AMERICAN ASSOCIATION FOR CANCER RESEARCH
Ut Cancrum Vincamus
1907

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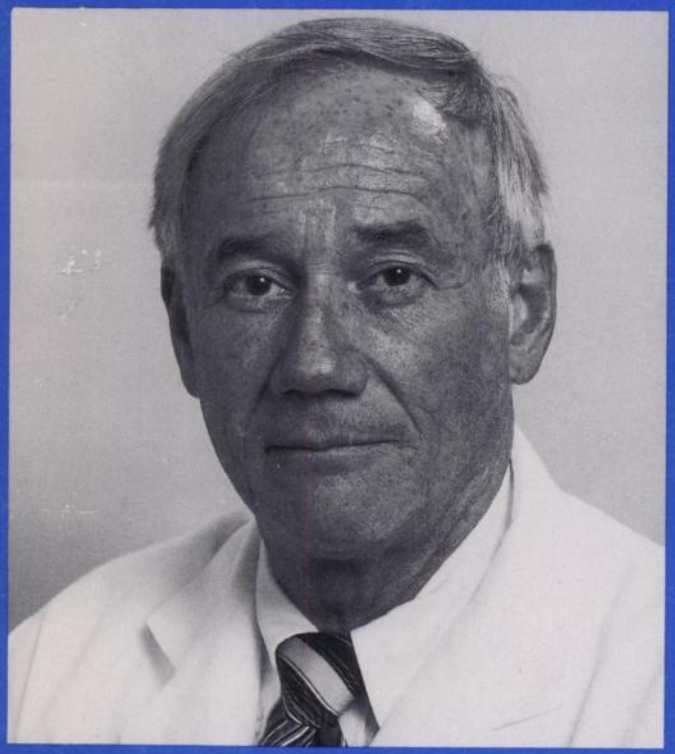
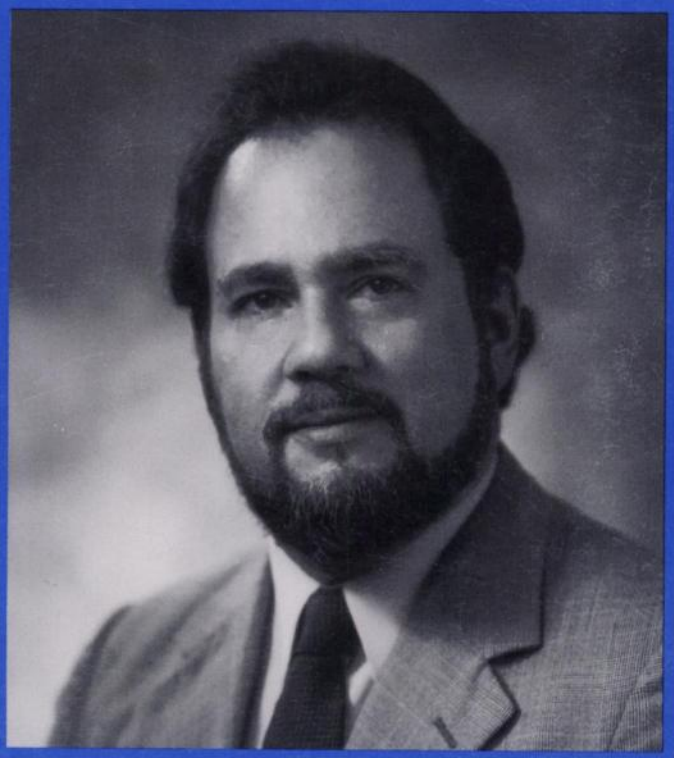
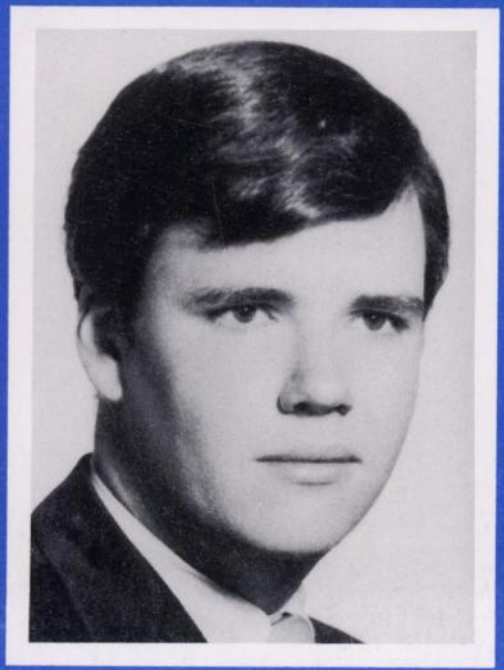






FOR GENERATIONS CANCER PLAGUED THIS FAMILY. THEN WE CAME INTO THE PICTURE.

It's a tragic coincidence that cancer has taken so many members of this family over the years.

It took Frank Domato in 1961. Patricia O'Hara Brown in 1974. And Serafino Gentile in 1982.

But the fact that the chain of tragedies has now been broken is no coincidence at all.

Over the last 40 years, research programs supported by the American Cancer Society have made increasing progress in the treatment, detection and prevention of cancer.

In 1985 alone, the Society funded over 700 projects conducted by the most distinguished scientists and research institutions in the country.

So it's no coincidence that in 1986, cancer did *not* take Debra Gentile—Frank Domato's great-granddaughter. Just as it didn't take hundreds of thousands of others who have been successfully treated for the disease.

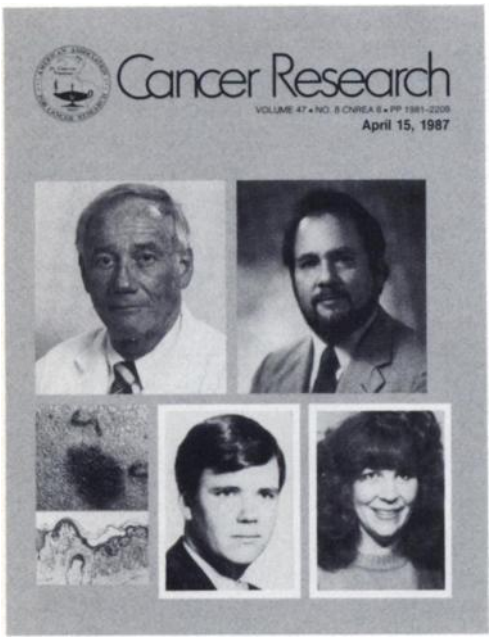
You see, we are winning.

But we need you to help keep it that way.

AMERICAN CANCER SOCIETY

Help us keep winning.

COVER LEGEND



The interdisciplinary approach to studying families at high risk of specific cancers represents a powerful tool with which to gain insights into the etiology and pathogenesis of neoplastic diseases in humans. The dysplastic nevus story provides an example.

In 1976, Dr. Michael J. Mastrangelo referred a melanoma-prone kindred to the National Cancer Institute. The proband of this family, Richard K., was convinced that the presence of melanoma in himself and his sister, father, and paternal uncle was not a coincidence. Dr. Mark H. Greene of the Epidemiology Branch of the National Cancer Institute undertook an evaluation of the family. He enlisted Dr. Wallace H. Clark, Jr., then Professor and Chairman of the Department of Pathology at Temple University, as a collaborator. They examined 26 members of Family K. and found a previously unsuspected melanoma in another family member and the presence of unusual melanocytic nevi on the skin of all family members with melanoma and several of their cancer-free relatives. Histological review of moles excised from members of this family revealed unusual features and reminded Clark of biopsies he had seen recently from another member of a melanoma-prone family, Susan B. After evaluating five additional melanoma families, Greene, Clark, and coworkers reported the clinical (J. Am. Med. Assoc., *239:* 744–746, 1978) and histological (Arch. Dermatol., *114:* 732–736, 1978) characteristics of this new preneoplastic disorder, which was provisionally designated the "B-K mole syndrome" after the first two families studied.

The study was expanded to include 14 high-risk families. With the recognition that a disorderly architectural pattern and cytological atypia of melanocytes were the salient characteristics of these unusual moles, they were renamed "dysplastic nevi" (Lancet, *2:* 1024, 1980). The clinical features of dysplastic nevi were delineated more fully (N. Engl. J. Med., *312:* 91–97, 1985), and follow-up of the 14 families documented that dysplastic nevi were the histogenetic precursors of the melanomas which arose in family members, who were at exceedingly high risk of developing this cancer (Ann. Intern. Med., *102:* 458–465, 1985). Genetic studies demonstrated that the melanoma and dysplastic nevus traits segregated in a manner consistent with autosomal dominant inheritance, indicated that both traits represented the pleiotropic effects of a single, highly penetrant gene, and suggested that this gene might be located on the short arm of chromosome 1, near the Rh blood group gene (Proc. Natl. Acad. Sci. USA, *80:* 6071–6075, 1983). This latter hypothesis has provided the basis for ongoing recombinant DNA studies designed to identify the melanoma/dysplastic nevus gene and its product.

Other laboratory studies, conducted using biological specimens obtained from these carefully characterized families, suggested the presence of subclinical immunological abnormalities and demonstrated that cultured fibroblasts and lymphoblasts from affected family members were unusually sensitive to the cytotoxic and mutagenic effects of ultraviolet radiation, a known melanoma risk factor (Int. J. Cancer, *30:* 39–45, 1982; Proc. Natl. Acad. Sci. USA, *81:* 1179–1183, 1984). Hereditary melanoma/dysplastic nevus syndrome has thus joined xeroderma pigmentosum as a human hypermutability disorder. This project also identified the existence of a nonfamilial form of dysplastic nevus [Cancer (Phila.), *46:* 1787–1794, 1980] which is present in at least half of all melanoma patients and in 2 to 5% of the general population. Thus, dysplastic nevi have emerged as the most common and best characterized precursor of melanoma (Lancet, *2:* 1076–1077, 1983) and have provided the basis for an elegant model of tumor progression in humans (Hum. Pathol., *15:* 1147–1165, 1984). Proper management of patients with dysplastic nevi "should significantly reduce the incidence of and mortality from cutaneous malignant melanoma" (J. Am. Med. Assoc., *251:* 1864–1866, 1984).

Pictured are: *left*, Wallace H. Clark, Jr., M.D., who was born in Georgia in 1924 and obtained the Doctor of Medicine degree from Tulane University in 1947; *right*, Mark H. Greene, M.D., who was born in New York State and obtained the Doctor of Medicine degree from Tufts University in 1970; and Susan B. and Richard K., now deceased, victims of the disease they helped to elucidate. A clinical photograph and a photomicrograph of a dysplastic nevus are also shown. We are indebted to Dr. Greene for the information and illustrations. We are also grateful to the families of Richard K. and Susan B. for permission to use their photographs.