

Reynoso G, Chu T M, Holyoke D, Cohen E, Nemoto T, Wang J-J, Chuang J, Gulnan P & Murphy G P. Carcinoembryonic antigen in patients with different cancers. *J. Amer. Med. Assn.* 220:361-5, 1972.  
[Roswell Park Memorial Inst., New York State Dept. Health, Buffalo, NY]

The paper shows that carcinoembryonic antigen (CEA) is present in normal individuals and in patients with a variety of cancers, not only gastrointestinal cancer. The paper convincingly demonstrates the positive correlation between antigenemia and clinical stage and sets the basis for the use of serial CEA measurements as monitors of therapy in cancer. [The *SCI*<sup>®</sup> indicates that this paper has been cited in over 295 publications since 1972.]

Gustavo Reynoso  
Department of Pathology  
Norwalk Hospital  
Norwalk, CT 06856

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"Cancer immunology was an exciting field of research in the late-1960s and early-1970s. The work of Sir Macfarlane Burnet<sup>1</sup> had led to the then widely accepted concept of immunological surveillance in cancer; alpha-feto protein had recently been discovered<sup>2</sup> and the Montreal group had just begun their long series of publications on the carcinoembryonic antigens (CEAs) of the human digestive tract.<sup>3</sup> It was believed at the time—in part because of extrapolation from animal models—that human cancer tissues contained antigens specific for malignancy and specific for the organ or site from which the antigen was isolated. Such a belief encouraged a great deal of enthusiasm in the use of tumor-specific antigens as potential laboratory tests for cancer.

"In such a climate of heightened expectations, it was important to put the ideas in perspective from a clinical point of view. To that effect, I organized a team of patholo-

gists, clinicians, biochemists, and immunologists to study the immunological basis and the methodological limitations of measuring CEA in plasma, in the normal population and in patients with cancer of different organs, and to correlate the findings with the tumor type and the clinical stage.

"The paper, in my opinion, has been so widely cited because the results of our work provided most of the fundamentals on which later research was based. First, we demonstrated that cross-reactive antigens, immunologically and physicochemically indistinguishable from CEA, are present in normal human subjects. Second, we showed convincingly that the claimed tissue specificity of CEA is not a fundamental property of the antigen itself. Rather, methodological variability can modify the apparent specificity. When such a finding was challenged by the Montreal group, we were able to show carcinoembryonic antigenemia in patients with non-endodermally derived cancer using their own antigen and antibody.

"Of more importance are the positive aspects of our work. We correlated antigenemia with tumor burden and clinical stage and predicted—with clinical and experimental data—the now well-accepted use of fetal antigens as tumor markers.

"The paper and the two or three that followed<sup>4-6</sup> were surprisingly well received by the scientific editors even though (or perhaps because) they contradicted the cancer-specific dogma of the time. It is, I believe, the publication of this paper that led to my appointment to the task force that developed the master plan for the national cancer program and later, in the implementation phase, to several of the review committees and study sections on immunodiagnosis of the National Cancer Institute.

"A happy thought: all of the young investigators whom I invited to collaborate in my group became cancer immunologists and remain active and productive researchers in the field to this time."

1. Burnet M. *Immunological surveillance*. Oxford: Pergamon Press, 1970. 280 p.
2. Abelev G I. Production of embryonal alpha-globulin by hepatomas: review of experimental and clinical data. *Cancer Res.* 28:1344-50, 1968.
3. Gold P & Freedman S O. Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. *J. Exp. Med.* 121:439-59, 1968.
4. Reynoso G, Chu T M, Gulnan P & Murphy G P. Carcinoembryonic antigen in patients with tumors of the urogenital tract. *Cancer* 30:1-4, 1972.
5. Chu T M, Hansen H J & Reynoso G. Demonstration of carcinoembryonic antigen in normal human plasma. *Nature* 238:152-3, 1972.
6. Chu T M & Reynoso G. Evaluation of a new radioimmunoassay method for carcinoembryonic antigen in plasma, with use of zirconyl phosphate gel. *Clin. Chem.* 18:918-22, 1972.