Methods for analysing AgNORs

In their interesting review on proliferation markers in tumours, van Diest and coworkers emphasise the importance of the assessment of AgNORs (nucleolar organiser regions), since AgNOR scores correlate well with other proliferation markers and can be used to estimate cell cycle time. The authors finalise the section with the statement "but at present these methods are difficult to apply in daily practice." At the moment, indeed, most of the working groups determine the silver stained area in the nucleus, which requires morphometry of course, and is time consuming. Yet we would like to remind readers that there are alternative methods for AgNOR analysis that do not depend on image analysis systems and can easily be applied in daily routine work. In our own investigations we have always emphasised the different morphological appearances of silver precipitations. AgNOR staining of cytological preparations from acute leukemias allows the differentiation of clusters (aggregations of precipitations) to gain a common matrix in the nucleus) and dots (small singular precipitations without a matrix).1 Our staining and counting procedures are standardised and the inter- and intraobserver variability is low. This alternative approach is justified because for acute leukemias there is a good correlation between the BrdU index and the mean number of clusters (r = 0.60) or the percentage of cells with one cluster (r = -0.63), bearing in mind that the correlation between the mean AgNOR size and BrdU shows a very similar value (r = -0.63).2 For chronic lymphocytic leukaemia (CLL) we also recommend making a differential count, separating cells with one or two complex nuclei and cells with clusters.3 The percentage of cells with clusters correlates well with the tumour mass score (r = 0.72) and lymphocyte doubling time (r = -0.74) and permits one to differentiate well between stable and progressive CLL. Furthermore the AgNOR pattern in CLL helps in the follow up monitoring of the patients and their response to chemotherapy.1,4

In summary, although we agree with others that measuring the AgNOR area provides very important information, especially with regard to the cell cycle time,5 we believe that there are alternative ways of analysing AgNORs which can be more easily applied in daily practice, but nevertheless are of equal pathophysiological and clinical relevance.


Cervical intraepithelial glandular neoplasia

Kurian and Al-Nafussi6 deserve our gratitude for shedding further light on the difficult subject of cervical intraepithelial glandular neoplasia. In particular, by establishing a ratio of 1.12:1 between the mean AgNOR size of invasive and non-invasive disease and of 0.96:1 for low grade and high grade in situ lesions, they provide a means by which pathologists may monitor their diagnostic performance using the principles outlined by Wakely et al in 1998. This will be particularly informative in the case of low grade lesions which could be easily overlooked or passed off as reactive changes. The classification of in situ glandular lesions of the cervix is the subject of much controversy—for example, two methods are described in a standard British textbook of gynaecological pathology,7 each of which differ from the method used in the current study, which has also dispensed the term adenocarcinoma in situ. Variations in diagnostic criteria and terminology between papers may go some way to explaining why the conclusions in this paper, where progression from low grade to high grade disease is assumed to occur, differ from those of Goldstein et al,8 who suggested that there was no morphological evidence to support the existence of a spectrum of endocervical glandular changes culminating in what they recognised as adenocarcinoma in situ. Finally, Kurian and Al-Nafussi’s study highlights the importance of the cervical smear test in detecting these lesions when it is used as part of a screening programme.

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Acknowledgements


Authors’ response

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1. It is a pleasure to read Dr Heatley’s response to our paper. The reason for abandoning the term adenocarcinoma in situ in our report is to conform with the new terminology for glandular lesions of the cervix. This is due to be released shortly in the Guidelines of Royal College of Pathology for reporting cervical biopsies.

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