current interest and updated with notable additions to various sections of different chapters.

The book is divided in 16 chapters, starting with the introduction of different concepts which are usually involved and commonly used in the study of environmental chemistry. The environmental segments and the natural cycles of the environment are introduced in the first chapter. Chapters 2–6 provide information about environmental segments such as atmosphere, hydrosphere, lithosphere, geosphere and biosphere respectively. Each chapter deals with composition, structure and chemical reactions involved in the different segments.

Impact of increase in population on environment is discussed in chapter 7 using concepts like doubling time, infant mortality, carrying capacity, food and natural resources. In chapter 8, the author introduces basic biochemical terms related to the environment. Chapter 9 is mainly focused on how the environment is influenced by the presence of toxic chemicals, e.g. carbon monoxide, nitrogen oxide, ozone, peroxyacetyl nitrate, cyanide, pesticide, etc. and some toxic elements such as arsenic, cadmium, lead and mercury. Chapters 10 to 12 deal with air, noise and water pollution respectively. Each topic separately emphasizes the cause, effect and control measures for bringing down pollution. In addition some instrumental techniques for the analysis of pollutants are discussed in brief in each chapter.

In chapter 13, the crisis of waste with its classification is studied, with special reference to treatment, waste management and recycling or reuse depending on the type of waste. In the next chapter, the most sophisticated and useful instrumental techniques for the environmental chemical analysis are discussed. They include neutron activation analysis, anodic stripping voltammetry, atomic absorption spectrophotometry, inductively coupled plasma emission spectroscopy, X-ray fluorescence, non-dispersive infrared spectrometry, Fourier transform infrared spetroscopy, chemiluminescence, gas chromatography and high performance liquid chromatography.

'There is enough on earth for everyone's need but not for everyone's greed.' On the basis of this thought, chapter 15 focuses on the availability of natural resources on Earth. Recent trends in environment destruction are discussed in the next chapter in the light of Earth summits, environmental impact assessment, environmental audit and action plan, etc. The state of global environment is discussed by considering human development, population and health. Different reports provide recent useful data on pollutants in the Indian metropolitan cities. The myths, ground realities, environmental policies and laws in the Indian context are discussed.

This book covers nearly every aspect of environmental chemistry in its updated and revised form. The popularity of the book is reflected by the fact that is in its seventh edition and was reprinted in the same year. The strength of this book is that it not only discusses the facts, but also gives remedies in the form of information, various reports and instrumental techniques in environmental chemical analysis. However, I feel that the author has not succeeded in correlating the relevance of biochemistry and environment in chapter 8.

Overall, the book has several commendable features and is informative. One of the most notable features of this book is that it is in lucid, easy and popular writing style. It is less intended for the specialists, but more for a generalist audience. It may also act as a ready reference for students, teachers and researchers in the field.

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Annual Review of Genomics and Human Genetics, 2013. Aravinda Chakravarti and Eric Green (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0139, USA. Vol. 14. 595 pp. Price: US$ 92.

Researchers, not only involved actively in the field of human genetics and genomics, but in different areas of biology, would find this volume useful. It covers a broad spectrum of contemporary topics, which are thematically oriented to human genetics and genomics, while they originate from different domains of biology such as immunology, neuroscience, pharmacology, evolution and ethology along with a number of ethical, social and legal aspects. Altogether, this volume contains 26 chapters that provide reviews of important and uniquely interesting perspectives that may be relevant to the advancement in genomics and human genetics research worldwide.

The book starts with an article by David J. Weatherhall on inherited disorders of hemoglobin. This review contains a historical account of thalassemia molecular genetics with a future perspective on proper management of these disorders globally. Chapter 2 deals with progress made in understanding the molecular genetic mechanisms of hypoxia tolerance in *Drosophila* and humans with more emphasis on the former. Authors discuss genetic factors that confer an advantage to cope with hypoxic condition in human high-altitude dwellers; however, a discussion of ethical and legal issues like 'gene doping' could have been an excellent addition in this review article.

The genomics of learning and memory in songbirds in chapter 3 is also an excellent addition to this volume. Songbirds are a unique model to understand memory and learning, since they have evolved a complex communication system that requires perceptual and motor learning. Learning is quantified in two contexts, song production learning that is restricted to males during the juvenile period and song recognition learning that occurs in both males and females throughout life. This learning and recognition is important to form associations with song-specific behaviour in birds. Early studies on zebra finch to determine the molecular nature of this response demonstrated a rapid response in four genes (*zif268*, *egr-1*, *NGF1-4* and *Krox-24*) when taped bird-songs were played back. The Songbird Neurogenomics Initiative (SoNG) sequenced the zebra finch genome and produced a cDNA microarray. This allowed gene expression changes to be documented according to age, sex, different regions of the brain and in various species. Learning and behaviour are not only influenced by auditory cues, but also by social, ethological, environmental and evolutionary aspects. These effects accumulate slowly but have finite behavioural impact. Overall Genomics

has accelerated our understanding of learning and memory. It has demonstrated that, this is a complex, cumulative and integrative interplay of multiple events rather than being an event controlled by a single master switch gene response. In chapter 4, the author stresses upon the probabilistic model of the spatial organization of the human genome and its consequences on long-range gene regulation. The importance of studying single-cell genome organization, impact of individual genetic variations on its spatial organization, and cell-type specific spatial organization are elaborately discussed. The authors feel the need of developing newer technologies, which would enable studying the spatial genome organization in a living cell since the current techniques like 3C or FISH can only study fixed cells.

Somatic cell reprogramming, alternately known as induced pluripotent stem cells (iPSCs), has brought immense promises in the field of regenerative medicine and developed a novel method to study human diseases. Although genetically identical, iPSCs undergo significant changes in their epigenetic landscape. In chapter 5 the authors deal with the wide variation of one such epigenetic modification, known as X-inactivation, between female human iPSC (hiPSC) and embryonic stem cells (ESCs). Comparative analysis of three different classes of hiPSCs based on the X-inactivation specific transcript (XIST) expression pointed towards the effectiveness of using hiPSCs for disease modelling or therapies. The authors further emphasized that the characterization of female hESCs and hiPSCs simply by assessing XIST expression in undifferentiated cells is not enough. XIST must be assayed in the differentiated state as well to clearly distinguish between class I and class III cells. Chapter 6 on understanding heritability using genetic interaction networks is an important inclusion in this book. The concept of genomic medicine essentially emanated from proper genotype–phenotype correlation in human diseases. However, pinpointing phenotypic effects of individual genetic alterations comes with innumerable practical and statistical challenges. Consequently, model organisms have come in handy to execute large-scale genetic interaction screening. The authors emphasize that despite relatively low conservation of individual genes and their pairwise interactions, the overall topology of genetic interaction networks and the connections between broad biological processes are somewhat similar in most organisms. Therefore, these general principles should provide a fundamental basis for mapping and predicting genetic interaction networks in humans. From a critical point of view, along with budding yeast, the authors could have discussed genetic interaction networks in higher order eukaryotes like zebrafish and mouse, which probably would have been more relevant for human interactome analyses.

Despite difficulties in genotype–phenotype correlation, efforts to understand the molecular mechanisms involved have spurred the development of methods to create targeted alterations in a normal genome, initially in mice and budding yeast and now in other species. Such genome engineering methods historically involved random mutagenesis followed by screening, target selection and true targeting. In chapter 7 the authors discuss techniques widely being used for genome engineering, which have profound effects on understanding disease processes. Independent research has suggested that double-strand breaks (DSB) in DNA significantly increase the efficiency of homologous recombination at such breakpoints. The ability of generating DSBs by nucleases was well characterized, but it could not be exploited to generate knockouts at the desired positions in the genome. What helped was the discovery of DNA binding proteins like the zinc-finger nucleases (ZFNs) and discovery of semi-independent nuclease domains to guide the nuclease to a user-defined target site. Several technologies like ZFNs, trans-activator like effector nucleases (TALENs) and nucleases based on the bacterial CRSIPR/Cas nucleases have now been developed. These new nuclease-based genome engineering methods have rapidly found a wide range of applications in guiding small insertions or deletions, preforming large deletions by excising intervening fragments using two different nucleases simultaneously, collapsing direct repeats, deleting entire chromosomes and more recently, for correcting single nucleotide polymorphisms in cells. ZFNs in particular are now in clinical trials to engineer HIV-resistant cells from HIV patients. The engineered resistant cells will then be used to repopulate infected patients for treatment. In the future genome engineering by nucleases can be used to generate new animal disease models, stem cell or human cell-based disease models and eventually perform gene and cell therapy.

Chapters 10, 13–15 deals with diverse aspects on the genomics of host–pathogen interactions. Chapter 10 begins by introducing the four theories that have prevailed in infectious disease biology, viz. microbial theory, ecological theory, immunological theory and genetic theory. Genetic theory is the focus of discussion in the remaining part of the chapter, contrasting it with the microbial and immunological theories. There is a nice argument built for genetic theory in the earlier sections; issues of conflict between immunologists, microbiologists, ecologists and geneticists are well articulated throughout the discussion. One shortcoming in the authors' discussion is that they do not bring in ecological theory, which could have really made the review comprehensive. Since environment has a major role in any infectious disease pathogenesis, more emphasis should have been given to this aspect. Furthermore, a unifying theory consisting of genetic and environmental (including microbial) factors could have been proposed as conclusion of the chapter. Instead, the authors next discuss eight infectious/immunological disorders (some included in the supplement) that have contributed to the genetic theory of infectious diseases from the 1950s from the perspective of both population and clinical genetics. These individual disease conditions are discussed rather comprehensively (especially the one on hepatitis C virus), but as pointed out earlier, no unifying theme seems to emerge from these discussions. With genome wide association study (GWAS) carried out on more than a dozen infectious diseases, the chapter could have been made more up-to-date by discussing these diseases and possible directions the field may be heading towards. However, the strength of the chapter is that the reader gets a good historical background of infectious diseases in the context of germline theory, and also read well-written summaries on eight different infectious/immunological disorders. Chapter 13 throws light on the emerging pathogens and their molecular identification and the role genomics has played in this area of infectious diseases. The chapter

seems to fulfil the unmet need that this area of infectious diseases has felt for sometime now, especially with the emergence of HTS technology. The authors give a detailed account of what is expected when an emerging pathogen is suspected, beginning with appropriate sample collection/preparation and suitable molecular methods for their detection. Chapter 14 on genomics of major histocompatibility complex (MHC) and human disease, offers the reader a comprehensive view on MHC and its association with human diseases. The concept of linkage disequilibrium (LD) is well narrated since it is important in association studies as MHC is known to have strong LD blocks and as pointed out, the MHC region has more association with human disease than any other region of the genome. Chapter 15 enlightens the readers on 12 immune-related disorders, which have been subject to GWAS and/or are part of the Immunochip consortium studies. Further, data is used from these studies to analyse functional significance of GWAS hits and perform pathway analysis. Moreover, the chapter gives a good background on genetic studies in immune-mediated disorders beginning with candidate gene studies, linkage studies; it extensively discusses GWAS, interpretation of GWAS hits, functional variant discovery and pathway analysis to understand disease biology.

Activating somatic mutations in the RAS gene family are oncogenic drivers in cancer. Chapter 16 deals with rasopathies, which are a defined group of medical genetic syndromes arising due to germline as opposed to somatic mutations in RAS genes and their pathways. Rasopathies are the largest known group of malformation syndromes affecting 1 in 1000 individuals. Some, but not all individuals, have an increased risk of cancer in various organs. Despite advent of genomic technologies and several drug trials, not all mutations leading to rasopathies have been identified, nor have all potential drugs been evaluated in clinical trials. Clearly, it is important to study these syndromes in greater detail to help define the best medical practices for each Rasopathy.

Genomic dissection of complex traits and associated diseases are well articulated in several chapters of this book. Complex diseases such as autism spectrum disorders, degenerative disc disease and osteoarthritis and melanoma have been discussed in chapters 9, 11 and 12 respectively. In connection with this, chapters 19 and 20 deal with two timely topics of quantitative traits dissection in mice and power of meta-analysis in GWAS. Both these chapters essentially discuss the advancement of statistical methodology to deal with high-resolution mapping in association studies. The take-home messages like 'statistical methods that combine haplotype mapping with near-complete catalogs of sequence variants segregating among inbred mouse strains, make it possible to test whether individual variants are functional' or 'larger GWA meta-analyses, could increase our knowledge by identifying new loci, thus increasing the proportion of variance explained and potentially also providing new insights into the biology of human disease' point towards a routine practice of these statistical methods as independent genomic research groups will publicly share data to form worldwide consortia.

A number of ethical issues are also included in this volume. In chapter 24, the authors discuss the trend of using pediatric-whole genome sequencing (P-WGS) and pediatric-whole exome sequencing (P-WES) for testing in children. Though genetic testing in children for some conditions is common, due to a huge drop in cost and time taken for WGS/WES, it is fast becoming an affordable and routine clinical option. Currently, WGS/WES is done as a part of research studies in childhood health conditions, or in children with serious undiagnosed health conditions to understand disease causation. Parents now express interest in obtaining genetic health information of their children and ask for provisions in pediatric care. However, the impact of knowing test results on children and their families, the mode of communication of such results by health professionals, clinical care decisions and reporting incidental findings that the children were not tested for which are revealed due to the genome-wide nature of sequencing, remain under studied. These are therefore major challenges which need to be overcome at the policy level, before routine adoption of such testing in pediatric care. It is evident that before implementation, P-WGS and P-WES must be proven to be more advantageous over existing tests in terms of accuracy and efficiency; it must contain actionable information that can ultimately improve overall health outcomes in children. More research needs to be focused on parental choice, return of test results, impact on children and families, supporting research at the infrastructural level, clinical training and policy making in order to adopt P-WGS/P-WES in pediatric healthcare practice.

Finally, this volume is a perfect and timely compilation review articles pertinent to human genetics and genomics. Investigators in the respective fields would definitely find this as a useful reference.

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Annual Review of Immunology, 2012. William E. Paul, Don R. Littman and Wayne M. Yokayama (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0139, USA. vol. 30. xi + 822 pp. Price: US$ 94.

Each year the *Annual Review of Immunology* (*ARI*) puts together a series of excellent reviews by leaders in the field in different areas of immunology. This volume is no different and areas covered can be broadly classified under distinct topics: immune cells and their biology, regulation of immune responses, etc.

The arsenals used by the adaptive immune responses in vertebrates are diverse. Jawed vertebrates utilize the B-cell receptor, T-cell receptor and major histocompatibility complex encoded molecules, whereas variable lymphocyte receptors (VLRs) play an important role in jawless vertebrates, e.g. lampreys and hagfish. VLRs consist of an array of leucine-rich repeats (LRRs) and consist of two broad types. The number of LRRs is variable with the sequences being highly divergent. VLRA is expressed on T cells, whereas VLRB is expressed on B cells and secreted as a multivalent protein. Interestingly, VLRA is expressed on thymus-like tissue present at the tip of gill