Cancer Research is presenting invitational autobiographies of elder cancer research workers. In the August issue, Waro Nakahara, director of the National Cancer Center Research Institute of Tokyo, Japan, contributes his pilgrim’s progress in cancer research, 1918-1974. It is a modest, informative essay, starting with his association with James B. Murphy at Rockefeller Institute at the time of Murphy’s involvement with lymphocytes and cancer immunity.

Cancer research has much to be modest about. Nakahara does not spare himself in recalling his non-reproducible inhibition by oleic acid of mammary tumors in mice. He wryly notes Gye’s announcement of the viral cause of cancer in 1925, and Fibiger’s work on nematode cancer of rats, which still remains to be replicated. For the United States, proud of its Cancer Acts of 1937 and 1971, it is timely to be reminded that the Japanese Cancer Institute and Hospital were established in 1934 and that Gann, the Japanese cancer research journal, is older than our cancer publications. We could have wished for recollections of the doyens of Japanese cancer research, Yamagiwa and Yoshida.

Nakahara’s and his associates’ contributions extend over many fields. He mentions specifically the work on toxohormone, 4-nitroquinoline-1-oxide, syncarcinogenesis, and experimental chemotherapy. Fifty of his 78 years have enriched cancer research. His leadership and mature wisdom will continue to be needed and used. (August)

The role of immune mechanisms in cancer remains a fertile research field, in spite of the dangers of over-optimistic enthusiasms. E. Robinson et al. (Aba Khousy School of Medicine, Haifa, Israel) studied lymphocyte cultures from 15 cancer patients and 15 normal individuals. Phytohemagglutinin (PHA) stimulated all but one of the normal cultures, and only four of the cancer-patient derived lymphocytes. Lymphocytes from cancer patients were not stimulated by
tumor cells from the same patients, whereas nine of the normal controls and cultures from patients with localized neoplasms were stimulated. Thus, lymphocytes of cancer patients in an advanced stage of disease mount a poor reaction to their specific tumor antigens and to non-specific stimulants such as PHA. (July)

S. H. Golub et al. (University of California at Los Angeles, California) compared immunocompetence in 50 patients with cancer by in vitro responses in lymphocyte blastogenesis and in vivo delayed cutaneous hypersensitivity reaction to DNBC and recall reactions to four microbial antigens. Carcinoma patients demonstrated impaired skin reactions, but the least impairment of blastogenesis reaction. Melanoma patients had notable defects in lymphocyte function tests but less impairment of the skin test reactions. Sarcoma patients were intermediate in both vitro and in vivo assays. (August)

Malignant melanoma is relatively uncommon, but its many unusual and unpredictable manifestations have generated wide clinical and research interest. Disseminated melanoma, which often afflicts young people, is one of the deadliest of cancers, for which available therapeutic approaches are unsatisfactory. L. H. Einhorn et al. (M. D. Anderson Hospital and Tumor Institute, Houston, Texas) summarize their experience between 1967 and 1973, on 426 patients. The median survival for all patients, from entry, was 4.7 months. The response rate to a variety of treatment regimens with DIC was 18 percent; the addition of BCNU appeared to increase the response rate of patients with pulmonary and visceral involvement. Patients with clinical involvement limited to the lungs or the subcutaneous and cutaneous tissues had better median survival experience of 10 and 11 months respectively. For CNS involvement, only radiotherapy to the brain with concomitant dexamethasone yielded temporary alleviation. Hepatic metastases were highly correlated with elevated LDH levels in the blood. (August)

Therapeutic approaches targeted at modifying immune responses would be greatly facilitated by more specific quantitative technics that would measure various manifestations of immunologic competence and reactivity.

One of the directions taken by contemporary therapy of disseminated cancer is the use of megadoses of chemicals followed by antidotal measures to sustain the host. Citrovorum factor “rescue” following massive antifolate therapy is an example of this approach. The concept has been applied to immunotherapy, in which a temporary graft-versus-host reaction is induced against leukemia.
M. M. Bortin et al. (Mount Sinai Medical Center, Milwaukee, Wisconsin) treated leukemic AKR mice with chemotherapy, radiotherapy and transplant of bone marrow and lymph node cells from an incompatible donor. The mice were then "rescued" from potentially lethal graft-versus-host (GVH) disease by killing the incompatible cells with specific antiserum plus chemotherapy. Finally, bone marrow transplants from compatible donors were used for hematopoietic restitution. Not only was a significant proportion of the treated animals cured of the transplanted leukemia, but the long-term survivors did not develop the spontaneous leukemia characteristic of this strain of mice. The authors postulate that in addition to the graft-versus-host (GVH) and graft-versus-leukemia (GVL) reactions, there might have been a graft-versus-virus (GVV) reaction. Extensions of these findings to the treatment of human leukemia are obvious. (August)

There are some 85 other reports in the July and August issues, to assure us that not all of cancer research is immunology and chemotherapy. Note is made, as an example, of the resurgence of interest in radioactive isotopes motivated by the 1969 discovery of Edwards and Hayes that carrier-free 67Ga has a high and rather specific affinity for neoplastic tissue. J. Clausen et al. (Institute of Neurochemistry, Copenhagen, Denmark) find that the radionucleotide is associated with transferrin. In tumor homogenates from patients injected intravenously with 67Ga for scintigraphy, 67Ga is preferentially bound to proteins in the nuclei fraction. Intracellular 67Ga is associated with a fast migrating substance with a molecular weight considerably lower than that of ferritin. (August)

Finally, Frank J. Rauscher, Jr., (director of the National Cancer Institute, Bethesda, Maryland) shares with us the complicated details of budget allocations for the National Cancer Program. Whatever other reactions individual analyses might elicit, there should be a sigh of relief at the probable 1974 reversal of the trends initiated in 1972. Let us hope it is not merely a temporary respite, and maintain our vigilance. (July)