

Annual Review of Genetics, 2007. Campbell, A. Johnson, Anderson, W. W. and Jones, E. W. (eds). Annual Reviews, 4139 El Camino Way, Palo Alto, CA 94306, USA. Vol. 41. 532 pp. Price not mentioned.

The *Annual Reviews* series is not only a great resource material for experts and peers in diverse fields, but is also a great educational odyssey for students. The volume under review is no exception, with several articles of great interest to both the specialists and students. The volume starts with reminiscences of Allan Campbell, outlining the developmental stages of the field of genetic mapping in λ -phage, providing the context of his parallel foray into the system of λ gal, which he developed almost single-handedly. Particularly noteworthy is the sense of collegiality among the research pioneers of the era of the fifties, when elegant genetical innovations of pioneers like Epstein, Benzer and others laid the foundation of bacterial and λ -genetics, without the benefit of the modern sequencing techniques.

This volume includes 21 more reviews, each of which starts with an abstract and concludes with summary points that highlight the take-home lessons. Overall, the volume can be subdivided into 3–4 major sub-areas, each having articles with a shared theme. Noble and Johnson describe the genetics of *Candida albicans*, a diploid human fungal pathogen that infects not only normal individuals, but also has emerged as a virulent pathogen among immunocompromised patients. Lack of clear diploid and haploid phases in the life cycle has necessitated development of clever gene knockout strategies for studying gene function, although the mechanism of virulence has been left unaddressed.

In a succinct and condensed article summarizing a large body of work, Klar describes how fission yeast has emerged as an important model organism for understanding the epigenetic mechanisms regulating gene expression and differentiation. He describes how the mating-type switching process in this yeast resembles the stem-cell lineage in higher eukaryotes, and how this is regulated by a strand-specific imprint at the mating-type locus itself. A major insight into the processes of silencing and imprinting is the integral role of DNA replication. Another impor-

tant epiphany is that DNA and its configurations resulting from association with epigenetic factors, like specific histone modifications (H3-Lys9 methylation caused by Clr4/Suv39 methyltransferase), and heterochromatin-specific protein (Swi6/HP1) have the ability to propagate themselves for a large number of generations both during mitosis and meiosis, thus constituting the unit of inheritance in sharp contrast to DNA alone. In a pattern similar in concept to immunoglobulin recombination, mating-type switching also exhibits the phenomenon of directionality such that the cells always switch to the opposite mating-type and several trans-acting switching factors play an important role in this copy choice mechanism. Most notably, the RNAi machinery plays a parallel role in silencing at the mating-type system, the effect being mediated through a *cenH* element highly similar in sequence to the *dg-dh* repeats of outer repeat region of centromere 2 (*cen2*). This phenomenon may represent recruitment and harnessing of an ancient invader surveillance mechanism that prevent uncontrolled expression of the invading virus-like elements, to the mating-type physiology, enhancing the genomic integrity and facilitating the long-term survival of fission yeast. Thus, fission yeast mating-type silencing can serve as a paradigm for various epigenetic phenomena in higher eukaryotes.

Along the same theme, Ekwall provides a concise review of the molecular mechanisms involved in centromere structure and function from budding yeast to fission yeast and higher eukaryotes, highlighting the role of epigenetic factors involved in gene silencing, including RNAi, nucleosome remodelling factors, histone chaperones, histone-modifying enzymes, transcription factors, RNA polII and importantly, centromere-specific histone H3, Cnp1 (CENPA) in organizing the centromeric structure and integrity. Expanding on the theme of the role of RNAi in gene silencing, Jose reviews evidence regarding how the double-stranded (ds) RNA, the key effector molecule in RNA interference, can deliver its effect over large distances in organisms like *Caenorhabditis elegans* and plants where mechanisms exist for transport of dsRNA from one cell to another, thus imparting anti-viral resistance. This characteristic provides scope for the dsRNA information to be passed onto germ cells, thus linking the sensing of the environment to

inheritance of the adaptation through RNAi mechanism.

Mechanisms of DNA replication in different organisms during the cell cycle are covered by Sclafani and Holzen, discussing issues about the complexity of replication origins in fission yeast and higher eukaryotes, and epigenetic control of their function and separation of the assembly of complexes involved in pre-replication and activation steps, ensuring lack of re-replication. Recombination during meiosis is critical for generating variation and is correlated with the occurrence of regular hotspots of recombination. Localization of such regions across mammalian genome provides data for sites of crossing over and recombination, although no precise cis-acting sequences have been identified. This interesting topic, which is important from the perspective of evolutionary and population genetics, has been reviewed by Arnheim *et al.*, stressing the need for future studies. Occurrence of chromosomal fragile sites (CFS), a defect involving generation of breaks and gaps on metaphase chromosomes following replication stress, has been reviewed by Durkin and Glover. Such sites frequently undergo rearrangements in tumour cells and are associated with trinucleotide and AT-repeat sequences. This disorder involves homologous and nonhomologous end-joining repair pathway and is monitored by ATR-dependent DNA damage checkpoint. Although several models are invoked, the mechanism of generation of CFS in normal and tumour cells and their possible role in cell-cycle progression remain to be understood. The mutagenic process of somatic hypermutation at the immunoglobulin loci by targeted action of activation-induced cytosine deaminase at CG basepairs, which is responsible for generating antibody diversity, has been reviewed by Teng and Papavasiliou.

Another set of articles addresses a variety of evolutionary issues. Using data on haplochromine fishes of Lake Victoria, Klein *et al.* review how the use of trans-species polymorphism in *MHC* genes to analyse population demographics spanning timescales of millions of years, has yielded the insight that new species can arise from large founding populations. Feschotte and Pritham update information on the varieties of transposons found among eukaryotes and discuss how they contribute to maintenance and diversification of the host genome architecture.

Dolinski and Botstein review the orthology relationships for a large number of genes among different eukaryotes, including yeast, *Arabidopsis*, mouse and humans, to show that proteins that are essential and/or interact with other proteins are generally conserved among species. More importantly, the way these proteins work in the context of large biological processes is also conserved among all eukaryotes. Underhill and Kivisild discuss how the use of Y-chromosome and mitochondrial DNA sequence variation has helped in arriving at recent insights into the nature of human migrations. Reyes-Prieto *et al.* discuss the endosymbiont theory about the origin of plastids among photosynthetic eukaryotes having occurred when a heterotrophic protist engulfed and retained a cyanobacterium in the cytoplasm, and review how the recent genomic and phylogenomic approaches have provided fresh underpinnings to the theory, with additional molecular evidence for gene flow from the endosymbiont to the host nuclear genome.

Programmed cell death of old differentiated cells and production of new cells by stem cells occur simultaneously in all tissues of all organisms and maintain a balance, which, if abrogated can cause diseases like cancer. Pellettieri and Alvarado review the phenomenon and discuss the utility of understanding the phenomenon in planarians, which exhibit both these processes. Cobaleda *et al.* discuss the issue of both normal and cancer stem cells sharing common mechanisms of development and the role of the zinc-finger transcription factor *SNAI2* in both processes. Interestingly, *SNAI2* seems to

be widely implicated in the initiation and development of human cancer and is, therefore, considered as a marker for malignancy and therapeutic target.

Lastly, application of systems approach to understanding development and differentiation is covered in different systems. Two component histidine kinase signal transduction systems help bacteria to sense, respond and adapt to diverse environmental factors, stress and growth conditions. Changes in phosphorylation and dephosphorylation are the chemical changes involved in transmission of information. Multiplicity of the sensor proteins, however, makes the issue of noise and crosstalk between different and off-targets a major concern. How specificity is achieved amid such complexity is reviewed by Laub and Goulian. Beckett reviews the hitherto unexpected role of biotin in transcriptional regulation through covalent linkage to biotin-dependent carboxylases that are found from *Escherichia coli* up to humans. Kroos reviews how the recent genomic and phylogenomic approaches have provided fresh underpinnings to the mechanisms involved in the formation of forespore in *Bacillus* sp. through cascades involving σ -factors, and fruit body development in *Myxococcus xanthus* using other transcription factors that function as enhancer binding proteins (EBP). While *B. subtilis* forms septum by synthesizing proteins that modify peptidoglycan to compartmentalize σ^F and σ^E in the forespore and mother cell, respectively, *M. xanthus* delays the process of commitment to after aggregation of cells and change of shape from rod to spherical one. Although dif-

ferent in details, both organisms execute networks involving autoregulatory, feed-forward and feedback loops to ensure proper temporal and spatial gene expression. Laub *et al.* review the elegant system of cell cycle and asymmetric cell division in *Caulobacter crescentus*, which is integrated with chromosome replication and morphogenesis by multiple feedback pathways. Key regulators (CtrA, GcrA, DnaA and CcrM) are synthesized in succession to regulate the expression of nearly 200 genes. The cell cycle programme is governed by the epigenetic mechanisms, sensors and signal transduction systems providing feedback for advancement of cell cycle, which involves dynamic sub-cellular localization of regulatory proteins. The master regulators are, in turn, degraded by multiple feedback loops. However, despite the advances, the pathways involving sub-cellular localization of proteins, regulation of protein stability, and the signals recognized by the sensors remain to be identified.

Overall, perusing through this volume has been an enjoyable, stimulating and educational experience. Most of the articles provide a concise and focused review of the subject matter. Many chapters conclude with future prospects defining the outstanding questions, providing an overall perspective and stimulus for thinking to both the expert and the neophyte.

JAGMOHAN SINGH

*Institute of Microbial Technology,
Sector 39-A,
Chandigarh 160 036, India
e-mail: jag@imtech.res.in*