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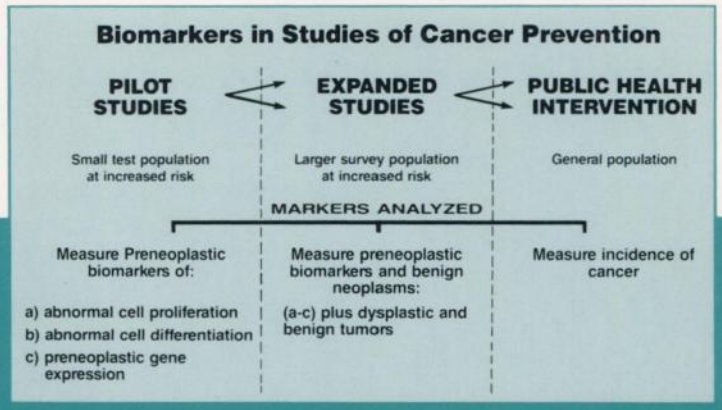
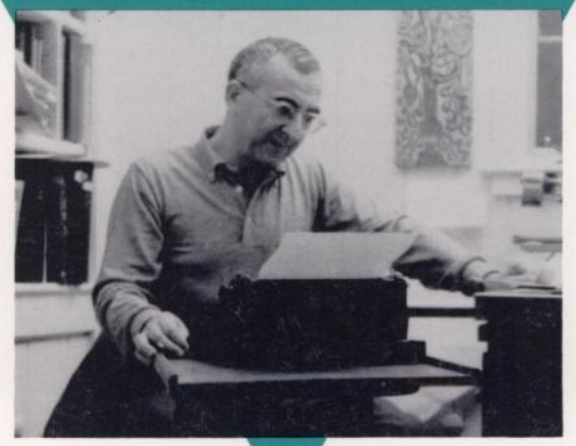
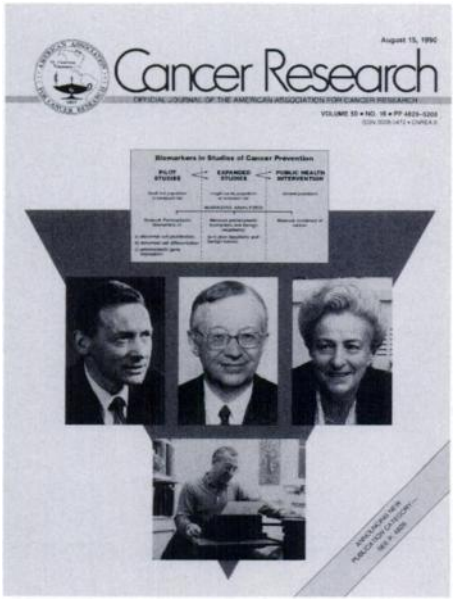




ANNOUNCING NEW PUBLICATION CATEGORY— SEE P. 4829

COVER LEGEND



Shortly after the preparation of tritium-labeled thymidine and its use in identifying duplicating chromosomes in *Vicia faba* [J. Taylor, P. S. Woods, and W. L. Hughes. Proc. Natl. Acad. Sci. (USA), *43:* 122–127, 1957], investigators at the Brookhaven National Laboratory demonstrated newly formed DNA in mouse nuclei and rapid epithelial cell proliferation in several organs [W. L. Hughes, V. P. Bond, G. Brecher, E. P. Cronkite, R. B. Painter, H. Quastler, and F. Sherman. Proc. Natl. Acad. Sci. (USA), *44:* 476–483, 1958]. The continual renewal of epithelial cells in rat small intestine had been noted earlier (C. P. Leblond and C. E. Stevens. Anat. Rec., *100:* 357–378, 1948) but could be further documented with tritiated thymidine (C. P. Leblond and B. Messier. Anat. Rec., *132:* 247–259, 1958). The mathematical basis of cell population kinetics was developed and applied to the small intestine of the mouse (H. Quastler and F. Sherman. Exp. Cell Res., *17:* 420–438, 1959), and to mouse colon (M. Lipkin and H. Quastler. J. Clin. Invest., *41:* 141–146, 1962).

These methods were extended to humans [J. W. Cole and A. McKalen. Gastroenterology, *41:* 122, 1961; M. Lipkin, P. Sherlock, and B. Bell. Nature (Lond.), *195:* 175–177, 1962], and the proliferative cell cycle kinetics, epithelial cell migration and extrusion rates, and spatial distributions of proliferating and differentiating epithelial cells were characterized in all areas of the human gastrointestinal tract (M. Lipkin, B. Bell, and P. Sherlock. J. Clin. Invest., *41:* 1380, 1962; *42:* 767–776, 1963; Gastroenterology, *45:* 721–729, 1963; B. Bell, T. P. Almy, and M. Lipkin. J. Natl. Cancer Inst., *38:* 615–628, 1967).

An expansion of the proliferative compartment was noted in precancerous lesions with failure of epithelial cells to undergo terminal differentiation [E. Deschner, C. Lewis, and M. Lipkin. Clin. Res., *393:* 1962; J. Clin. Invest., *12:* 1922–1928, 1963; J. W. Cole, and A. McKalen. Cancer (Phila.), *16:* 998–1002, 1963; E. Deschner, M. Lipkin, and C. Solomon. J. Natl. Cancer Inst., *36:* 849–857, 1966], and the same abnormalities were found in rodents following the injection of a colon carcinogen [U. Lors, B. Wiebecke, and M. Eder. Z. Ges. Exp. Med., *151:* 297–307, 1969; N. Thurnherr, E. Deschner, E. Stonehill, and M. Lipkin. Cancer Res., *33:* 940–945, 1973].

These abnormal characteristics of epithelial cell proliferation and differentiation are observed in the multistep evolution of human gastrointestinal neoplasms, chemical carcinogenesis in the gastrointestinal tract, and in human cancer-prone epithelial cells in high-risk individuals (E. Deschner and M. Lipkin. J. Natl. Cancer Inst., *44:* 175–185, 1970; F. Troncale, R. Hertz, and M. Lipkin. Cancer Res., *31:* 463–467, 1971). The quantitative analysis of proliferating and differentiating colonic epithelial cells in high-risk human subjects is being applied in attempts at cancer prevention through studies of early effects of chemopreventive agents on these intermediate biomarkers [H. J. R. Bussey *et al.* Cancer (Phila.), *50:* 1136–1141, 1982; M. Lipkin and H. N. Newmark. N. Engl. J. Med., *343:* 1381–1384, 1985; Cancer Res., *49:* 248–254, 1989].

We are indebted to Dr. M. Lipkin for information and photographs. *Top left:* Henry Quastler, M.D., 1908–1963, radiobiologist, Biology Department, Brookhaven National Laboratory, Upton, NY; *top right:* Charles Philippe Leblond, M.D., Ph.D., Professor and Chairman, Emeritus, Department of Anatomy, McGill University, Montreal, Quebec, Canada; *bottom left:* Martin Lipkin, M.D., Member and Attending Physician, Memorial Sloan Kettering Cancer Center, New York, NY, and Professor of Medicine, Cornell University Medical College; *bottom right:* Eleanor Deschner, Ph.D., Associate Laboratory Member, Memorial Sloan-Kettering Cancer Center, New York, NY.

John H. Weisburger