LETTERS TO THE EDITOR

Markers to study human colonic cell proliferation

EDITOR,—We noted with interest the paper by Kubben et al (Gut 1994; 35: 530–5) on a comparison between proliferating cell nuclear antigen (PCNA) and ex vivo bromodeoxyuridine (BrdU) labelling. We have compared PCNA labelling in 86 human colorectal tumours to iododeoxyuridine (IudR) labeling after in vivo administration using both flow cytometric and immunohistochemical methods.1

In contrast with the authors’ findings, we have not found a significant correlation between the two labels. This was despite correcting for the presence of IudR labeled daughter nuclei (a problem that has not been discussed in this paper) and using a variety of fixatives when assessing PCNA labeling. In our experience, the strongest correlation seen has been on comparison between IudR labeling assessed immunohistochemically and PCNA labeling after fixation in methanol (r=0.38, p=0.015). Fixation methods seem to affect the identification of PCNA in different parts of the cell cycle2 and the apparently higher expression of PCNA than BrdU in Kubben’s paper reflects this.

As we have stated before,1 we feel that in comparisons such as this, it is necessary to analyse a much greater number of specimens from a greater number of subjects and attach less clinical significance to a weak correlation that is statistically significant.

M S WILSON
P P SCHOFIELD
Department of Surgery,
Christie Hospital NHS Trust,
Manchester M20 9BX


Reply

EDITOR,—We are grateful to Wilson and Schofield for their comment on our study. Wilson and Schofield did not find a significant correlation between proliferating cell nuclear antigen (PCNA) and in vivo iododeoxyuridine (IudR) immunohistochemistry in 86 human colorectal tumours. The higher expression of PCNA than BrdU in our study ascribe to the fixation method used.

Two populations of PCNA are present during S phase. One is nucleoplasmic, present in short term G2 cells, and not apparent in cells fixed in organic solvents such as methanol or ethanol. The other form is associated with DNA replication sites and cannot be extracted with organic solvents.1–3

Our results are comparable with those of Weisgerber et al,4 who used an organic solvent as fixative as well, and slightly lower of those of Riso et al,5 who used formalin fixation (Table). Riso showed a decreasing correlation between PCNA and BrdU immunohistochemistry with increasing dysplasia of the tissue under investigation.

The progressive increase of PCNA expression with increasing dysplasia seems to be related to both hyperproliferation and hypoplastic deregulation of PCNA synthesis. Although they do not provide sufficient technical details, the interesting results of Wilson and Schofield are in agreement with our study and the work of Weisgerber et al and Riso et al.

F J G M KUBBEN
A PEETERS-HASEVEOETS
L G J B ENGELS
C G M BAETEN
B SCHUTTE
J W ARENDS
R W STOCKBRUGGER
G H BLIJHAM
Academic Hospital,
Department of Internal Medicine,
Maasricht, The Netherlands

Correspondence to:
Dr F J G M KUBBEN
University Hospital,
Department of Gastroenterology and Hepatology, Building 1, CL D, MC 6000.
2300 RC Leiden, The Netherlands

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J H Baron and A W Harris

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