
Apoptosis and Inflammation. James D. Winkler (ed.). Birkhäuser Verlag, P.O. Box 133, CH-4010, Basel, Switzerland. 1999. 244 pp.

In human society, suicide often seems an irrational and impulsive act. Not so in the society of cells in an organism. Like obedient soldiers making a personal sacrifice for the common good, excess cells, or those that pose a threat to the well being of the organs, often commit suicide on command via an orderly process called programmed cell death/apoptosis. Although recognized in 1842 by Carl Vogt, the most recent re-discovery of cell suicide was in 1972 when the term apoptosis was adopted. A couple of years ago people had real doubt about apoptosis being involved in disease. Now almost everyone is sold on the idea. The past few decades have seen a spontaneous rise in the number of papers being published in the field of apoptosis. The vulnerability to different death signals and the ability to be saved from death by different inhibitors of apoptosis varies from cell type to cell type.

Apoptosis is a highly regulated process that is involved in physiological as well as in pathological conditions. There is extensive and growing understanding of the role of apoptosis and apoptotic signals in inflammatory and immune cells. This book has concentrated on this aspect and also focused on the key role of apoptosis in inflammatory and immune diseases. James D. Winkler set out in this book, to provide a comprehensive, conceptual, introductory account of the characteristics of apoptosis, its regulation and its role in diseases. This is followed by 12 chapters. Each chapter deals with a specific topic and the links between the topics and chapters are strong. Although the morphological characteristics of apoptosis are fairly universal across cell types, the molecular events that initiate, mediate and execute an apoptotic signal are intricate and vary between cell types. A series of intracellular changes that activate a proteolytic cascade which progressively dismantles structures and the cell ultimately degrades its DNA and dies.

The chapter on signalling cascades of apoptosis has focused on glucocorticoids, Fas and T cell receptor. Glucocorticoids stimulate apoptosis in immune cells and are used to suppress inflammation. Activation of a protease cascade is a biochemical hallmark of glucocorticoid-receptor induced apoptosis and is also common to Fas and T cell receptor (TCR). The protease caspase-3 cleaves a number of downstream targets such as poly ADP ribose polymerase (PARP), laminin B1, serum response element binding proteins (SREBPs), DNA fragmentation factor (DFF). Agents which inhibit dATP, cytochrome C release from mitochondria or block caspase action, block DNA degradation and apoptosis. Findings suggest a role of Fas-mediated apoptosis in induction of peripheral tolerance and/or in the antigen-stimulated suicide of mature T cells. Mutation in *Fas* gene leads to autoimmune disorders.

Thereafter the book is organized essentially into two major parts; one dealing with apoptosis in the regulation and function of T and B lymphocytes, granulocytes, haematopoietic cells, chondrocytes, keratinocytes and the second deals with involvement of apoptosis in diseases related to these cell types, i.e. rheumatoid arthritis (RA), osteoarthritis (OA), lupus and lupus-like syndromes, psoriasis and renal disease, dealing with the fundamental analysis and with clinical and therapeutic correlation by different authors working in these fields. There is also a chapter on arachidonic acid which has reviewed *in vitro* and *in vivo* studies that have examined the relationship between arachidonic acid metabolism and cell proliferation with special emphasis on apoptosis.

There has been a major focus in understanding the association of total dietary fat and specific types of fat with cancer risk. In regard to inflammatory cells, proliferation of T cells is suppressed by poly-unsaturated fatty acids (PUFA) in several studies and a pro-apoptotic effect of PUFA has been reported. It is important to point out that major molecular events that link arachidonic acid metabolism and PUFA to cell proliferation or apoptosis are currently poorly understood, fur-

ther progress needs to be made to resolve controversial findings and inconsistencies in this area to provide new opportunities to utilizing old and new drugs that influence arachidonic acid metabolism and to treat diseases such as inflammatory and cancer.

There is sufficient evidence establishing granulocyte apoptosis leading to phagocytic clearance as an important injury limiting granulocyte disposal mechanism capable of promoting resolution of inflammation as discussed in the next chapter. There does seem a realistic prospect of being able to direct granulocyte apoptosis for therapeutic gain and researchers are looking at the prospect of selectively triggering cell death in population of granulocytes which are causing the injury. In hematopoiesis inflammatory cytokines can induce many of the changes by regulating apoptosis of hematopoietic cells. Thus cytokine inhibition can provide a potential means to interfere with cytokine network and offer relief of systemic complications associated with increased or decreased blood cell numbers. Chondrocytes are differentiated mesenchymal cells which play a role in skeletal development, maintenance and repair. Apoptosis can be induced in chondrocytes by several distinct mechanisms. Keratinocytes, the epithelial cells prevent the entry of toxic environmental agents. Keratinocyte apoptosis is seen in many biological circumstances such as epidermal differentiation, certain skin diseases and graft vs host disease. Recent evidence suggests that keratinocytes can modulate the epithelial immunological environment by expression of Fas ligand and granzyme B and can kill cytotoxic lymphocytes.

Immunological cytotoxicity is one of the most important consequences of immunological activation producing selective destruction of cellular targets by humoral or cellular effector mechanisms and apoptosis. Apoptosis is also a key mechanism for eliminating autoreactive lymphocytes, activated lymphocytes and non-specific effector cells during different phases of inflammation. Defective induction of apoptosis is believed to allow persistence of autoreactive T cells and production of auto antibody-

ies in autoimmune diseases as discussed in the last few chapters in the second part of the book. The difference in apoptotic susceptibility is used in treatment of many types of inflammatory and immunological diseases. Keratinocyte apoptosis has been described in many immunological skin diseases such as lichen planus, graft vs host disease, photosensitive lupus and psoriasis. Environmental triggers such as viruses, sunlight and drugs can dysregulate apoptotic pathway or pathways for immune clearance and result in chronic inflammatory diseases. A large number of viruses have been associated with development of chronic infection which lead to autoimmune diseases either by persistent or latent viral antigen or molecular mimicry. Modulation of apoptosis may play a role in pathogenesis of arthritis associated with infection of adenovirus, baculovirus, HIV and influenza virus. Inhibition of apoptosis is associated with persistent infection, latency enhancement of viral production whereas promotion of apoptosis facilitates virus spread and release. Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting synovial tissue in multiple joints. There is a strong evidence to suggest a role of CD₄⁺ T cells as well as of activated macrophages and fibroblasts like synoviocytes which destroy articular structure in chronic RA disease. Inadequate apoptosis appears to play a significant role in the increased cellularity in the synovial tissue. Interventions aimed at enhancing apoptosis in the synovium are emerging as potentially effective forms of treatment. Osteoarthritis (OA) is the most frequent musculoskeletal disorder, especially in the aging population. There is reduction in chondrocyte cell number due to apoptosis involving a number of multiple molecular pathways. The pathogenesis of systemic lupus erythematosus (SLE) is multifactorial and multigenetic. Chronic inflammation associated with it is thought to be due to loss of self-tolerance and apoptosis defects. Fas and Fas ligand regulate NFκB, kinases, phosphatases, bcl-2 family members, interleukin 1-β converting enzyme (ICE) and FLICE (FADD-like ICE) fam-

ily members which may be dysregulated in patients with SLE. There is strong evidence for involvement of apoptosis in acute renal failure but it is not clear whether it is involved in disease progress or the repair process or both. Thus a direct connection of apoptosis with numerous disease states has been established and the number of examples will probably increase as more apoptosis and disease regulation genes are identified, and their biochemical activities established. Opportunities for novel therapy may then become apparent.

I trust that both experienced and new researchers alike will read this book as a primer on what is new and possible in apoptosis and immune system. This book will serve as a useful resource material and guide for biochemists/researchers who wish to understand the role of apoptosis, particularly in immune/inflammatory disease. The number of references to the primary literature is fairly large, i.e. more than 850. It covers a small number of topics in depth and with relevant detail. In summary this book will find an appreciable but limited audience.

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Proton Pump Inhibitors: Milestones in Drug Therapy. L. Olbe (ed.). Birkhäuser Publication. 1999. 264 pp. Price: SFr 188/DM 238.

Innovation has become the industrial religion of the new millennium. Healthcare business sees it as the key to

increasing profits and market share. For more than 100 years it has been known that gastric acid secretion is not the only but an essential causative factor in the pathogenesis of acid-related diseases. Thus reduction of acid secretion became a major therapeutic goal. For quite sometime, surgical procedures (gastric resection and vagotomy) were used as effective interventions in the management of peptic ulcer diseases. The introduction of potent inhibitors of acid secretion, that is the H₂ receptor blocking agent cimetidine and its analogues in the late seventies and the even more potent proton pump inhibitor omeprazole and its analogues in the late eighties have revolutionized therapy. Around the world, the rhetoric of innovation has replaced the redundant products or surgical approaches in the management of peptic ulcer disorders.

This new monograph series – *Milestones in Drug Therapy* – highlights new therapeutic developments of proton pump inhibitors, which have provided significant steps forward in the fight against peptic acid disease. Each book in this series generally deals with an individual drug or drug class, which has altered the approach to therapy. Experts in the field place emphasis on the scientific background to the discoveries and the development of the therapy, with an overview of the current state of knowledge of the drugs. The series is aimed at a broad readership, covering biochemistry, pharmacology and clinical aspects, as well as revealing the personal stories behind the scientific developments. *Proton Pump Inhibitors* presents the story starting from the initial observation of classical experiments to the launch of four proton pump inhibitors in six chapters namely: the discovery and development of the proton pump inhibitor; mechanism of action; the pharmacology of proton pump inhibitors; pharmaceutical considerations; clinical experience with proton pump inhibitors and socio-economic impact of acid-related diseases. Modern drug discovery mostly relies on identification and characterization of potential targets by genome research, molecular biology, combina-

torial chemistry and automated screening. But the first chapter takes the reader back by thirty-three years and gives narration how director Ivan Östholm initiated an innovative research project in the gastrointestinal field at Astra Hässle using classical screening methods. It is worthwhile for all researchers engaged in drug discovery research to read the development of the first proton pump inhibitor – omeprazole – starting from a chemical structure with an observed antisecretory effect but also severe toxic effects that had to be eliminated. As

always, the basic and the applied research operate hand in hand to optimize the delicate balance between efficacy and safety of a new drug.

The second chapter starts with the landmark paper of William Prout presented at the Royal Society Meeting on 11 December 1823, stating that 'On the Nature of Acid and Saline Matters Usually Existing in the Stomach of Animals'. He was the first to identify the hydrochloric acid in the gastric juice of many species and was able to quantify the free and total acid. Further, work on acid secretion in isolated frog mucosae in the 1960s paved way to identify the molecular target involved in acid production. This chapter gives a detailed biochemical description of the gastric H^+ , K^+ ATPase and its gastric acid secretion inhibition potentials. The third chapter gives greater details of animal pharmacology and clinical studies pertaining to proton pump inhibitors. Overviews compare omeprazole and other proton pump inhibitors and discuss their pharmacology, including the mechanism of action, the effect on *Helicobacter pylori* infection and the consequences of profound inhibition of gastric acid secretion. The fourth chapter deals with physicochemical properties of omeprazole, lansoprazole, pantoprazole and rabeprazole; oral formulation principles, dosages; influence of food and antacids; parenteral dosage forms and pharmaceuticals delivery system for other routes of administration of proton pump inhibitors.

The clinical experience with proton pump inhibitors in acid-related dis-

eases is reviewed in the fifth chapter with focus on gastro-esophageal reflux disease, peptic ulcer diseases including *Helicobacter pylori*, non-steroidal anti-inflammatory drugs associated ulcers and Zollinger–Ellison syndrome. Socio-economic impact including aspects that concern both the individual and society are dealt with in the last chapter. Here the authors provide some background of concepts like prevalence and incidence of acid-related disorders, emphasizing the important aspect of quality of life, direct and indirect cost (pharmacoeconomic) associated with acid-related disorders and its total socio-economic impact.

Overall this book gives information about the problem faced in launching a tailor-made drug for a specific target; the dramatic changes in the outcome of

results in the treatment of peptic ulcer disease and its impact on pharmacoeconomics. It is written by eminently qualified scientists from industry, academics and clinicians. This volume is intended not only for those active in research into proton pump inhibitors but also for those with an interest in peptic ulcer disorders.

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Geology of Rajasthan: Status and Perspective. P. Kataria (ed.). Department of Geology, M. L. Sukhadia University, Udaipur, 1999. pp. 250. Price: Rs 400.

Rajasthan State constitutes the bulk of Aravalli Craton which preserves a fascinating geological record from 3500 million years ago to the present. Rajasthan is geologically well known for its Proterozoic rocks of the Aravalli mountains which throw light on the operation of plate tectonics in the distant past. It has a singular and complete example of acid magmatism in the Malani Igneous Suite. A wide array of Quaternary formations provide valuable evidence of neotectonics, and throw new light on the lost Vedic river Sarasvati. The Thar Desert presents a unique example for the study of desert geology. Rajasthan has major lead-zinc (and copper) deposits and a host of useful industrial minerals including the famous Makrana marbles and alluring gemstones. It is not surprising that such an attractive geological tapestry has spawned several new edited volumes on the geology of the region. For example, the Geological Society of India has published two Memoirs (No. 7, 1988 and No. 31, 1995), besides a textbook on *Rajasthan Geology* by S. Sinha-Roy and others in 1998. B. S. Paliwal edited a volume on the Indian Precambrian (1998), a large part of which is devoted to Rajasthan geology. The present volume which represents the proceedings of the seminar with the same title is brought out to felicitate the distinguished Professor A. B. Roy on his retirement from the University of Rajasthan (now called M. L. Sukhadia University). It contains nine thematic as well as review papers contributed by specialists in their respective fields.

The volume begins with a comprehensive update on the regional geology of Rajasthan by A. B. Roy and P. Kataria, which provides a balanced appraisal with emphasis on the stratigraphic classification proposed by A. B. Roy and his associates. B. Sreenivas and coworkers describe geochemical changes across one of the major hiatuses in earth history at the Archaean–Proterozoic boundary/transition about 2500 million years ago. They confirm the widely documented change in the earth's record, viz. decrease in the abundance of Cr, Ni, Sc in the Proterozoic rocks compared to the

Archaean, from the Aravalli rocks of Rajasthan.

S. Sinha-Roy deals with his favourite subject of Precambrian plate tectonics as applied to Rajasthan, with emphasis on Rakhabdev and Phulad ophiolites marking two major sutures between tectonic blocks at 1500 and 1100 Ma respectively. S. K. Bhushan describes two major felsic magmatic events in Rajasthan, namely, the Erinpura and Abu granites (800–900 Ma) formed by anatexis during collision, and the Malani volcanic and plutonic suite (730–750 Ma) formed by rift tectonics related to ‘hot spot’ activity. D. S. Chauhan describes the evolution of the largest sedimentary basin (Marwar basin) formed in Neoproterozoic to Cambrian time. Anil Bhandari provides an excellent overview of the Phanerozoic stratigraphy of the major sedimentary basins of western Rajasthan, viz. Jaisalmer, Bikaner-Nagaur and Barmer. He makes a brief mention of possible hydrocarbon resources and lignite in these basins. Amal Kar traces the evolution of landforms carved by aeolian and fluvial processes in the Quaternary, with special emphasis on the development of Thar Desert with its dunes and saline depressions (ranns) like Mithi, Desai, Glines, Kesli, Kinra, Sambant and others. Mithi, Desai, Glines, Kesli, Kinra, Sambant of classification and genesis of the metallic mineral resources of Rajasthan, prominent among them being the well-known deposits of zinc and lead at Agucha, Zawar and others. There are also other potential deposits of copper, gold, silver, tin, tungsten and uranium in Rajasthan. The book has the concluding paper on the industrial minerals and decorative stones of Rajasthan by M. K. Pandya and others. The important minerals in this category are phosphorite, soapstone, asbestos, gypsum, salt, ochre, limestone, graphite, wollastonite, fluorite, calcite, etc. The marbles of Rajasthan are famous the world over. Rajasthan is also well known for its precious stones like garnet.

This volume encompasses all aspects of Rajasthan geology leaving out groundwater resources and geo-environmental problems. This book is printed and bound well, although the reproduction of figures could have been better. The volume is a very valuable addition to our knowledge of Rajasthan geology and is useful for teachers, students and professional geologists.

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Sex, Color, and Mate Choice in Guppies. Anne E. Houde. Princeton University Press, 41 William Street, New Jersey 08540, USA. 1998. Price not stated. xii + 210 pp.

The motivational forces that drive mate choice in animals and the underlying mechanisms guiding sexual selection have fascinated students of evolution right from the time of Charles Darwin. A number of animal species including the celebrated, but relatively unstudied, peacock have served in attracting attention to what is arguably one of the most fascinating areas of evolutionary biology. But no species has achieved more to further our understanding of the interrelated processes of mate choice and sexual selection than the lowly guppy.

The Trinidadian guppy (*Poecilia reticulata*) is a small tropical live-bearing fish, native to the streams and rivers of Trinidad and Tobago and adjacent areas of South America. They have now been introduced all over the world, especially for mosquito control in ponds in tropical countries, and have finally found their way into home aquaria and into the hearts of most fish enthusiasts.

Guppies are best known for their conspicuous colour patterns and the untiring courtship of females by the males of the species. Much of the earlier work on this fish therefore concentrated on the genetics of colour pattern inheritance, reproductive biology and the ecological genetics of the species. Some of the most intensive recent research has however been conducted by behavioural ecologists, who have found that the guppy mating system makes guppies especially useful in the study of sexual selection and mate choice. The extent to which such research has been successful is clearly evident when the author Anne Houde points out that guppies are unique among the species in which the mechanisms of sexual selection have been addressed in that it has been possible to make specific predictions about evolutionary outcomes on the basis of the characteristics of different natural populations.

The colour patterns of guppies, ex-

pressed only in males, are complex but usually consist of spots, speckles and lines of black, white, red, orange, yellow, green blue and violet – sometimes rather iridescent. What is more interesting, however, is that these unique colour patterns exhibit tremendous heritable variation among individuals. Male guppies usually inherit much of the colour patterns of their fathers intact, and this has been shown to be due to colour polymorphism being genetically sex-linked to the X-, or more commonly, to the Y-chromosome.

Taking off from here, the author expertly summarizes and synthesizes the current scientific literature to address the question of why males have evolved their spectacular colour polymorphism. A leading researcher in this area of enquiry today, Houde clearly emphasizes the role of female mating preferences in the evolution of male colour patterns, particularly those with bright orange spots, as also in the sexual selection of their elaborate courtship displays.

Sexual selection in guppies has thus led to the evolution of a number of conspicuous traits – elaborate colour patterns and courtship displays – which may be favoured by female choice but may also bring about increased risk of predation. Differences in the mating success of males seem to be most influenced by female choice for male colour patterns, rather than by male display behaviour or other traits such as male–male competition, thus leading to the selection of certain preferred colour patterns. Different as-

pects of guppy mating behaviour, including courtship displays by males and active mate choice by females, however, appear to be constrained by the presence of predators, to the extent that population levels of female choosiness can often directly depend on specific predator regimes.

Although direct female choice clearly affects the outcome of sexual selection on male traits, it is still not clear how females exactly choose their mates. What is rather interesting, however, is that there is now increasing evidence that mating preferences of female guppies can be modified by prior experience. Females may thus either choose a male on the basis of her observations of past interactions between a specific male and other females, or on the basis of the phenotypes of males they have experienced in the past.

Houde's analyses also provide fairly convincing evidence that female mating preferences can vary genetically and therefore undergo evolutionary change. Particular preference of individual females, for example, can often remain fairly constant over time and consistent differences in choosiness across local populations of females can be clearly documented. Artificial selection experiments, of course, have now conclusively established that differences in female preferences do indeed have a genetic basis and that such preferences may be forced to evolve in response to direct or indirect selective pressures.

Why should females prefer to mate



The Trinidadian guppy (*Poecilia reticulata*).

with males with bright orange spots? Orange and other carotenoid-based pigments cannot be synthesized in guppies and can therefore only be acquired through their diet. Accordingly, it has been suggested that high concentrations of such pigments in certain males could indicate their ability to forage actively and efficiently – a signal that such males may be qualitatively ‘better’ than their paler counterparts. Attractive as such a ‘good genes’ hypothesis may be, several studies have failed to document whether female guppies that mate with brighter males do indeed produce offspring of greater vigour. Obviously, the jury is still out on this critical issue.

Finally, guppies have provided valuable support to the idea that the evolution of female mating preferences and male sexual traits are interdependent. These two traits have thus tended to evolve in parallel across populations and covary genetically within at least some local populations. This is, however, in striking contrast to certain other species of fish like the swordtails or the Tungara frog where female preferences and male traits do not coevolve but arise independently. A triumph, once again, for biology – the science of diversity – that stubbornly refuses to be reigned into conformity.

Anne Houde concludes her labour of love with an excellent chapter that summarizes succinctly our current state of knowledge about mate choice and sexual selection in guppies, and frankly highlights the glaring lacunae that have yet to be filled in. We still need to discover, for example, the sensory basis for female mating preferences, the behavioural rules that females use in selecting their mates, whether female mating preferences invariably lead to sexual selection on male traits, and, perhaps most surprising,

the underlying reason why guppy colour patterns are so polymorphic. She also includes an appendix that provides practical details for designing tests for mate choice experiments and outlines methods for measuring male colour patterns and male mating success – a most welcome addition to this excellent treatise.

Houde’s own work addresses a number of areas that are of interest in sexual selection, including the remarkable degree of plasticity and evolutionary lability of sexual behaviour in guppies, geographic variation in mating preferences, possible mechanisms for the evolution of female mating preferences, and the role of sexual selection in speciation. Given her remarkable range of research interests and, above all, her love for this small unique fish swimming actively in the sun-drenched shimmering waters of a Trinidad stream, it is not surprising that we have here a brilliant account of ~~a model system – a must for the bookshelves of both, a student of sexual selection as also the mature guppy researcher.~~

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Faunal Diversity in India. J. R. B. Alfred, A. K. Das and A. K. Sanyal (eds). ENVIS Centre, Zoological Survey of India, Calcutta. 1988. 495 pp. ISBN 81-85874-19-0. Price: India: Rs

600/Foreign \$ 50; £ 40.

In the context of India’s commitment to inventory, monitor and conserve our precious faunal diversity, the Environmental Information System (ENVIS) Centre on Faunal Biodiversity, set up by the Ministry of Environment and

Forests, Government of India in the Zoological Survey of India (GSI) at Calcutta, has taken up this stupendous task of collecting and collating the available information as a state-of-the-art publication on *Faunal Diversity in India* as a commemorative volume in the 50th year of India’s independence.

This is a sequel to the pioneering attempts by the Zoological Survey of India on two previous significant publications, viz. *The State of Art Report: Zoology* and *The Animal Resources of India* in 1980 and 1991, respectively. A total of 57 articles contributed by experts provides an up-to-date information on the status, distribution, biological diversity, endemism, value, threats and conservation strategies of protozoa followed by all over phyla of the animal kingdom. Each chapter is appended by selected valuable references pertinent to the respective group. These accounts are preceded by an overview of faunal diversity incorporating information on biogeographic zones and biotic provinces in India, estimated number of described species with estimated percentages of endemism, as well as the number of experts both in and outside the ZSI on different faunal groups. A one-page black and white figure in a blue background giving an idea of morphological dimensions of the respective taxa adds to the value of the book.

It is unfortunate that, in spite of painstaking efforts by the editors, omission of some important groups like e.g. Ephemeroptera (mayflies) is conspicuous. I hope this will be included in future publications.

This compendium is a veritable source of reference for teachers, researchers and environmentalists, who are committed to check the continuous and ongoing depletion of valuable faunal diversity due to natural and man-made impacts on their habitats and life history.

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