

### Annual Review of Genetics, 2018.

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The editors of this series have been bringing out in-depth reviews about the most recent developments of contemporary topics in molecular as well as classical genetics. This volume is a compendium of latest information on the topics of both basic as well as applied genetics encompassing 25 thought-provoking review articles with informative illustrations. The listing of summary points, concluding remarks and future research directions at the end of article is of immense benefit to researchers to ponder over the subject. The present volume covers a wide range of topics relating to epigenetics (2 articles) microbial genetics (3 articles), developmental biology (4 articles), plant breeding (2 articles), biology of ageing (2 articles), molecular genetics and cancer biology (11 articles).

The volume begins with an autobiography article by Frederick M. Ausubel in which he describes his work on using genetic engineering technologies to transfer the ability to fix nitrogen from prokaryotic nitrogen-fixing (*nif*) genes to the model plant *Arabidopsis thaliana*. For the last 35 years, he has been studying host–pathogen interactions using *Arabidopsis* and the nematode *Caenorhabditis elegans* as host models. The article covers his associations with other renowned scientists of his time and their influence on his work.

In recent years, the belief that the genetic code is the sole basis for biological inheritance has been challenged by the innovation of trans-generational epigenetic inheritance<sup>1</sup>. Bošković and Rando highlight how epigenetic information is inherited in multi-cellular organisms from one generation to the next. Further, the article discusses about the induction of heritable epigenetic changes by genetic or environmental perturbations. Germline-specific features of chromatin structure, cytosine methylation and small RNAs are briefly reviewed in this article. The neural crest cells (NCC) are transient multipotent stem cell population that migrate collectively to various locations throughout the embryo and contribute a number of cell types to several organs. Recently, NCC have become an attrac-

tive model for developmental and evolutionary biologists, as well as cancer biologists and pathologists. Szabó and Mayor describe the cellular interactions, the molecular mechanisms and the chemotactic cues of NCC migration in a region-specific manner.

Hippo signalling is an evolutionarily conserved network that controls growth and regeneration of organs by regulating cell proliferation, apoptosis and stem cell self-renewal. Down-regulation of Hippo signalling promotes uncontrolled cell proliferation, impairs differentiation and is associated with cancer. Misra and Irvine review the current understanding of Hippo signalling and highlight recent developments in the elucidation of its regulatory mechanisms (extracellular signals/membrane receptors) and biological functions. Other articles highlight the structural maintenance of chromosomes (SMC) complexes such as cohesin (consists SMC1 and SMC3), condensin (consists SMC2 and SMC4) and the SMC5/6 complex (consists SMC5 and SMC6) are the key regulators of chromosome dynamics, structure and function in eukaryotes<sup>2</sup>. SMC5/6 plays a crucial role in maintaining genome stability and in DNA repair. Nevertheless, how SMC5/6 promotes chromosome stability is largely unknown. Aragón summarizes recent research developments on structure, function and molecular details of SMC5/6 complex in the stability and dynamics of eukaryotic genomes.

The dynamic nature of chromatin is defined by histone chaperones as they can deposit and evict histones in different tissues at different times in the cell cycle. The article by Grover *et al.*'s focuses on the molecular details of canonical and variant H3–H4 histone chaperone pathways that lead to histone deposition on DNA. They further highlight replication-coupled and replication-independent histone deposition via alternative histone chaperone pathways.

Although in prokaryotes more than half of the genes in the genome are organized into linearly positioned operons, eukaryotic genomes possess very small number of genes organized into operons also known as metabolic gene clusters. Nützmann *et al.* describe the metabolic functional gene clusters for primary and secondary metabolism in fungi and plants. The article highlights the origins of functional gene clustering and how these clusters are regulated. Opachaloephan *et al.* overview the epigenetic

regulation of caste development and behaviour pattern in eusocial insects. This article emphasizes interesting mechanisms of histone modification, DNA methylation, juvenile hormones and odorant receptors to determine genetic and epigenetic regulations of social behaviour in eusocial insect colonies. Other article deals with the multiple levels of mitonuclear coregulation primarily at the time of transcription and translation (by Isaac *et al.*). Galupa and Heard provide a comprehensive review on mechanisms of X-chromosome inactivation (XCI) and influence of XCI on genome function in the context of developmental biology.

In the last decade novel archaeal phyla such as *Korarchaeota*, *Thaumarchaeota*, *Bathyarchaeota*, *Woesearchaeota*, *Aigarchaeota*, *Nanoarchaeota* and *Lokiarchaeota* are identified by cultivation independent modern sequencing approaches including metagenomics and single cell sequencing<sup>3</sup>. Recent developments in systems biology and next generation sequencing techniques enable us to understand interaction and regulation networks of non-coding RNAs (ncRNAs) in archaeal domain. Current knowledge of small, non-coding RNAs with important functions for the archaea lifestyle and their adaptation to extreme environments are extensively reviewed by Gomes-Filho *et al.* The article focuses on RNA metabolism at elevated temperatures in hyperthermophilic archaea and reveals elevated amounts of RNA-guided RNA modification and virus defense strategies. Further, evolution of fragmented ncRNA genes in archaeal domain has been emphasized with appropriate illustrations.

One of the fascinating fields in the evolutionary biology of prokaryotes is the battle for survival between bacteria and bacteriophages. Stanely *et al.* review the most recent developments in evolutionary arms race between bacterial encoded CRISPER-Cas adaptive immune system and phage evolved anti-CRISPER protein inhibitors. The article describes the potential mechanisms of action of anti-CRISPERs in bacteriophage infection. Other highlights in this volume include article by Wallace *et al.* on the four different stages of plant breeding programmes for achieving global food security in the 21st century; Zhang and Vijg describe somatic mutations in clonal lineages of mammals with a focus on their possible functional consequences in human disease and ageing.

Synapses are the sites of communication between neurons and their formation is mediated by a wide variety of genes encoding synaptogenic proteins (e.g. neuroligins, neuroligins, cadherins, ephs/ephrins, integrins, etc.). One of the protein families that is implicated in synapse wiring but poorly understood is the immunoglobulin superfamily (IgSF). Cameron and McAllister highlight the critical role of IgSF molecules in synapse formation particularly in the context of vertebrate brain. The authors anticipate that deducing the IgSF code for synapse formation may eventually lead to novel treatments for psychiatric disorders caused by defected IgSF-induced synapse wiring.

Reviews describing various aspects of chromosome structure function and dynamics are well compiled in this volume. Lange provides an elaborate review on current knowledge of shelterin-mediated telomere protection and highlights differences between human and mouse shelterin. Shelterin structure, DNA binding features and shelterin accessory factors are comprehensively addressed in this article. Seeber *et al.* discuss critical regulators of chromatin mobility in response to DNA damage. This review suggests that centromeric tethering, telomeric tethering, microtubules and actin filament influence chromatin mobility.

One of the major challenges in biomedical research is to understand the interface between the ageing process and the manifestation of age-associated diseases. Although different research activities are currently being conducted to understand the process of ageing<sup>4</sup>, there is no unifying concept that explains better the complex biology of ageing. Two review articles especially focus on this issue. Mertens *et al.* emphasize the key features of ageing that appear to drive neurodegeneration and age-associated diseases. They discuss the extent to which induced pluripotent stem cells reflect aged neurons.

As a whole this is a highly informative volume that consists of various high quality articles on key issues in genetics. Molecular biologists will find a number of articles in this volume extremely interesting as promised by its earlier volumes. This volume provides major research findings in contemporary topics and opens up new research avenues towards understanding some long standing questions from different sub-fields of genetics.

1. Lind, M. I. *et al.*, *Heredity*, 2018, **121**, 205–209.
2. Diaz, M. and Pecinka, A., *Genes*, 2018, **9**, 36.
3. Brochier-Armanet, C. *et al.*, *Nat. Rev. Microbiol.*, 2008, **6**, 245–252.
4. López-Otin, C. *et al.*, *Cell*, 2013, **153**, 1194–1217.

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#### **Annual Review of Physiology, 2019.**

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This volume of *Annual Review of Physiology* starts with two articles on the fate and function of mitochondria. The first article on the ‘Evolving concepts of mitochondrial dynamics’ focuses on the issues of mitochondrial fusion, mitochondrial fission, trafficking pathways and mitophagy. The article brings into focus mitochondrial dynamics in the heart which is the most energy-dependent and mitochondrial-rich mammalian organ (accounting for a third of the weight of cardiomyocytes). While the article is primarily physiological, the authors draw attention to the possible role of mitochondrial function in the genesis of cardiac hypertrophy which is not an uncommon clinical condition. The second article on the ‘Maintenance of skeletal muscle mitochondria in health, exercise, and ageing’ addresses a significant health issue at a population level. The ageing population in all countries of the world is steadily increasing and one of the issues of increased longevity is sarcopenia or the loss of skeletal muscle mass, with all its attendant sequelae. In young populations physical inactivity affects skeletal muscle quality. The authors provide compelling cellular evidence for the positive role of exercise in mitochondrial biogenesis and the maintenance of muscle mass, and the case for

providing exercise as a non-pharmaceutical method to enhance mitochondrial function in ageing and muscle disease. These studies are particularly important because they add valuable support and enhance the physiological understanding of the large number of physical activity interventions already completed and underway. This article resonates with the very last article of the book which focuses on the ‘Physiology of optimising health with a focus on exercise as medicine’. The article has a telling quotation of Sir Edward Stanley – ‘those who think they have not time for bodily exercise will sooner or later have to find time for illness’. This article has particular relevance in India where the prevalence of physical inactivity is particularly high and where chronic non-communicable diseases such as diabetes, hypertension, and coronary heart disease, among a host of other illnesses are increasing. Exercise is protective against these diseases and this has been shown in a variety of epidemiological study designs including observational cross-sectional studies, cohort studies and intervention studies. While the article reviews much of the public health data, it also focuses on the physiological basis of these physical inactivity–disease relationships by exploring the link between low physical fitness, abdominal adiposity and inflammation, muscle as an endocrine organ and the anti-inflammatory actions of myokines. The article is timely but also underscores the large relatively unexplored area of the physiology of physical inactivity and sedentary behaviour. While to most people it is intuitive that if exercise protects against disease, sedentary behaviour must be bad, there is only now an emerging body of data which explores the specific physiological sequelae during sustained physical inactivity such as prolonged sitting, immobilization, bed rest, etc. This is an area which I hope will be covered in future editions of the *Annual Review of Physiology*.

The maternal changes that occur during pregnancy has been the subject of considerable investigation for reproductive physiologists. The rapidly growing foetus demands an adequate blood supply in the pregnant women. This is achieved through an expansion in plasma volume, an increase in cardiac output, a reduction in peripheral resistance and an increased uteroplacental blood flow of the order of 10 to 20 times. Uteroplacental