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Letters to the Editor

Confocal microscopy of idarubicin localisation

Sir

We have read with interest and some surprise the paper recently published in the *British Journal of Cancer*: Confocal microscopy of idarubicin localisation in sensitive and multidrug resistant bladder cancer cell lines (*Br. J. Cancer* 1996; **74**: 906–909) by Duffy, Hayes, Cooper and Smart, from Southampton.

A factor that has not been taken into account by the authors and which would significantly modify their conclusions is the fact that there is a 98% quenching of fluorescence when an anthracycline is intercalated between DNA base pairs. This means that the nuclear signal of anthracycline fluorescence has to be multiplied by 50 to be compared with the cytoplasmic nuclear signal. The confocal microscopic study performed by the authors is in no way quantitative and the rough comparison of the visual signals (cytoplasm vs nuclear) cannot bring any conclusions concerning the subcellular distribution of the drug. The differences pointed out by the authors between doxorubicin and idarubicin are not sustained by any quantitative data and cannot be interpreted. We would advise the authors to use confocal microspectrofluorometry, a technique that allows absolute measurements of anthracycline nuclear concentration (Gigli et al, 1988, 1989). Such a technique applied to idarubicin has already been performed in Reims and has led to the conclusions that the behaviour of idarubicin is not qualitatively different from that of doxorubicin or other anthracyclines.

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Confocal microscopy of idarubicin localisation – reply

Sir

Professors Manfait and Robert highlight the difficulty in interpreting nuclear/cytoplasmic fluorescence in the presence of quenching. This is a dilemma addressed in our original article and our findings regarding this phenomenon are presented in Figure 5. The data show that differences in fluorescence quenching between idarubicin and conventional anthracyclines (in free solution with DNA) appear insufficient to account for the consistent differences in nuclear/cytoplasmic fluorescence observed in our studies. We have also more recently repeated the studies using nuclei isolated from our cell lines by zaponin in the presence of protease and phosphatase inhibitors. Idarubicin fluoresces in stripped nuclei as effectively as epirubicin. We will publish these results as soon as possible in view of their relevance to this controversy. Overall, we feel that we have demonstrated a distinction between intracellular idarubicin fluorescence and that of less lipophilic anthracyclines that is not explained by fluorescence quenching phenomena.

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Colorectal carcinoma: some reflections on bile flow through the terminal ileum

Sir

I have just read with great interest the paper by Boutron et al (1996). They suggest that the type of dairy product might be the important factor with regard to prevention of colorectal tumours.

It is widely believed that bile salts may have some role in colorectal carcinoma (CRC) (Nagengast, 1988; Garewal et al, 1996). The enzyme diamine oxidase (DAO), which is a major catabolic enzyme for histamine, is found in highest concentration