Reply

We would like to reply to the letter of Drs. R. P. Bird and T. P. Pretlow referring to the article by G. Caderni et al. published in Cancer Research (1).

Drs. Bird and Pretlow criticize the choice of the term “dysplastic crypt foci” that we used throughout the paper to describe lesions of the colon induced by DMH,1 which were identified by coloring the entire colon surface with methylene blue, according to the method originally described by R. P. Bird (2).

With this method animals treated with colon carcinogens show a number of intensely stained foci which are currently classified according to the number of crypts they contain (2–5).

In the original paper published by Dr. Bird these carcinogen-induced colon lesions are defined “aberrant crypts” or “aberrant dysplastic crypts” interchangeably (2). Papers by other authors published in the same period describe this kind of colonic lesions as “focal disturbances of the mucosal surface” or “mucosal lesions” (6).

In later publications (3–5), on the contrary, Dr. Bird has consistently used the term “aberrant crypt foci” to describe the same lesions. According to a widely accepted nomenclature “aberration” means “abnormality, deviation and abnormal variant,” whereas dysplasia indicates “incomplete or aberrant development of a part, system or region of the body” (7). In this respect the term “dysplastic crypts” seems to be appropriate for early carcinogen-induced colon mucosa lesions, since they are never observed in the normal colon of experimental animals and appear to be the result of disorderly development of the mucosa structure induced by colon carcinogens.

Moreover, the fact itself that these foci are more intensely stained with methylene blue compared to the surrounding mucosa, indicates an alteration of the normal architecture of the colonic crypts that can rightfully be defined as dysplasia (8).

In a recent work, published 2 months after our paper appeared in Cancer Research (9), Dr. Bird and coworkers made an attempt of distinguishing between different classes of aberrant crypts, by studying some histological longitudinal sections and classified them using two different criteria of dysplasia (presence of nuclear elongation and nuclear stratification), which produced a grading system varying from 0 to 4 according to the progressive severity of the dysplasia. According to this paper the aberrant crypts that show grade 4 dysplasia appear with a lag of 19 weeks after carcinogen treatment and their percentage increases with time. On the basis of these results Dr. Bird and coworkers propose to classify just a few of the aberrant crypts as “dysplastic crypts.”

In order to make this classification Dr. Bird and coworkers analyzed a few longitudinal sections of some aberrant crypts (from 2 to 6) and graded them with the system described above. Given the fact that the total number of aberrant crypts observed in rats treated with 125 mg of DMH is about 100, this attempt is like “looking for a needle in the haystack,” using Dr. Bird’s own expression (10).

It should also be noted that classifying dysplasia only on the basis of the appearance of nuclei of the cells lining the crypts might be inherently erroneous, because it does not take into consideration other important parameters like “tissue architecture . . . and cytoplasmic differentiation” (8). Moreover, this approach has not yet been accepted and validated, and there is no proof yet in the literature that it will be better correlated with colon carcinogenesis compared with previously used procedures.

Generally speaking, we feel that there is an extreme need of methods that would allow discrimination among different types of early carcinogen-induced lesions of the colon and correlate them with the development of malignant tumors. This need is well documented by a recent publication of Hardman et al. (11) in which no correlation between aberrant crypt foci number and colon cancer was observed in rats treated with DMH. Better methods of classification, possibly not based on morphological characters alone, might have a stronger correlation with colon carcinogenesis.

To distinguish between aberrant and dysplastic crypts, like Dr. Bird and Dr. Pretlow propose, by means of a random selection of a small number of lesions analyzed with conventional histology, would kill the purpose of a method which was devised as a short-term system for studying the modulation of carcinogenesis in experimental animals. Such a method, in fact, allows the quick visualization of a large number of lesions that can represent the overall response of the mucosa of the treated animals.

We do think, however, that it would be helpful if all the workers of the field, for the sake of clarity, were willing to adopt the nomenclature proposed by Drs. Bird and Pretlow. However, we are convinced that we are discussing here a minor problem of nomenclature, the solution of which does not entail any apparent progress in this field.

Professor Piero Dolara
Dr. Giovanna Caderni
Department of Pharmacology
University of Florence
50134 Florence, Italy

References

Received 9/30/91; accepted 5/15/92. 1The abbreviation used is: DMH, 1,2-dimethylhydrazine.
Correspondence re: Giovanna Caderni et al., Effect of Dietary Carbohydrates on the Growth of Dysplastic Crypt Foci in the Colon of Rats Treated with 1,2-Dimethylhydrazine. Cancer Res., 51: 3721–3725, 1991—Reply

Piero Dolara and Giovanna Caderni


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