Age related decrease of AgNOR activity in acute and chronic lymphocytic leukaemias

In their interesting article Pedrazzini and co-workers demonstrated that in bone marrow cells the proportion of silver stained nucleolar organiser region (AgNOR) positive metaphases decreased as a function of age. The authors compared these results with the observations of an age dependent decrease in the number of AgNORs in stimulated human lymphocytes, related in the literature, which could be caused either by a loss of proliferative activity or a by progressive inactivation of ribosomal RNA (rRNA) genes with aging. This question prompted us to perform additional statistical analysis on previously published data of adult patients with acute lymphoblastic (ALL), acute myeloid (AML), or chronic lymphatic leukemia (CLL). In the patients with ALL (n = 11) there was a negative correlation between age and the following: (1) the mean number of clusters/cell (Pearson’s \( r = -0.62, p = 0.02 \)) (fig 1) and (2) the percentage of cells with bromodeoxyuridine (BrdU) incorporation (\( r = -0.55, p = 0.04 \)). When in a partial correlation the variable “percentage of cells with BrdU incorporation” was held constant, the correlation between age and mean number of clusters/cell decreased (\( r = -0.36, p = 0.14 \)). There were no significant correlations between age and the number of metaphases per cell. These results suggest that the age dependent decrease of AgNOR clusters in ALL is the result of reduced proliferation, but additional factors cannot be excluded. However, in the patients with AML (n = 21) we could not find a correlation between age and the parameters mentioned above (fig 1).

Patients with CLL (n = 48) showed a negative correlation between age and the percentage of cells with AgNOR clusters (\( r = -0.54, p < 0.001 \)). It is interesting to note that the subgroup of patients with progressive CLL (n = 25) revealed a significant negative correlation (\( r = -0.34, p = 0.04 \)), whereas this was not seen in patients with stable disease (n = 23; \( r = -0.18, p = 0.20 \)) (fig 2).

Partial correlations with the variable “tumour doubling time” kept constant revealed an increased absolute value of the correlation coefficient for all the patients grouped together (\( r = -0.78, p < 0.001 \)) and for patients with stable disease (\( r = -0.32, p = 0.07 \)), but not for patients with progressive disease (\( r = -0.34, p = 0.04 \)). Thus, our findings suggest that patients with stable and progressive disease have different proliferation characteristics and that there are factors other than proliferative activity that influence the age dependency of AgNOR expression. Finally, we would like to emphasise that the AgNOR parameter that correlated best with age was the cluster, confirming previous studies on the importance of differentiating AgNOR precipitations qualitatively.

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Basic Molecular and Cell Biology. 3rd ed. Latchman D, ed. (£14.95.) BMJ Publications, 1998. ISBN 0 7279 1195 3. The existence of a new edition of this worthy primer on transcriptional control, with contributions from many of the big names in the field. Inevitably, in a book with so many authors, the quality of the chapters is a little variable, and in some cases the language is distinctly idiosyncratic, but overall the standard is good and the volume has some real gems, such as the chapters by Davies and Hastie on tumour suppression factors, Gilman and Vignais on the RAS family, and Wasylyk and Nordheim on the efs family of proteins. These exhibit the qualities of the best chapters in that they are insightful, synthetic, and full of an intellectual energy rare in reviews as expert and rigorous as these.

The level at which the book is aimed is quite high but, thanks to good chapters describing the basis of transcriptional control and the relation of the structure of transcription to factors to their function, anyone with a background in biochemical, genetic, or biomedical science would expect to get a great deal from this book.

A must for every library and one of the few books at this price that I would buy for myself. Papavassiliou should be congratulated in welding such a huge area into such a rewarding and useful book.

PAUL SCHOLFIELD


From time to time books appear that allow one to fill worrying holes in one’s knowledge in an effortless and absorbing way. Rare as these events are, I was delighted to find such a treat in the new multi-author work edited by Athanasios Papavassiliou, recently published by Springer-Verlag.

I am sure that I am not alone in finding it difficult to beat a path through the jungle of transcription factors, which proliferate with every issue of Cell and present a bafflingly complex array of activities and nomenclatures. In this book, Papavassiliou has, first and foremost, done an excellent job in establishing some kind of understandable “taxonomy” for the transcription factor zoo and, more importantly, has included in this volume articles on transcription processes and their biology. Although based mainly on an approach from the molecules up, rather than the biology down, this volume still succeeds in being a superb and up to date primer on transcriptional control, with contributions from many of the big names in the field.

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importance in normal and altered physiology, is not indexed or (as far as I can see) mentioned in the text.

The individual authors are almost entirely from the UK and, as is so often the case, London based contributors are prominent numerically. However, these observations do not detract from the potential usefulness of this volume to the non-specialist, including pathologists in training for the MRCPath examination. In general, more specialised readers would find that the most up to date information is lacking here, but that is inevitable with any book in this very rapidly expanding field. The volume is well edited and none of the chapters is too terse or too prolix.

Will the fourth edition be in two volumes?

JOHN CROCKER, Editor


Cancers with a viral aetiology are a fascinating subset of human malignancies. On the one hand, they continue to illuminate fundamental mechanisms underlying the neoplastic process; on the other, they offer some of the best opportunities for immune intervention in that process. The roll call of incriminated agents is surprisingly diverse and includes members of the hepadna, papilloma, herpes, and retrovirus families. Consequently, any text designed, as this one is, to introduce undergraduate/postgraduate students to human tumour virology has a lot of ground to cover. For each agent, one needs as background both the viral epidemiology and enough molecular detail on virus genome structure, replication strategy, and lifecycle to allow a meaningful discussion of the evidence for a tumour association. Faced with these demands, most of the individual virus chapters manage to convey their essential message without cutting too many corners, but only just! I particularly liked the clear mechanistic exposition of the likely role of human papillomaviruses in cervical carcinogenesis and the very accessible review of human T lymphotropic retroviruses and leukemogenesis, still a relatively under researched area. For those of an opportunistic bent looking to enter the field, a chapter on the Kaposi’s sarcoma associated herpesvirus, HHV-8, illustrates just how much there is still to learn from this newly discovered agent.

The book therefore gives useful overviews of the main candidate human tumour viruses. What could have been given greater prominence, I felt, were the common themes that the individual chapters serve to illustrate; for instance, the type of evidence required to establish a bonafide virus–tumour association, the interplay of epidemiology and molecular biology, and the importance of cancer in immunocompromised patients as a touchstone for the discovery of new agents. These are all alluded to in the “Introduction” but the message is not reinforced. Another central theme, the prospects for prophylactic and/or therapeutic vaccines, is rightly given its own chapter; but here again there is a danger that, for the undiscerning reader, the principles might be lost in the detail. Yet, would tumour virologists need not be discouraged, this is still a useful handbook, with more than enough in its pages to interest and engage.

A B RICKINSON


When I was a junior doctor studying for the membership of the Royal College of Physicians, I used to attend the Grand Rounds that were held at Queen’s Square, London. We were dazzled by the skills of the eminent neurologists as they pinpointed exactly the lesion causing the neurological signs. With the advent of sophisticated scanning techniques, we were then able to visualise these lesions, even if the aetiology of many of the diseases remained obscure. Molecular neurogenetics has begun to offer us unique insights into the nature of many neurological diseases as well as a variety of novel targets for therapeutic intervention. Joe Martin has collected together an internationally renowned panel of experts and provides an excellent introduction into the principles and practice of molecular neurology. I particularly enjoyed Stanley Prusiner’s account of the discovery of prion diseases. The value of this book to students and junior medics is that it captures the excitement and glamour of molecular neurogenetics. It does not profess to be a comprehensive textbook but more an introduction to the science. However, the book will be of value to senior clinicians and scientists who do not have time to follow this expanding and rapidly moving field in the scientific literature. The text is easy to follow and the illustrations are first class. The book even contains an epilogue detailing recent advances that have occurred since the chapters for this volume were submitted.

E W HILLHOUSE