

## The Role of an NCI Comprehensive Cancer Center in Fostering Basic and Translational Research of Rare Hematologic Disorders

Since its establishment in 1986, the H. Lee Moffitt Cancer Center & Research Institute has focused entirely on cancer care, research, education, and prevention and has served as the focal point for cancer-related interests and activities at the University of South Florida. In recognition of its excellence in scientific research and clinical care, Moffitt Cancer Center was designated a Comprehensive Cancer Center by the National Cancer Institute in 2001, a status recently renewed in 2006. After 20 years, the Cancer Center's mission remains the same: to contribute to the prevention and cure of cancer.

Central to the achievement of the Cancer Center's goals has been the interdisciplinary approach to cancer care and research performed by 270 physicians and scientists who are supported by over 2,000 employees and 200 volunteers. Currently, the Cancer Center consists of six research programs structured under the umbrella of the Moffitt Research Institute (MRI), a 162-bed hospital that in 2005 admitted 6,273 inpatients, an outpatient clinic with over 212,000 visits per year, a comprehensive cancer screening program, an active community education division, and affiliations with several national cooperative groups (SWOG, RTOG, GOG, NSABP) and other Florida hospitals. In addition, the Lifetime Cancer Screening and Prevention Center provided screening services to 18,229 people.

As a result of the significant growth in patient volume, Moffitt Cancer Center is well poised to conduct basic, translational, and clinical research for not only the most common type of malignancies but also those malignant disorders that due to their rarity are not well studied. As discussed below, by assembling a complementary team of basic scientists, physician-scientists, pathologists, and clinicians within the Lymphoma Section at Moffitt Cancer Center, we have been able to develop basic and translational research programs in mantle cell lymphoma and peripheral T-cell lymphomas, two rare malignant disorders.

### Basic and Translational Research in Lymphomas

In 2003, the Malignant Hematology Division at Moffitt

Cancer Center initiated an interdisciplinary Lymphoma Section with the goal of bringing together hematologists/oncologists, hematopathologists, cytogeneticists, and basic scientists sharing a particular interest in the biology, diagnosis, and treatment of lymphomas. Reminiscent of the rapid growth observed in the Cancer Center, the Lymphoma Section also experienced a progressive increase in the number of lymphoma patients being evaluated and treated in our institution. The number of visits to our Lymphoma Clinic has reached 3,500 per year, and in 2005 approximately 500 new lymphoma patients were evaluated in our Section. This growth offered a unique opportunity to not only study the biology, molecular genetics, immunology, and epidemiology of B- and T-cell lymphomas, but also contribute to the identification and validation of novel therapeutic approaches for these malignancies. Our experience to date has been that the development of a comprehensive basic and translational research program in lymphomas, especially for rare subtypes, requires the fulfillment of the following:

- Adequate number of patients and an interdisciplinary team of basic scientists, physician-scientists, and clinicians willing to work together to "attack" these diseases.
- Appropriate collection, banking, and distribution of primary lymphoma tissue.
- Appropriate data management support.

### Adequate Number of Patients and an Interdisciplinary Team Approach

Our initial strategy to increase the number of patients with rare hematologic disorders such as mantle cell lymphoma (MCL) and T-cell lymphomas was to provide patients with these malignancies and their treating oncologists/hematologists with access to innovative clinical trials conducted at Moffitt Cancer Center. For instance, the starting point for our research efforts in MCL was the opening in the fall of 2004 of a phase II vaccine clinical trial using the GM-CSF/CD40 ligand bystander vaccine approach for patients with untreated or relapsed MCL. For vaccine preparation purposes, this clinical trial required an excisional lymph node biopsy at the time of enrollment, which was performed

by the principal investigator, Sophie Dessureault, MD, PhD, a surgeon who shares a particular interest in immunotherapy and vaccine approaches. With the opening of this investigator-initiated clinical trial came an increase in the MCL patient population seen at Moffitt Cancer Center and a parallel increase in collection and banking of primary human MCL cells. Given that only a portion of the excised lymph node was needed for diagnostic purposes and vaccine preparation, we found ourselves with an increasing number of MCL samples that could potentially be used to validate findings that basic scientists in our institution were already obtaining in MCL cell lines and other types of malignant B-cell lines. After fulfilling appropriate regulatory requirements, primary human MCL cells were made available to these investigators who soon became the backbone of our scientific efforts in MCL.

To foster further collaborative and integrated efforts among scientists and clinicians sharing the common interest of understanding the biology, genetics, and immunology of MCL, we then established weekly meetings to discuss the diagnosis and management of new MCL patients seen at Moffitt Cancer Center. We also scheduled monthly scientific meetings to discuss research data generated in MCL cell lines and in primary tissue obtained from MCL patients. As a result of our interdisciplinary approach to this rare hematologic disorder, we were able to create a Program Project entirely devoted to the study of MCL. This Program Project, titled *Biologically Targeted Therapy for Mantle Cell Lymphoma*, was submitted to the National Cancer Institute in October 2006.

A similar approach is being used to build a clinical and research program focused in T-cell lymphomas. Under the direction of Lubomir Sokol, MD, PhD, from the Lymphoma Section at Moffitt Cancer Center, and Frank L. Glass, MD, from the Department of Dermatology at the University of South Florida College of Medicine, we first established a joint Cutaneous Lymphoma Interdisciplinary Clinic (CLIC) in which patients affected with these disorders can be seen simultaneously and/or sequentially by both specialists. This team is supported by other specialists with expertise in radiation oncology, photopheresis, psoralen ultraviolet A (PUVA) treatment, immunotherapy, dermatopathology, and hematopathology. Such an approach, together with the opening of novel clinical trials for patients with T-cell malignancies, has resulted in the rapid growth in the number of patients with T-cell lymphomas being referred to our institution for evaluation and treatment. Having established a solid patient base as well as adequate T-cell lymphoma banking, we are now bringing together basic scientists and physician-scientists from different programs and divisions across the Cancer Center. This multidisciplinary approach will lead to the development of an integrated research effort into the

biology, intracellular signaling, molecular genetics, and immunology of T-cell lymphomas, and it will generate (within the next 18 to 24 months) a Program Project focusing in these uncommon malignancies. An example of this integrated effort to conquer T-cell lymphomas is discussed in this issue of *Cancer Control*, in which Dr Sokol and Dr Glass as guest editors have assembled a distinguished group of experts to discuss relevant topics in the biology, diagnosis, prognosis, and treatment of T-cell lymphomas.

### **Appropriate Collection, Banking, and Distribution of Primary Lymphoma Tissue**

Central to the successful development of a basic and translational research program in MCL and T-cell lymphomas was the establishment in early 2004 of a centralized Lymphoma Tissue Bank under the direction of Jianguo Tao, MD (MCL), and Hernani D. Cualing, MD (T-cell lymphomas). This tissue banking is under the umbrella of the Moffitt Cancer Center Tissue Bank (MCC Tissue Bank) and is in compliance with the University of South Florida-IRB and Privacy Board recommendations and in adherence with government-regulated Good Laboratory Practice (GLP) standards. Operating under IRB-approved informed consent protocols, the Lymphoma Tissue Bank has been able to collect, process, bank, and distribute lymphoma cells from fresh and cryopreserved tumor, frozen tissue blocks, and paraffin-embedded tumor blocks to lymphoma investigators within the Cancer Center. The tumor tissue includes solid lymphoma mass, bone marrow aspirates, and blood and body fluid collections from MCL and T-cell lymphoma patients. Since its creation, the Lymphoma Tissue Bank has played a pivotal role in providing Moffitt investigators with access not only to high quality, well-annotated human specimens but also to associated clinical, molecular, and phenotypic data.

### **Appropriate Data Management Support**

Recently, Moffitt Cancer Center established a bioinformatics system with the goal to integrate tissue banking, the laboratory database, and the clinical database into one common interface. The Lymphoma Tissue Bank, in close interaction with the Biostatistics & Data Management Core at Moffitt Cancer Center, is taking advantage of this in-house bioinformatics expertise to establish an integrated lymphoma bank/clinical database that would allow us to maintain a centralized resource of all prospectively collected and banked specimens. We are planning to incorporate into this database the new findings obtained in a specific MCL or T-cell lymphoma tissue provided to Moffitt's investigators. In the near future, we expect that we will have not only the demographics, clinical outcomes, tissue diagnostic characteristics, and/or imaging studies for a specific MCL or T-cell lymphoma patient, but also new scientific knowledge

about the status of the apoptotic, signaling, and/or immunologic pathways in lymphoma samples being evaluated by investigators at Moffitt Cancer Center.

As can be gathered from above, the development of a basic and translational research program focusing in rare hematologic disorders relies strongly in a coordinated group effort that shares clinical and scientific expertise as well as tools, resources, and experimental models available in each researcher's laboratories. Such an integrated scientific effort would likely discover novel molecular targets and would provide the framework for subsequent development of innovative therapies for not only MCL and T-cell lymphomas but also for more common types of lymphoid malignancies. In the absence of such an interdisciplinary and integrated approach and/or limits in the availability of human tissue for research, such a goal will take longer to be achieved.

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