase (HDAC) activities, and histone acetylation at H3K9 and H4K16 histone moieties. DNA hypermethylation, reduced HAT activities, increased HDAC activities, and lowered H3K9-H4K16 acetylation affected the expression of the candidate genes cumulatively. A leptin-deficient pattern of obesity was thus observed in our study population [6]. Therefore, understanding the anthropometric scenario of the study population, followed by planning lifestyle modifications, dietary management, and epitherapeutic approaches, could exert a cumulative role in controlling obesity, thereby aiding in policy-making.

Koyel was unaware of all these research findings. Yet she recently came across the term 'Ozempic', the viral anti-obesity drug shining in the global market. Semaglutide, the principal component of Ozempic (marketed by Novo Nordisk), is a glucagon-like peptide 1 receptor (GLP-1R) agonist commonly used to treat type 2 diabetes mellitus. This popular drug, considered a 'miracle for weight loss', acts on appetite suppression, generating a quantitative reduction in body weight. It mimics the GLP-1 hormone, thereby successively enhancing insulin production in response to elevated blood glucose. The primary concept of Ozempic and similar drugs is to make one feel fuller to avoid excess eating [7]. The behavioural alteration is not a suitable solution for the betterment of one's metabolic activities. Overuse and the demand for Ozempic would soon result in a worldwide crisis of this drug, rendering the diabetic patients unable to access their life-sustaining medication [8]. Dr. Emma Beckett considers semaglutide unable to cure obesity, rather a potential for increasing fat-phobia among the patients [9]. Reports archived in the drugs.com repository state 54% of reviewers of 2023 had a positive experience with semaglutide, while 24% reported a negative experience [10]. A more effective alternative to reduce the stubborn visceral fat is bariatric surgery. But this practice comes with a lot of adverse effects, including nutritional deficiency, anemia, osteoporosis, neuropathy, infertility, bleeding, infection, hernias, bile reflux, stomach ulcers, blood clots, bowel adhesion, obstructions, anastomotic leaks, and even death [11]. In this context, anti-obesity treatment with semaglutide is a safer option. Yet, several side effects also accompany semaglutide usage. Nausea, diarrhoea, abdominal pain, bloating, weakness, and headache are some common symptoms, with the 'Ozempic face' being the most pronounced. Rapid and excessive weight loss induced by semaglutide may lead to loss of facial adipose tissue, resulting in skin laxity and wrinkles, a condition popularly known as 'Ozempic face'[12]. A case study on a 54-year-old female patient with a history of hypertension, hyperlipidemia, and depression, administered with 0.5mg semaglutide weekly, showed a significant negative impact on her mental health [13]. The emergence of adverse effects linked to Ozempic has intensified efforts to develop safer and more effective therapeutic strategies.

Natural bioactive compounds possess strong antioxidant properties and potential therapeutic properties with minimal toxic side effects. Plant derivatives like polyphenols, including curcumin, quercetin, resveratrol, catechins, tannins, etc., with anti-inflammatory, anti-obesity, and anti-carcinogenic properties, are widely explored as bioactive therapeutics [14]. The dietary polyphenols can be considered as free from adverse health effects [15]. Identification of a suitable alternative to a conventional anti-obesity drug requires targeted ligand-receptor-specific epitherapy with the concept of modern drug designing using molecular dynamics. Our study concentrated on investigating the potential of curcumin and quercetin, the natural compounds extracted from turmeric and berries, as potential GLP-1R agonists. Docking, the prediction of the binding affinity of the ligand and the respective protein, was followed by a molecular dynamics simulation, where a time-dependent behavior of the receptor-ligand complex in a pseudo-natural environment was observed. Quercetin was observed to promote a more stable and compact conformation with the GLP-1R complex. Both the ligands, curcumin and quercetin, were seen to have unique properties in regulating the stability of the studied receptors, GLP-1R, LEPR, and PPARG. An additional validation of the study was observed through an in vitro study with mature 3T3L1 adipocytes. A combination of dose with curcumin and quercetin (15+20 μM) was found to be effective in reversing the adiposity-generated epigenetic alterations when administered for 72 hours. DNA methylation, HDAC activity, H3K9 acetylation, and

H4K16 acetylation reflected a significant improvement with treatment. The promising role of curcumin and quercetin as HDAC inhibitors and GLP-1R agonists was well established.
Future investigations should focus on validating these results in animal models and clinical settings to establish their efficacy, safety, bioavailability, and optimal dosing regimens. The development of advanced delivery systems, such as nanoformulations, may enhance the bioavailability and therapeutic effectiveness of these phytochemicals. Additionally, exploring their potential as adjuncts or alternatives
to current anti-obesity therapies, including GLP-1 receptor agonists, could pave the way for safer and more sustainable obesity management strategies.
Koyel wondered whether the answer to sustainable weight management might soon be found in her own kitchen.



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Announcement

1. The All India Congress of Genetics and Genomics proudly announces the "**First Dhananjoy and Parvati Giri Oration Award**," instituted in honor of the parents of **Dr. A. K. Giri,** an eminent scientist and former Secretary-Convener of AICGG. The award will be conferred on **Prof. David A. Polya, Professor of Environmental Geochemistry and Health at the University of Manchester, UK**, on **February 7, 2027**, in Kolkata, India

Webinars

- **Third Webinar**

Topic: Resurrecting ancient health code: Next-Gen Intelligent solutions from Ayurveda's lost algorithms

Speaker: **Prof. (Dr.) Mitali Mukerji,** Professor, Department of Bioscience & Bioengineering Affiliate Faculty at School of Artificial Intelligence and Data Science (AIDE) & Centre for Emerging Technologies for Sustainable Development (CETSD) Indian Institute of Technology Jodhpur

Date: Tuesday, 28 July 2026, Time: 7:30 PM (IST) Platform: Google Meet

- **4th Webinar**

Topic: Hidden world of microbial communities, genomics and how bacteria evolve

Speaker: **Dr Prabhu Patil,** Senior Principal Scientist and Professor AcSIR, CSIR-Institute of Microbial Technology, Chandigarh, INDIA.

Date: 30 September 2026, Time 7.30 pm IST, Platform: Google Meet

Invitation for Articles

Invitation for the quarterly e-Newsletter AICGG

We warmly invite eminent researchers, scientists, professors, and distinguished members to contribute scholarly articles aligned with the theme of our newsletter ***Genomic Horizons***. Contributions may take the form of concise scientific articles, **typically one to two pages in** length (**1000 to 1500 words**), that reflect ongoing research, insights, or perspectives relevant to our field.

Format for articles (Word Doc, Times New Roman, Font size 12)

Theme: **Molecular Crossroads: Genes, Environment, and Human Risk**

Title:

Name of author (s):

Affiliations:

Email Address of Corresponding author:

Article Body: In addition to the text, figures/images/tables/schematic diagrams may be included as relevant

References: 10 (maximum in APA style)

Articles should reach us by 15th December 2026 for the next issue to be published in **January 2027.**

Email address for sending articles: 2006.nilanjana@gmail.com and vikas.srivastava@csir.res.in

"Genes are like the story, and DNA is the language that the story is written in." — Sam Kean