Cancer Research

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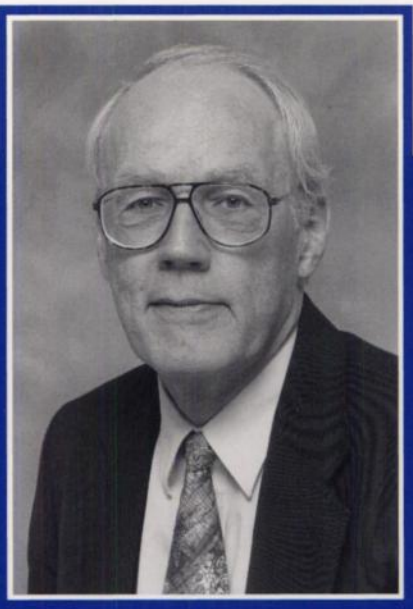

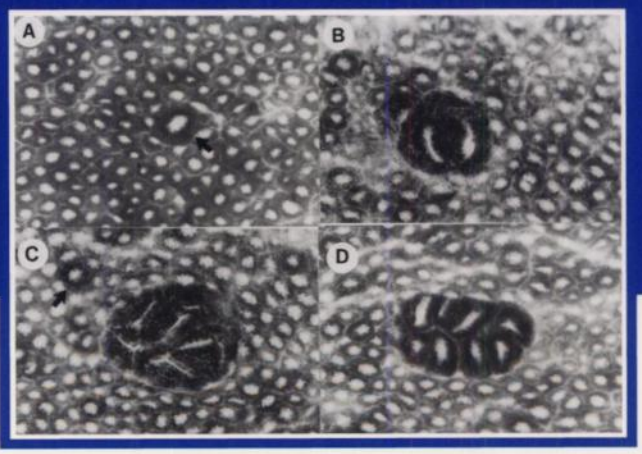

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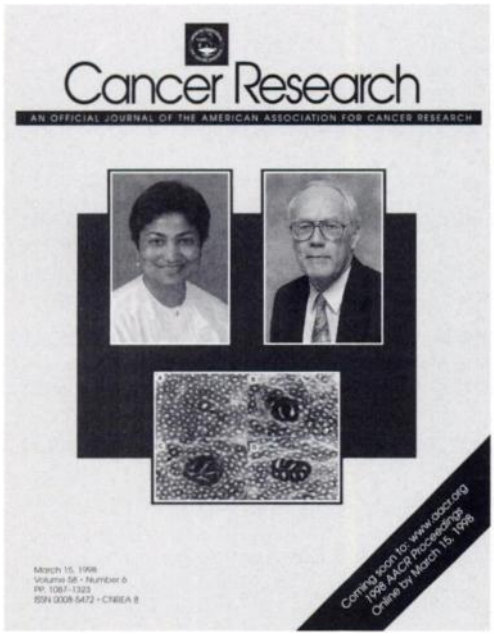
COVER LEGEND



Dietary factors play an important role in the etiology and prevention of a variety of cancers. Animal models have been especially valuable in assessing dietary etiological elements associated with colon cancer. To screen potential initiators or modulators of colon carcinogenesis, a simple and economical system was needed to quantify preneoplastic changes in rodent colons. Work on the histogenesis of colon cancer documented the presence of altered crypts exhibiting hyperproliferation, dysplasia, and altered crypt morphometry. Thus, the early changes in colonic crypts could be visualized by examination of the whole colonic mucosa. The presence of aberrant crypts (ACs) in the whole mount of methylene blue stained colonic mucosa was first reported by Ranjana Prasad Bird (*left*) in 1987 (Cancer Lett., *37:* 147, 1987). ACs were visualized microscopically and were easily distinguished from the millions of surrounding normal crypts by their large and irregular luminal openings, a thicker epithelial lining, and a pericryptal zone. In the cover illustration (*bottom*), the frames A, B, C, and D denote the presence of four foci with more than one crypt and the morphological heterogeneity among the AC. The arrow emphasizes the presence of an aberrant crypt focus (ACF) with one crypt (x40). ACs were present in carcinogen-treated murine colons, whereas they were absent in colons with marked hyperplasia and those that were not exposed to a carcinogen. Some ACs showed dysplasia, the key feature of preneoplastic lesions, and hence, they might represent preneoplastic lesions. Their number and growth features could be used to identify initiators and modulators of colon carcinogenesis. These studies were conducted at the Ludwig Institute for Cancer Research in Toronto, Ontario, Canada, directed by W. Robert Bruce (*right*), in a broad program of basic and applied research on cancer prevention strategies in high risk individuals. It was systematically demonstrated that: (*a*) ACF were induced by colon carcinogens in a dose- and species-dependent manner; (*b*) they grow at different rates; and (*c*) their number and growth were modified by the modulators of colon carcinogenesis and, of considerable relevance, they predicted the tumor outcome (Cancer Res., *48:* 6183, 1988; Cancer Res., *48:* 6187, 1988; Cancer Res., *49:* 1236, 1989; Cancer Res., *51:* 5270, 1991; Carcinogenesis, *12:* 969, 1991; Carcinogenesis, *12:* 2093, 1991).

In 1991, Dr. Bruce and colleagues (Hum. Pathol., *22:* 287–294, 1991; Cancer Epidemiol. Biomark. Prev., *1:* 57, 1991) and also Theresa P. and Thomas G. Pretlow and colleagues (Cancer Res., *51:* 1564, 1991; Gastroenterology, *111:* 772, 1996) reported the presence of ACF in the methylene blue stained whole mount of human colons. The morphological and genotypic features of ACF in human colons were similar to those in animal colons and demonstrated the importance and relevance of basic research in animal models to the clinical situation. The use of the ACF system to study modulators has accelerated remarkably in the last five years, for it provides a simple and economical tool for preliminary screening of potential chemopreventive agents, and it permits a quantitative assessment of the mechanisms of colon carcinogenesis (Cancer Lett., *93:* 55, 1995). Sequential analyses of ACF with different growth features and histological atypia allows dissection of the disease process at the cellular and molecular level and exploration of the concept that carcinogenesis is a multistep process involving serial colonal selection and expansion of transformed cells leading to a malignant phenotype (Am. J. Pathol., *149:* 381, 1996).

Dr. Bird received her undergraduate degree in Biology (University of Ranchi, India, and University of Waterloo, Ontario, Canada) and her M.Sc. (1977) and Ph.D. (1981) in Nutritional Sciences in the area of Nutritional Toxicology (University of Guelph, Ontario, Canada). She joined the Ludwig Institute for Cancer Research in 1982, initially investigating the role of dietary components in colon cancer. Dr. Bird soon recognized the difficulties of reaching such a goal with existing methodologies. She searched for a simple system that would allow quantitative assessment of the stepwise process of colon carcinogenesis and thus focused on aberrant crypts. She attributes her ability to discover and apply the procedure in part to her basic instincts as a "biologist." Currently, Dr. Bird is Professor, Department of Foods and Nutrition, at the University of Manitoba (Winnipeg, Manitoba, Canada), teaching at the undergraduate and graduate levels. The main focus of her research program is to define and refine the biology and growth regulation of ACF and to understand the role of nutrients in the pathogenesis of colon cancer. In Manitoba, she was a recipient of the Women in Science Career Award of the Natural Sciences and Engineering Research Council of Canada (1991–1996). She received a Rh Institute Award for excellence in interdisciplinary research in 1990. Dr. Bird also was honored with the Borden Award in 1996 by the Canadian Society for Nutritional Sciences for her contributions during the past five years to the field of nutritional sciences. Dr. Bird has been a member of the American Association for Cancer Research (AACR) since 1989.

Dr. Bruce obtained a B.S. in Chemistry at the University of Alberta in 1950 and a Ph.D. in Physics at the University of Saskatchewan in 1956, and he completed his M.D. at the University of Chicago in 1958. He began studies in radiobiology and experimental chemotherapy at the Ontario Cancer Institute in 1959, concentrating on the cellular and proliferative basis for the selectivity of the therapeutic agents in animal models and clinical studies. His interest turned to the cellular biology of spermatogenesis as a tool for evaluating exposure to environmental agents. He used record linkage in the assembly of patient cancer records from multiple sources and the generation of population-based cancer data. He initiated studies of the origin of colorectal cancer in 1975 with the demonstration of mutagenic compounds in feces, which were later identified as "fecapentaenes" (Cancer Res., *49:* 1236, 1989). He was concerned with the long duration and cost of laboratory and clinical studies that depended on cancer endpoints and focused on presumed biomarkers of cancer risk, on the development of polyp recurrence in clinical studies, on proliferation measures in animal and clinical studies, and on the appearance of nuclear aberrations or apoptosis in experimental studies. He was immediately struck with the importance of Dr. Bird's observation of ACF and worked with her on the demonstration of ACs following exposure to known colon carcinogens and on the growth of the ACF. He extended the studies with the demonstration of ACF in the human colon with Luca Roncucci (now in Modena, Italy) and Alan Medline (Toronto).

At present, Dr. Bruce is at the Department of Nutritional Sciences, University of Toronto, using the ACF assay to examine the effect of thermolyzed foods and insulin resistance on colon carcinogenesis. Dr. Bruce became an AACR member in 1963. He served on the Board of Directors from 1979 to 1982 and on the Membership Committee in 1980. He has also been on the Editorial Board of the AACR journal *Cancer Epidemiology, Biomarkers & Prevention* since its inception, first as a member of the Editorial Advisory Board (1991–92), then as an Associate Editor (1993–). Dr. Bruce received the Dameshek Award of the American Society of Hematology in 1970 and the O. Harold Warwick Prize, the National Cancer Institute of Canada Eli Lilly Award, in 1995. He was elected a Fellow of the Royal College of Physicians and Surgeons of Canada in 1978 and of the Royal Society of Canada in 1980.

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