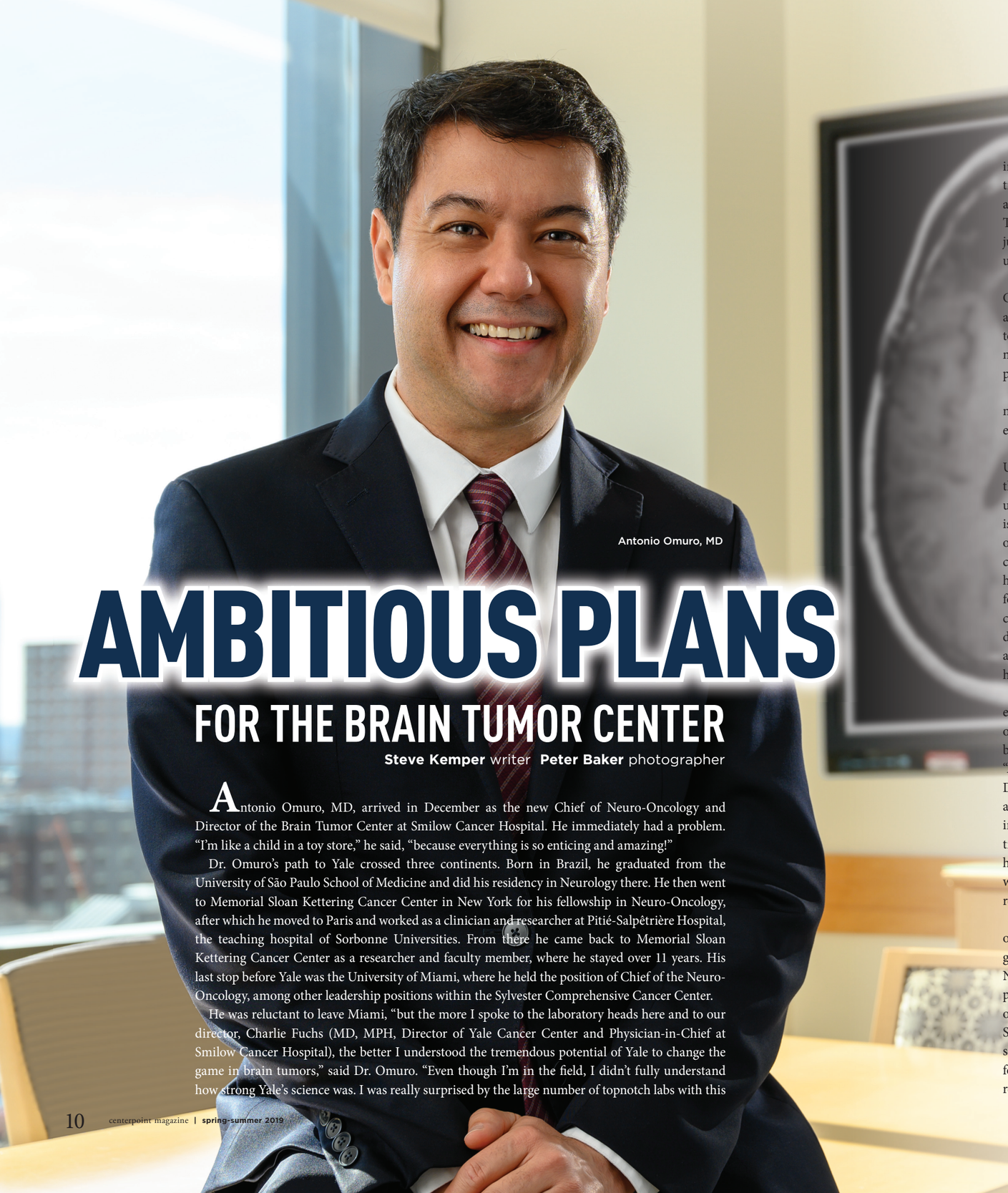

Antonio Omuro, MD

AMBITIOUS PLANS

FOR THE BRAIN TUMOR CENTER

Steve Kemper writer **Peter Baker** photographer

Antonio Omuro, MD, arrived in December as the new Chief of Neuro-Oncology and Director of the Brain Tumor Center at Smilow Cancer Hospital. He immediately had a problem. "I'm like a child in a toy store," he said, "because everything is so enticing and amazing!"

Dr. Omuro's path to Yale crossed three continents. Born in Brazil, he graduated from the University of São Paulo School of Medicine and did his residency in Neurology there. He then went to Memorial Sloan Kettering Cancer Center in New York for his fellowship in Neuro-Oncology, after which he moved to Paris and worked as a clinician and researcher at Pitié-Salpêtrière Hospital, the teaching hospital of Sorbonne Universities. From there he came back to Memorial Sloan Kettering Cancer Center as a researcher and faculty member, where he stayed over 11 years. His last stop before Yale was the University of Miami, where he held the position of Chief of the Neuro-Oncology, among other leadership positions within the Sylvester Comprehensive Cancer Center.

He was reluctant to leave Miami, "but the more I spoke to the laboratory heads here and to our director, Charlie Fuchs (MD, MPH, Director of Yale Cancer Center and Physician-in-Chief at Smilow Cancer Hospital), the better I understood the tremendous potential of Yale to change the game in brain tumors," said Dr. Omuro. "Even though I'm in the field, I didn't fully understand how strong Yale's science was. I was really surprised by the large number of topnotch labs with this incredible talent. I knew about their work individually but had not tied them together around the Yale name, until now. It seems to be a bit of a kept secret, like a gem waiting to become a beautiful jewel. The intellectual capital and the resources here are unparalleled. It's just a matter of grouping them together and put them to the best use."

Dr. Omuro has lots of plans, and expansion of the Brain Tumor Center is central to them. He sees it as a clearinghouse for collecting and distributing information on the vast amount of research related to brain cancer that occurs throughout Yale. He also sees it as a meetinghouse where basic scientists can find clinical partners for projects that can turn research ideas into new therapies.

Advances in the treatment of brain cancers are desperately needed. "There hasn't been a major breakthrough for over 30 years," explained Dr. Omuro.

To begin, he has started to inventory all the labs throughout Yale University currently working on basic and translational research that could be applied to the treatment of brain tumors. So far he's up to over 20 labs. "And the list keeps growing," he said. "What is interesting is that many of these investigators were not aware of what the others were doing, and they didn't know how to get clinical support to help them develop their new ideas and test their hypotheses in patients. We are going to give these investigators a forum in which to present their work, exchange ideas, and establish collaborations. We are also providing them with advice to best determine the kind of experiments and select new treatments that are most likely to have a path forward for clinical development, and hopefully fund the best projects."

He ticked off several possibilities for collaborations. For example, the lab of Murat Gunel, MD, Chair of the Department of Neurosurgery, has been doing whole exome sequencing on all brain tumor patients operated on at Smilow for several years now. "A host of projects can come out of that genomic information," said Dr. Omuro. "We have investigators trying to understand the tumor and the role of each identified mutation. Yale is also very strong in immunology and brain microenvironment, and we have people trying to understand the interactions between the tumor and the host. It's a complicated process, and we have these ultra-specialists working on all aspects of it, but they have to talk to each other if we really want to make a difference."

Together with Dr. Gunel, Dr. Omuro has also been working on the arduous process of assembling an application for a SPORE grant (Specialized Programs of Research Excellence) from the National Cancer Institute. SPOREs are given to institutions of proven excellence who submit projects that show strong promise of moving quickly from basic scientific findings to clinical testing. SPORE projects require intensive multidisciplinary collaborations, so Dr. Omuro sees the application process as another opportunity for Yale scientists to share resources, exchange ideas, fine-tune research, and fast-track lab breakthroughs to the clinic.

Once all of Yale's labs are sharing their information on brain tumors, Dr. Omuro hopes to create a platform that uses artificial intelligence (AI) and machine learning (ML) to deepen and expand the application of the information. Some labs have started to use the enormous data science resources available at Yale, but others researchers have not accessed AI and ML yet. Dr. Omuro plans to set up a platform where investigators can learn which labs have these technologies and how they are being used, and can request help to meet their needs. He also wants to bring these technologies into clinical research and direct patient care.

"We have our own machine learning laboratory, led by Sanjay Aneja (MD)," said Dr. Omuro, "and he will help us with clinical developments and to improve the care of our patients, for instance by using AI resources to help physicians improve safety and predict outcomes."

He mentions a pilot project that is using deep learning methodologies to analyze patients with primary central nervous system (CNS) lymphoma. "We hope we will be able to predict, from the beginning, who will be cured and who will not be cured by existing treatments, based only on analysis of the first MRI scan," he said. "This type of technology is in its infancy when it comes to health care, but we want Yale to have a prominent role in its development, and we are ahead of most institutions."

The Center will also focus heavily on the development of clinical trials based on Yale science. Dr. Omuro singles out two projects. While investigating multiple sclerosis (MS) in his lab, David A. Hafler, MD, Chair of the Department of Neurology, discovered that expression of an immune check point called TIGIT was decreased in MS patients but increased in patients with glioblastoma. That is, TIGIT was protecting brain tumor cells by suppressing the immune system's T-cells. Dr. Hafler wondered whether targeting TIGIT would release T-cells to do their job against the cancer. He has been investigating that in laboratory models, and a clinical trial is expected to begin sometime this summer.

Dr. Omuro's other example is the work of Ranjit Bindra, MD, PhD, Associate Professor of Therapeutic Radiology and Experimental Pathology. Dr. Bindra discovered that a PARP inhibitor called olaparib can suppress the IDH-1 mutations common in gliomas. This innovative and promising immunotherapy is now in Phase 2 clinical trials at Yale and elsewhere. Dr. Bindra is one of the Brain Tumor Center's co-directors, along with Jennifer Moliterno, MD and Veronica Chiang, MD. The center's leadership team is working together to transform all these ideas and vision into real progress for the benefit of brain tumor patients.

"These are the kinds of opportunities that Yale makes possible," said Dr. Omuro, as enthusiastically as a child in a toy store.