

# JOHNS HOPKINS

MEDICAL INSTITUTIONS

## Department of Pathology

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The Board of Directors of  
Lauren's First and Goal Foundation  
1002 B Bartlett Loop  
West Point, NY 10996

Dear Ladies and Gentlemen:

On behalf of all of us in the Division of Neuropathology in the Johns Hopkins Department of Pathology, I want to again extend our sincere appreciation for the generous support we receive from the Lauren's First and Goal Foundation. Because of you, we have the crucial resources our team of dedicated researchers needs to continue moving our pediatric brain tumor research forward, for all of us.

I am pleased to provide you with a summary highlighting the team's activity over the past year. Our overall research focus remains unchanged: (1) to identify molecular changes in pediatric low-grade gliomas, predominantly pilocytic and pilomyxoid astrocytomas (PA/PMA), that facilitate more accurate diagnosis; (2) to search for molecular "weak spots" that can serve as the targets of new, more effective therapies; and (3) to develop new models of these tumors, and testing agents in the laboratory and clinic that target specific molecular alterations.

- 1) As reported in prior updates, support from Lauren's First and Goal has allowed us to use a technique known as "conditional reprogramming of cells" to attempt to grow various types of pediatric low-grade gliomas in culture. These have been shared with an NIH-sponsored repository where they will soon be used to screen for new drugs which may slow their growth. We are also working in our laboratory to test new therapies using these models in zebrafish.
- 2) We recently collaborated with the laboratory of Hui Zhang, Ph.D. at Johns Hopkins, which has developed a pipeline for looking at changes to thousands of protein phosphorylation sites in tumors cells. We used this to better understand how pediatric gliomas driven by mutations in "BRAF" become resistant to therapy. A copy of the paper describing this work is attached. (Maxwell MJ et al. Unbiased Proteomic and Phosphoproteomic Analysis Identifies Response Signatures and Novel Susceptibilities After Combined MEK and mTOR Inhibition in BRAFV600E Mutant Glioma. *Mol Cell Proteomics* 2021; Jul 21. PMID: 34298159). We plan to expand on this technique, using additional models and treatments to develop more precise and effective mechanisms for patient care.
- 3) Drs. Charles Eberhart and Fausto Rodriguez recently helped to author a comprehensive review article on pilocytic astrocytomas. A copy of the paper, which acknowledges the support of Lauren's First and Goal, is attached. (Milde T, Rodriguez FJ, Barnholtz-Sloan JS, Patil N, Eberhart CG, Gutmann DH. Reimagining pilocytic astrocytomas in the context of pediatric low-grade gliomas. *Neuro Oncol* 2021; Oct 1;23(10):1634-1646. PMID: 34131743). We are currently working with this international group to compare our new models with other models of pilocytic astrocytomas to determine which will be most effective for preclinical testing.

- 4) As we have previously shared, Drs. Rodriguez and Eberhart are among the select group of pathologists and oncologists from around the world drafting a new World Health Organization (WHO) classification scheme for brain tumors, including pediatric low-grade gliomas. This new edition was delayed, but hopefully will be published before the end of 2021. Dr. Eberhart has also been selected as part of the editorial board for the new WHO classification of Eye Tumors, which will include pilocytic astrocytoma and other gliomas of the optic nerve.

Finally, I want to share with you that Dr. Rodriguez left Johns Hopkins in October 2021 to join the University of California, Los Angeles, where he will be the Director of Neuropathology. We plan to continue collaborating with him on our PA/PMA research and wish him the best in his new leadership position.

Despite the continuing challenges of the pandemic, with your help, our team has continued to make important advances in the diagnosis and treatment of pediatric brain tumors. Lauren's First and Goal Foundation continues to be an invaluable partner in raising awareness and research support, helping us to bring hope to the children and their families living with these tumors. For that, we are deeply grateful.

Wishing you and your families a very happy Thanksgiving!

Warm regards,



Charles Eberhart, M.D., Ph.D.

Charlotte A. Wilson and Margaret K. Witener Professor of Ophthalmology  
Professor of Pathology, Ophthalmology and Oncology  
Director of Neuropathology  
Chief of Ophthalmic Pathology

Attachments

cc: Michaela McAuliffe, Assistant Director of Development, Department of Pathology