
**Dr Barnes and Gillett comment:**

We thank Dr Trere for his interest in our editorial. He is obviously a keen proponent of this technique, however, the value of AgNORs in pathology remains controversial, as denoted by the large number of conflicting publications. In response to his footnotes 2 and 3 of our editorial, we would like to confirm our original points.

The accurate identification of AgNORs is highly dependent upon tissue preparation and mounting techniques. During fixation, silver deposition and hence loss of NOR definition can occur as a result of variations in tissue thickness, the use of different fixatives and prolonged fixation times. These features also affect the amount of non-specific staining, which can cause problems with the accurate identification of AgNORs.

The universally accepted method of evaluating AgNORs. Counting methods have evolved in order to obtain as much information as possible about demonstrable NORs and have counted as discernible NORs, others have counted the number of NOR clusters and satellites, whilst further groups have incorporated the AgNOR distribution pattern into their assessment. As we have previously shown, there is marked variation in the numbers of cells assessed, 100–200 being the usual number, far less than would be evaluated when staining with a proliferation marker such as Ki67 or KI67. By Dr Trere's own admission these enumerative methods are "time-consuming and subjective". However, manual counting is the only method of evaluating open to most pathologists, who do not have the necessary equipment to carry out computer aided image analysis. Most studies have combined AgNOR scores with established methods of predicting prognosis and directly with clinical outcome. Whether AgNORs are associated with proliferation or cell proliferation requires further clarification.

There are studies which have shown AgNORs to be associated with patient prognosis but among these, the prognostic value of AgNORs is less than in the more established methods and in some cases do not provide independent prognostic information when included in multivariate analyses.

In conclusion, we stand by our previous statement that AgNORs were of great interest when they were one of the few methods of assessing proliferative activity in formalin fixed, paraffin wax embedded material. As a prognostic marker, AgNORs have now been superseded by other methods, in particular the development of the Ki67 associated antibody, which are easy to use and are open to more standardised quantification.

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**Correspondence**

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This book provides a series of practical demonstrations, which may be undertaken by students themselves, to illustrate some of the fundamental concepts of genetics. It is aimed at first year undergraduates with questions and reassurances on each topic. The authors find themselves in the curious position of having to defend the use of practical laboratory work in courses on genetics which are also practical and succinct.

The book was first published in 1951 and is now in its 10th edition and therefore clearly has found a niche in this particular market. No doubt the book has evolved a great deal since the first edition but unfortunately some mutations have crept in over this period of time.

In the chapter on "Linkage and Crossing-over" somatic mapping is explained in great detail in the section on human gene mapping. Other approaches (for example, in situ hybridisation) are dealt with in one line—surely unusual for a textbook published in 1995. In the chapter on "Human Chromosomes" the chromosome pairs 17 and 18 are transposed in one figure (Fig 11.3) and the ISCN karyotype for Turner syndrome is incorrectly given as 47,XY; X versus 47,XXX. In the same chapter the cytogenetic consequences of the presence of the Philadelphia chromosome, observed in chronic myeloid leukaemia, are incorrectly described.

One is left with the impression that some parts of this book may have evolved faster than other parts. The book may be useful for classic genetic experiments but care should be exercised in relying upon it as a source of instruction and information in those areas undergoing rapid development such as human gene mapping, which will benefit from revision for the next edition.

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