EDITORIAL

Closing the Gap: Working Toward Effective Therapy for DIPGs

Diffuse intrinsic pontine gliomas (DIPGs) are aggressive tumors that affect primarily elementary school-aged children. Affected children present with fewer than 6 months of symptoms and have characteristic physical findings and radiographic imaging. Unfortunately, in spite of decades of attempts, no treatment has been found to cure DIPGs, though radiation therapy does prolong survival for a few months. The median survival of these tumors is a meager 9-11 months.

In this issue of Current Neuropharmacology, experts in the field of DIPG research present the issues of interest and potential growth for this burgeoning field. Drs. Infinger and Stevenson begin a thoughtful conversation about the diagnosis of DIPGs [1]. As is widely known, DIPGs were once diagnosed after a biopsy. However, in the 1990s, the approach to DIPG diagnosis was changed dramatically, making this the only brain tumor that is reliably diagnosed without tissue confirmation. Initially, this change was made to diminish the unwanted side effects of biopsies. However, a long-term and unintended consequence of this change was a paucity of molecular information about these tumors. In an era of molecularly guided therapies, DIPG therapy lags behind.

To deal with this quandary, Drs. Johung and Monje share the state of the development of therapeutic targets for DIPGs [2]. In their hands, DIPG tumor cells reveal genomic and epigenomic profiles to reveal the disease mechanisms and possible targets. They discuss the dissemination potential of DIPGs as well as a potential cell of origin for DIPG cells. Most interestingly, they describe the histone mutations now defining DIPGs, within the H3 histone family. The majority of these mutations occur in the H3F3A gene, which encodes histone H3.3. Histone mutations might well provide therapeutic targets for DIPGs as our understanding of these complex and resistant tumors continues to develop.

Drs. Hashizume and Gupta follow with an in-depth description of patient-derived DIPG tumor models [3]. They review the challenges in the development of clinically relevant xenograft models for DIPG, as the cell lines previously used are not ideally similar to de novo brain tumors and there are challenges in the replication of tumors in the tiny pons of the commonly used murine models. They also describe the advances in in vivo animal imaging that have provided additional information related to the growth and development of these orthotopic models. Finally, they educate us about the development of these patient-derived cell lines and the challenges and opportunities for learning within the confines of cellular and animal models of DIPGs.

Dr. Broome and her colleagues then discuss the state-of-the-art in targeting nanotechnology approaches for successful delivery of chemotherapy into the cellular milieu of DIPGs [4]. They discuss the barriers to the treatment of DIPG, both anatomic and molecular, and a few ideas on how to circumvent both of these barriers. They elaborate on a variety of nanoparticles and the benefits of each group and the various administration routes that might seen as options for the treatment of DIPGs and other high grade gliomas.

Finally, Dr. Souweidane and his colleagues directly address a novel chemotherapy administration route under investigation for the treatment of DIPGs [5]. Convection-enhanced delivery of chemotherapy offers the advantages of directly delivering chemotherapy into the area of disease, a chemotherapy delivery challenge which has not previously been circumvented. The challenge of direct infusion of chemotherapy into a restricted area, such as the pons, is one of engineering as well as biology. They address the many design challenges in the development of this approach and make a persuasive argument that convection-enhanced delivery of chemotherapy may be both safe and effective in the management of DIPGs. We are waiting, with eager anticipation, for the results of Dr. Souweidane’s current clinical trial investigating this precise question.

REFERENCES


Amy-Lee Bredlau, MD
(Guest Editor)
Director, Pediatric Brain Tumor Program
Assistant Professor, Sullivan Scholar
Pediatric Hematology/Oncology
Medical University of South Carolina
135 Rutledge Avenue, MSC 558
Charleston, SC 29425
USA
E-mail: bredlau@musc.edu