Investigating New Brain Tumor Therapies

C. David James, PhD, Neurological Surgery, Biochemistry Molecular Genetics

For 30 years, C. David James, PhD, has focused on understanding how gene alterations lead to malignant brain tumors – research he uses to identify novel treatments for patients.
In one recent paper published in *Nature Medicine*, he and colleagues demonstrated in mice that a small molecule inhibitor can reverse a histone mutation found in the majority of patients with diffuse intrinsic pontine, delaying tumor growth and prolonging survival.

The goal of his research is to identify therapeutic agents and treatments that improve outcomes for brain tumor patients.

James joined the Feinberg faculty in 2014 from the University of California San Francisco. He is a professor of Neurological Surgery and Biochemistry and Molecular Genetics, vice chair of research in the Department of Neurological Surgery and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Q&A

What are your research interests?
I have a longstanding interest in the study of the molecular, cellular and biological aspects of human brain tumors. In association with this interest, I have developed a number of unique model systems based on the serial propagation of human brain tumors as subcutaneous xenografts in immunocompromised mice. This approach to tumor cell propagation has been shown to better preserve tumor characteristics as manifested in patients than tumor cell propagation in cell culture. In association with the development of these models, my laboratory utilizes numerous techniques to investigate brain tumor growth and response to novel agents that are administered singularly or in combinations to animal subjects, following subcutaneous tumor transfer to the brains of immunocompromised mice.

What types of collaborations are you engaged in across campus (and beyond)?
Of the collaborations I've become involved in with Northwestern faculty, I'm especially enthusiastic about interactions between our pediatric brain tumor research group and the lab of Ali Shilatifard, PhD, chair of Biochemistry and Molecular Genetics. Pediatric brain tumors are presenting some interesting opportunities to study the importance of histone modifications in cancer development and Shilatifard is a renowned expert on the role of histone modifications in regulating gene expression. Through our interactions with Shilatifard and his laboratory, I feel as though I'm getting an advanced education in an area of cancer molecular biology that is emerging as a subject of keen interest in the development of novel therapeutic approaches for improving cancer patient treatment outcomes.

How did you become interested in this area of research?
As a graduate student, I studied c-myc oncogene translocations in Burkitt lymphoma and became hooked on investigating how somatic mutations cause normal cells to become tumor cells. I carried that interest into my postdoctoral training, where there were substantial resources for studying gene alterations in brain tumors. Little was known about brain tumor gene alterations at that time – it was 1986. My subsequent career path has therefore been a result of an intersection between my inherent interests, resource availability and the opportunity for discovery in studying gene alterations in an organ system for which little was known about the cancer-associated genetic etiology.

How is your research funded?
I have received research support from several philanthropic organizations, including the Pediatric Brain Tumor Foundation, the James S. McDonnell Foundation, Voices Against Brain Cancer and Accelerate Brain Cancer Cure. In addition, my research has been continuously supported by one or more NIH grants since 1991, with current NIH funding to extend into 2021.

What do you enjoy about teaching and mentoring young scientists in the lab?
The mentor-mentee relationship is bidirectional with respect to learning. The energy, inquisitiveness and creative thinking of young investigators stimulates my own thinking, such that, at the end of the day, I feel I learn as much from trainees as they learn from me. By continually being asked the question of "Why?" from young investigators, I have to constantly reevaluate the basis of my own thinking and opinions, with the end result being the growth and continuous evolution of my understanding regarding cancer origin, progression and treatment.