

Epigenetics

Ciba Foundation Symposium, June 24-26, 1997

Adam S. Wilkins

In late June, a group of 30 molecular developmental biologists and geneticists met at the Ciba Foundation in London for a 3-day symposium on the subject of 'epigenetics'. As the chairman, **Alan Wolffe** (NICHD, Bethesda), explained in his opening remarks, the term 'epigenetics' has been used in two somewhat different senses. The original definition was that of C. H. Waddington⁽¹⁾, who defined epigenetics as all those 'interactions of genes with their environment that bring the phenotype into being'. Today, however, the term is most often used to denote all those somatically heritable changes in gene expression that do not involve changes in DNA sequence. Although the majority of talks dealt with epigenetics in this second and narrower sense, Waddington's broader functionalist perspective, when one includes the internal cellular milieu as part of the environment, was never far from view. In addition, evolutionary questions about the origins and adaptive values of various epigenetic mechanisms were addressed at various points.

An evolutionary perspective, in fact, was provided in the first full talk, given by **Adrian Bird** (University of Edinburgh). Bird introduced the subject of DNA methylation, the best characterized mechanism for maintaining repressed states of gene expression. He pointed out that while much attention has been focussed on DNA cytosine methylation as a pervasive silencing mechanism in both higher plants and vertebrates, it is a comparatively minor event in the genomes of most organisms. Even in the invertebrate chordates (amphioxus, sea squirts) only a relatively few 'compartments' of the genome are methylated, with just a small number of genes being heavily methylated. One aspect of the origin or early evolution of the vertebrates must have been a substantial increase in methylation, and its utilization as a gene silencing event, in addition to an approximately fourfold increase in DNA content that took place in the evolution of vertebrates from cephalochordates. These two events may be related, in that enhanced silencing capacity may serve to reduce transcriptional 'noise', as argued by Bird in an earlier publication⁽²⁾. He also described the properties and differences in action of two proteins, MeCP1 and MeCP2, that bind methylated cytosines in vertebrate genomes and which undoubtedly play a part in methylation-induced silencing. Methylation of cytosines, in this view, does not directly repress transcription, but serves as the first step in a repression process, which is mediated by other molecules.

Alan Wolffe then described some *in vitro* titration experi-

ments which demonstrate that methylation of cytosines simply sets the stage for repression. He emphasized the importance of the nucleosomal context in achieving methylation-induced silencing and suggested that folding into nucleosomes may facilitate more efficient binding of the methyl cytosine-binding proteins. He also reviewed evidence to show that allowing a round of replication permits both more efficient *in vitro* nucleosome assembly and repression of basal transcription.

Methylation, however, is but one of several mechanisms of silencing of gene expression. Several talks dealt with transcription-silencing mechanisms in lower eukaryotes, in particular in the two main yeast model systems, fission yeast, *Schizosaccharomyces pombe*, and budding yeast, *Saccharomyces cerevisiae*. These mechanisms do not involve methylation but specific encoded proteins. **Shiv Grewel** (NCI, Frederick, Maryland) described the genes that have been identified in *S. pombe* which are involved in repression of the silent cassettes of the mating type locus in this organism. He discussed the evidence that the repressive state associated with particular cassettes can influence not only the directionality of switching (which silent cassette can be put in place for activation) but also the frequency of recombination in the region. The evidence implicates a 'heterochromatin'-like state surrounding the silenced cassette. Although there is a certain frequency of spontaneous reversion to activity (about 0.5-1% switching per generation), the silenced state can also, remarkably, be transmitted through meiosis.

Robin Allshire (MRC Human Genetics, Edinburgh) and **Susan Gasser** (ISREC, Epalinges, Switzerland) described epigenetic states associated with specific chromosomal structural features, namely centromeres in *S. pombe* and telomeres in *S. cerevisiae*, respectively. As described by Allshire, centromeres in *S. pombe* are normally underacetylated. If one inhibits the deacetylase with trichostatin, however, permitting higher levels of acetylation, the centromeres are partially destabilized and this 'derepressed' state can then be propagated in the subsequent absence of trichostatin. Gasser compared and contrasted the molecular requirements for silencing at the mating type loci in *S. cerevisiae* and that associated with the telomeres. Telomeric silencing is less 'tight' than mating type locus silencing and does not require all the molecules associated with the latter, e.g. Sir1p (the protein encoded by silent repression 1, *sir1*) is not required. Although telomeric silencing seems to be a non-

Alzheimers Disease And Related Conditions A Ciba Foundation Symposium

M Lipman



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Alzheimer's Disease and Related Conditions G. E. W. Wolstenholme, Maeve O'Connor, 2009-09-16 The Novartis Foundation Series is a popular collection of the proceedings from Novartis Foundation Symposia in which groups of leading scientists from a range of topics across biology chemistry and medicine assembled to present papers and discuss results The Novartis Foundation originally known as the Ciba Foundation is well known to scientists and clinicians around the world

Symposium on Alzheimer's Disease and Related Conditions Ciba Foundation, Gordon Ethelbert Ward Wolstenholme, 1970
Alzheimer's disease and related conditions: a Ciba Foundation symposium, ed Ciba Foundation, **Alzheimer's disease and related conditions**, 1970 **Ciba Foundation Symposium - Alzheimer's Disease and Related Conditions**, 2008

Concepts of Alzheimer Disease Peter J. Whitehouse, Konrad Maurer, Jesse F. Ballenger, 2003-05-27 As the essays in this volume show conceptualizing dementia has always been a complex process With contributions from noted professionals in psychiatry neurology molecular biology sociology history ethics and health policy Concepts of Alzheimer Disease looks at the ways in which Alzheimer disease has been defined in various historical and cultural contexts The book covers every major development in the field from the first case described by Alois Alzheimer in 1907 through groundbreaking work on the genetics of the disease Essays examine not only the prominent role that biomedical and clinical researchers have played in defining Alzheimer disease but also the ways in which the perspectives of patients their caregivers and the broader public have shaped concepts **Self, Senility, and Alzheimer's Disease in Modern America** Jesse F. Ballenger, 2006-03-31 Ballenger's work contributes to our understanding of the emergence and significance of dementia as a major health issue

Alzheimer's and Parkinson's Diseases Abraham Fisher, Israel Hanin, Chaim Lachman, 2012-12-06 This book is the outcome of an international conference held at the Aviya Sonesta Hotel in Eilat Israel on March 24-27 1985 This was the 30th in a series of the annual OHOLO Conferences sponsored by the Israel Institute for Biological Research Participants in this Conference consisted of scientists from four teen countries represented a broad spectrum of research interests and included a well balanced representation from academia clinical institutions and pharmaceutical industry The book includes talks poster sessions and a comprehensive general discussion all from the proceedings of this conference In the interest of assuring a rapid publication of the novel information reviewed this book has been prepared in camera ready format We are cognizant of the fact that several typographical errors may exist in the text and that there are variations in style and typeface of the various chapters This we felt was a reasonable compromise for the sake of speed and efficient transmission of valuable scientific information No body is perfect The success of the conference and hence the quality of this book are attributable to the extensive efforts of a large number of extremely capable individuals These include members of the Scientific Organizing Committee and the Technical staff of the OHOLO Organization Of course the conference could not have succeeded without the high quality of the presentations and the enthusiastic participation of the contributing scientists

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Progress in Alzheimer's and Parkinson's Diseases Abraham Fisher,Israel Hanin,Mitsuo Yoshinda,2012-12-06 This book represents the fourth in a series of international conferences related to Alzheimer's AD and Parkinson's PD diseases The first one took place in Eilat Israel in 1985 the second in Kyoto Japan in 1989 and the third in Chicago IL USA in 1993 This book incorporates the proceedings of the Fourth International Conference on Progress in Alzheimer's and Parkinson's Diseases held in Eilat Israel on May 18 23 1997 This Conference was the 41st in the series of annual OHOLO Conferences sponsored by the Israel Institute for Biological Research IIBR It was also conducted under the auspices of the Alzheimer's Association Ronald and Nancy Reagan Research Institute USA The Conference was attended by 550 participants from 28 countries representing a broad spectrum of research interests and included a well balanced representation from academia clinical institutions and pharmaceutical industry The four and one half day meeting served as an excellent medium for surveying the current preclinical and clinical developments in AD PD and other related disorders The scientific program was divided into 24 oral sessions and daily poster sessions The conference culminated in a round table discussion There were 122 talks and 161 posters This book incorporates a combination of both **Alzheimer Disease**

Robert Becker,Ezio Giacobini,2012-12-06 *Alzheimer Disease: The Changing View* Robert Katzman,Katherine Bick,2000-05-22 This book details how Alzheimer Disease went from being an obscure neurologic diagnosis to a household word The words of those responsible for this revolution are the heart of this book Dr Robert Katzman and Dr Katherine Bick leaders in Alzheimer research and policy making interview the people responsible for this awakening of public consciousness about Alzheimer Disease from 1960 to 1980 They speak with the scientists public health officials government regulators and concerned relatives and activists responsible for taking this neurodegenerative disease out of the back wards through the halls of Congress and on to the front page The reader will learn how the explosive increase in research funding and public awareness came about how physicians and psychiatrists established diagnostic criteria how drugs were developed that offer hope for sufferers and how the Alzheimer's Association was born Written in the words of those responsible for the widespread recognition of this neurodegenerative disease The authors are recognised as leaders in Alzheimer research and policy making

Aging 2000: Our Health Care Destiny Charles M. Gaitz,T. Samorajski,2012-12-06 The seventeenth annual symposium sponsored by the Texas Research Institute of Mental Sciences was held October 23 26 1983 in Houston Texas The theme was Aging 2000 Our Health Care Destiny This volume on biomedical aspects and a companion volume on psychosocial aspects include edited versions of the presentations by about 80 speakers Their papers were directed at practitioners researchers and medical educators who will be active and productive in the year 2000 and we focused on those who would influence the evolution of care of elderly persons during the next 17 years We chose topics that would be of

particular interest to teachers and current planners in the disciplines concerned with delivery of health and social services We believe that having a core of more qualified and better trained practitioners will help the population of aged persons achieve a higher level of physical and mental health life satisfaction and happiness to find better coping techniques and control of environmental stresses and to attain personal and social goals Our Goals While preparing for the symposium we knew that the status of the art in 1983 obviously would be the base from which we would work but we asked our speakers to give priority to future planning and directions *Hannah's Heirs* Daniel A. Pollen,1996-09-05 In *Hannah's Heirs* Dr Pollen tells the compelling story of Hannah's family and their monumental contributions to the fight against Alzheimer's disease

Hormones of the Limbic System ,2010-07-07 First published in 1943 *Vitamins and Hormones* is the longest running serial published by Academic Press The Editorial Board now reflects expertise in the field of hormone action vitamin action X ray crystal structure physiology and enzyme mechanisms Under the capable and qualified editorial leadership of Dr Gerald Litwack *Vitamins and Hormones* continues to publish cutting edge reviews of interest to endocrinologists biochemists nutritionists pharmacologists cell biologists and molecular biologists Others interested in the structure and function of biologically active molecules like hormones and vitamins will as always turn to this series for comprehensive reviews by leading contributors to this and related disciplines This volume focuses on hormones of the limbic system Longest running series published by Academic Press Contributions by leading international authorities **Modern Stereotactic**

Neurosurgery L. Dade Lunsford,2012-12-06 As in any multiauthored textbook penned by When I was first approached by the publisher of this volume Martinus Nijhoff Boston I writers of diverse backgrounds and interests explored the possibility of writing a personal *Modern Stereotactic Neurosurgery* to some monograph on contemporary stereotactic extent suffers from incompleteness Future surgery After a review of available literature volumes no doubt will include many additions several aspects became apparent First no cur from other authors who also are important rent readily accessible multiauthored text de specialists in the field Because not all authors signed to survey the field was available Those write in the same style or even language we books that were available tended to heavily have attempted to achieve a more cohesive text emphasize theory physiology and anatomy in the editorial process Each chapter has been Second stereotactic surgeons were considered subdivided into pertinent headings for easier abstruse and for too long were relegated to a reference Because of my own background status outside of the mainstream of neuro some readers will note an Americanization as surgery This attitude probably reflected the opposed to anglicization of the chapters insufficient explanation of the practical uses While many chapters comprise primarily sum and advantages of stereotactic technique maries of the authors work within the field Third in recent years the field has expanded each author was encouraged to review the liter so rapidly that it has become a major compo ature in that discipline if appropriate *Pathological Neurochemistry* Abel Lajtha,2013-03-14 More than for any other volume of the *Handbook of Neurochemistry* the chap ters in this volume on *Pathological Neurochemistry* deal with the

interface of the laboratory bench with the patient's bedside. Most of the chapters reflect the confluence of basic scientists, clinical investigators and physicians. Considered here are many of the more important disorders that afflict the nerves, muscles, spinal cord and/or brain of mankind throughout the world. There are well over 500 such disorders. And our understanding of their nature and of measures for effective prevention or treatment depends significantly on application of the biochemical disciplines that characterize neurochemistry. Before World War II any attempt to compile a volume on pathological neurochemistry would have been largely descriptive and very rudimentary as such handbooks by Hans Winterstein (1929) and Irvine Page (1937) and others demonstrate. But thanks to the many major advances in research and technology in the postwar decades we now stand at the threshold of understanding how to manage many of the major neurological disorders and we may expect more such delineations in the immediate decades ahead. Neurochemistry defined broadly has played a central role in this extraordinary turn of events progressing from what J. L. W. Thudichum in 1884 called objects of anxious empiricism to his anticipation of the proud exercise of chemical precision. *Neurobiology of Aging* J. Ordy, 2013-06-29. Aging is one of the most universal and inevitable social and scientific challenges confronting man. The lives of all multicellular organisms begin with conception, extend through phases of development, maturity, senescence and finally end in death. Man is no exception but has the unique feature of a complex brain. It plays an integrative role in adaptation to the physical and social environments through reflexes, conditioning and more complex forms of learning. The brain is a repository for both inherited and acquired information. With the development of speech and the formation of symbolic language the human brain has made it possible to transmit information culturally horizontal to other members of society in addition to genetic vertical transmission to progeny. This horizontal transmission which has reached its highest form in man is a powerful extension of genetic transmission. The brain may provide man all that is of importance in life. It has played a key role in the evolution of life by maintaining and extending the life span. Many mental or intellectual capacities of man reach a peak in early adulthood, remain relatively constant throughout maturity and then appear to decline during senescence. Behaviorally there appears to be a decrease in sensory, learning and motor functions with aging in all mammalian species. As integrated adaptive control systems, the brain and neuroendocrines have been closely associated with the homeostatic adaptation to environmental challenges throughout the life span. *Epidemiology of Aging*, 1975.

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