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) labelling after in vivo administration using both flow cytometric and immunohistochemical methods.

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 labelled daughter nuclei (a problem that has not been discussed in this paper) and using a variety of fixation methods when assessing PCNA labelling. In our experience, the strongest correlation seen has been on comparison between IudR labelling assessed immunohistochemically and PCNA labelling 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 cycle and the apparently higher expression of PCNA than BrdU in Kubben’s paper reflects this.

As we have stated before,1,2 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 F SCHOFIELD
Department of Surgery,
Christie Hospital NHS Trust,
Manchester M20 9BX


Reply

EDITOR,—We note the interest the correspondence raised by Drs Wilson and Schofield in our paper on the study of PCNA and BrdU levels. Although we did not see any significant correlation between the two methods, the difference in result was not great (0.26) and the authors have not commented on the fact that the highest levels of BrdU were seen in the lowest grade adenocarcinomas.

Correlation of BrdU and PCNA immunohistochemistry on human colorectal tissue

<table>
<thead>
<tr>
<th>Author</th>
<th>Tissue</th>
<th>Subjects (n)</th>
<th>r</th>
<th>p value</th>
<th>Mab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kubben</td>
<td>Normal</td>
<td>0-63</td>
<td>&lt;0.05</td>
<td>19A2</td>
<td></td>
</tr>
<tr>
<td>Weisgerber</td>
<td>Normal</td>
<td>0-6</td>
<td>0.011</td>
<td>19A2</td>
<td></td>
</tr>
<tr>
<td>Riso</td>
<td>Low grade adenoma</td>
<td>0.5</td>
<td>0.01</td>
<td>PC10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High grade adenoma</td>
<td>0.61</td>
<td>0.01</td>
<td>PC10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma</td>
<td>0.55</td>
<td>0.015</td>
<td>PC10</td>
<td></td>
</tr>
<tr>
<td>Wilson</td>
<td>Adenocarcinoma</td>
<td>0.38</td>
<td>0.015</td>
<td>PC10</td>
<td></td>
</tr>
</tbody>
</table>

Mab=monoclonal antibody against proliferating cell nuclear antigen; r=correlation coefficient.