Title

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Journal

The Oncologist, 20(11)

ISSN

1083-7159

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Publication Date

2015-11-01

DOI

10.1634/theoncologist.2015-0323

Peer reviewed

The Oncologist®

Tribute

Susan Bates, M.D., and Antonio "Tito" Fojo, M.D., Ph.D.: Thirty Years of Research, Discovery, Service, and Mentorship at the National Cancer Institute

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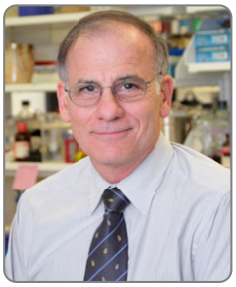
To reckon him who taught me this Art equally dear to me as my parents

Hippocrates

This summer, Dr. Susan Bates and Dr. Antonio "Tito" Fojo announced that they would be leaving the National Cancer Institute (NCI) after more than 30 years of research, teaching, mentorship, and clinical practice. They are transitioning to the Herbert Irving Comprehensive Cancer Center at Columbia University and to the James J. Peters Veteran's Administration Medical Center in New York City. They will be greatly missed in Bethesda, Maryland. At the NCI, their work, integrity, and dedication culminate in a long legacy on the nature, rigor, and focus of translational cancer research, in the lives of numerous trainees, whose own careers received a vital push under their guidance, and in the hearts of hundreds of patients and families, who benefitted from being cared for by these outstanding researchers and master clinicians. We write this as two graduating oncology fellows who benefitted from their wisdom and support these past 3 years, but we are certain we speak for many others.

Susan E. Bates, M.D.



Antonio "Tito" Fojo, M.D., Ph.D.

Although no canonical definition exists for what constitutes a "master clinician," two anecdotes help to convey why Susan and Tito have clearly achieved this caliber. During one of our training conferences, Dr. Bates presented a patient of hers who had experienced an intracranial relapse of HER-2-positive breast cancer and was successfully treated with surgery, radiation, and trastuzumab. Taking trastuzumab alone, she had been without evidence of disease for 10 years [1]. Despite this successful outcome, Dr. Bates was not seeking praise by relating the case; instead, she sought our opinions. Was there anything we would do differently, such as stopping trastuzumab? She posed the question graciously, with open-mindedness, eager to consider other thoughts, even from fellows with far less experience. Such are the traits of an excellent teacher.

With patients, Dr. Fojo's manner is friendly, focused, and caring. He is unflinchingly honest, careful in his choice of words, encouraging, funny, tender, and always kind. We believe that if all the classes in medical school that purport to teach doctor-patient skills were replaced with one afternoon in Tito Fojo's clinic, we would all be better physicians. We recall one particularly tough conversation he had with a patient, which led one of us to comment that he had done it so well. Tito gave a soft smile and replied, "After 30 years, I can't say that I'm good at it. You never are, but I try each year to be a little better."

In both Susan and Tito there is a deep humility—the cardinal virtue of the physician who understands there is much art beyond the science of medicine. Despite their many accomplishments, years of experience, hundreds of publications, and knowledge of the field, they have never stopped seeking to be "a little better" each year.

Antonio "Tito" Fojo began his clinical fellowship in medical oncology at the National Cancer Institute in Bethesda in 1982. He inherited his panel of patients from Susan Bates, a rising second-year fellow. From the moment they entered the NCI, their careers were closely linked. In the three decades that followed, they would be close collaborators. Their work has impacted topics as diverse as the molecular mechanisms of drug resistance, the in vivo kinetics of tumor growth, the methodology of clinical trials, and, forthcoming, the problem of selective reporting and publication bias in the oncology literature.

Each has had their own unique success. Susan focused on the mechanisms of multidrug resistance, helping to identify the important role of transporters such as ABCG2 and P-glycoprotein

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[2]. In the late 1990s, Susan identified a promising compound, FR901228 or depsipeptide, from preclinical work [3]. She helped to elucidate the mechanism of action and would later serve as principal investigator in a multi-institutional, international phase II trial of that drug [4]. Depsipeptide is better known as romidepsin, and Susan's work led to the submission of a New Drug Application and approval of that compound for two indications. She is among the few translational scientists who have brought a novel compound from bench to bedside. With more than 250 publications, Susan has become an important leader in oncology, particularly in drug development. She sits on the editorial boards of multiple journals, including Clinical Cancer Research and ***The Oncologist***. At the NIH, Susan served as head of the Molecular Therapeutics Section and has mentored dozens of clinical and research fellows.

Tito is known for his work on strategies to reverse cancer chemotherapy resistance. His translational work on microtubule-stabilizing agents helped to optimize the delivery of paclitaxel and aided in the clinical development of the epothilone B analog, ixabepilone [5]. Tito has shown in careful empiric work that the tumor growth rate (both with and without medication) and fraction of tumor killed are more faithful representations of a drug's anticancer properties than is progression-free survival or response rate, two indirect measures of these biologic concepts [6]. At the NCI, his clinic has focused on adrenal cancers and neuroendocrine malignancies, providing important clinical care and expertise for these rare tumor types.

In recent years, Tito has commented on the state of cancer drug development. In this Journal—just 2 years after the remarkable success of imatinib, when the field of oncology was riding high on the hopes that all cancer would succumb similarly to targeted therapy—Tito was among the first to liken the unbridled enthusiasm for targeted therapy with the dot-com stock market bubble [7]. It was the first of many of his commentaries that now seem prophetic. In 2009, with Christine Grady, Tito was one of the first oncologists to recognize and criticize the unsustainable increase in cancer drug prices [8]. In that report, Fojo and Grady [8] argued that cetuximab, if used routinely to treat non-small-cell lung cancer and based on the results of the First-Line ErbituX in lung cancer (FLEX) trial, would cost society $440 billion for the marginal gain of 1.2 months of life. Fojo would champion this cause in the popular press [9], as well as in his treatise on the topic, *Unintended Consequences of Expensive Cancer Therapeutics—The Pursuit of Marginal Indications and a Me-Too Mentality That Stifles Innovation and Creativity* [10].

Through these writings and his research, Tito has become a thought leader in oncology, sitting on the editorial boards of multiple journals. At the NCI, he served as the head of the Experimental Therapeutics Section and, for nearly a decade, was program director of the medical oncology fellowship program. He is currently a member of the U.S. Food and Drug Administration's (FDA) Oncologic Drugs Advisory Committee and is oft-quoted in the press. He has mentored hundreds of fellows over the years. Just as in his clinic, with fellows, Tito is willing to tackle even the most challenging cases.

Sanjeeve Balasubramaniam, a graduate of the NCI oncology fellowship and now a medical reviewer at the FDA, worked closely with Susan and Tito for the past decade. About them, Sanjeeve says, "Tito and Susan both served as mentors to many fellows over the years at NCI, but their counsel always exemplified two qualities that they bring to all of their human interactions, regardless of context: compassion and nurturing. I saw this in their approach to trainees, as well as colleagues seeking counsel, and, of course, with the many patients who seek treatment at NCI, usually after multiple prior lines of chemotherapy and with few remaining options. They are both tenacious in their manifestation of compassion, leaving no avenue unexplored, no stone unturned, whether it be for patients or fellows. But most importantly, this compassionate quality is evident in all of their communications: with trainees, colleagues, patients, and one another, and this is what has impacted me so deeply in my years with them, forever changing my relationships with my patients, and my family and friends."

1982 was an important year in cancer medicine. Vincent DeVita was entering his third year at the helm of the National Cancer Institute, and the NCI budget surpassed 1 billion dollars [11]. There was optimism that cancer would soon be defeated. Tito and Susan had just begun what would be long and illustrious careers at the National Cancer Institute. During those early years, they worked closely with Dr. Bruce Chabner, at that time a principal investigator and chief of the newly formed Clinical Pharmacology Branch, before becoming Scientific Director of the NCI and Director of the Division of Cancer Treatment, a position he held until 1995. Recalling his long relationship with both Tito and Susan, Dr. Chabner says, "These fine physician scientists have been invaluable to the conquest of cancer. They have been unselfish, devoted, caring friends and colleagues to a generation of NCI patients, trainees, and faculty, a remarkable team in an era when cancer research as a clinical science came of age."

On a personal note, we recall how Tito and Susan shared the Monday clinic. Their backroom was a hive of activity and the location of many spirited oncology debates. About those debates, there was only one safe bet: if you disagreed with Tito, you might occasionally be right. If you disagreed with Susan, you could, sometimes, have a point. But, if you found yourself disagreeing with both of them, you were bound to be wrong. During 30 years at the NIH, Susan and Tito have proven to be good doctors, good researchers, and good people. In this life, that is as good as it gets.

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Susan with Bruce Chabner

Susan and Tito

Susan and Tito, still collaborating