

«SPITZENMEDIZIN VERBESSERT DIE ZUKUNFT DER KINDER»
FREITAG, 2. SEPTEMBER 2022



Inputreferat 3

Prof. Dr. Javad Nazarian

Direktor Hirntumor-Institut, Children's National Hospital Washington &
Leiter DMG Forschungszentrum Universitäts-Kinderspital Zürich

Dr. Javad Nazarian is the Scientific Director of the Brain Tumor Institute at Children's National Hospital in Washington, D.C and the Head of DMG Research Center at University Children's Hospital, Zurich Switzerland. He is also an Associate Professor of Pediatrics at the George Washington University School of Medicine and Health Sciences in Washington, D.C. In his role, Dr. Nazarian has formed national and international collaborations to establish a translational and multi-disciplinary team focusing on childhood high grade gliomas.

Dr. Nazarian's research focus has been understanding the molecular pathways driving childhood brain cancers and, most importantly, finding ways for rapid translation of laboratory findings to the clinic. His research groups in Zurich and at Children's National Hospital in Washington DC, have extensive expertise in developing biorepositories, disease preclinical models, performing molecular analyses, drug assays, and correlative studies for ongoing clinical trials, including utilization of liquid biopsy and low intensity focused ultrasound. His laboratory at Children's National houses one of the most comprehensive and well annotated brain tumor biorepositories in the world. This has enabled the team to conduct extensive studies toward understanding mutations that drive tumors and the genomic landscape that can help to drive the development of novel mechanisms for targeted therapies. He has recently expanded his research group at Children's National to focus on Neurofibromatosis type 1 (NF1) transformed low-grade gliomas (LGGs). This research includes associated gliomas with a special emphasis on NF1-associated transformed anaplastic LGGs. His team is developing new avenues of research into childhood and young adult NF-associated LGGs with a special emphasis on transformed high-grade gliomas.

Dr. Nazarian is an expert in forming and leading national and international collaborations, and in disease/pathway-focused team building. He currently serves on the Scientific Committee and Executive Board of the Children's Brain Tumor Network. Additionally, working in close collaboration with Pacific Pediatric Neuro-Oncology Consortium (PNOC), Dr. Nazarian has established a working group encompassing 18 international institutions across North America, Europe and Australia. The Diffuse Midline Glioma-Adaptive Combinatory Trial (DMG-ACT) team's primary goal is to generate hypothesis derived preclinical data, test across institutions, validate using multiple preclinical DMG models, and provide input to the clinical team. The team's goal is to accelerate the discovery of clinically translatable therapies for the treatment of childhood brain cancers. Since inception in January 2020, the DMG-ACT team has generated data to support two new clinical trials with adaptive arms for children diagnosed with diffuse midline gliomas.

Dr. Nazarian earned his B.S. in Biochemistry from Florida State University and his M.Sc. and Ph.D. in Genetics from The George Washington University School of Medicine and Health Sciences.

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Recent and Notable Publications:

- Bonner ER, Waszak SM, Grotzer MA, Mueller S, Nazarian J. Mechanisms of imipridones in targeting mitochondrial metabolism in cancer cells. *Neuro Oncol.* 2021 Apr 12;23(4):542-556. doi: 10.1093/neuonc/noaa283. PMID: 33336683; PMCID: PMC8041338. <https://pubmed.ncbi.nlm.nih.gov/33336683/>
- Kambhampati M, Panditharatna E, Yadavilli S, Saoud K, Lee S, Eze A, Almira-Suarez MI, Hancock L, Bonner ER, Gittens J, Stampar M, Gaonkar K, Resnick AC, Kline C, Ho CY, Waanders AJ, Georgescu MM, Rance NE, Kim Y, Johnson C, Rood BR, Kilburn LB, Hwang EI, Mueller S, Packer RJ, Bornhorst M, Nazarian J. Harmonization of postmortem donations for pediatric brain tumors and molecular characterization of diffuse midline gliomas. *Sci Rep.* 2020 Jul 2;10(1):10954. doi: 10.1038/s41598-020-67764-2. PMID: 32616776; PMCID: PMC7331588. <https://pubmed.ncbi.nlm.nih.gov/32616776/>
- Lee S, Kambhampati M, Almira-Suarez MI, Ho CY, Panditharatna E, Berger SI, Turner J, Van Mater D, Kilburn L, Packer RJ, Myseros JS, Vilain E, Nazarian J, Bornhorst M. Somatic Mosaicism of IDH1 R132H Predisposes to Anaplastic Astrocytoma: A Case of Two Siblings. *Front Oncol.* 2020 Jan 14;9:1507. doi: 10.3389/fonc.2019.01507. PMID: 32010615; PMCID: PMC6971203. <https://pubmed.ncbi.nlm.nih.gov/32010615/>
- Mueller S, Jain P, Liang WS, Kilburn L, Kline C, Gupta N, Panditharatna E, Magge SN, Zhang B, Zhu Y, Crawford JR, Banerjee A, Nazemi K, Packer RJ, Petritsch CK, Truffaux N, Roos A, Nasser S, Phillips JJ, Solomon D, Molinaro A, Waanders AJ, Byron SA, Berens ME, Kuhn J, Nazarian J, Prados M, Resnick AC. A pilot precision medicine trial for children with diffuse intrinsic pontine glioma-PNOC003: A report from the Pacific Pediatric Neuro-Oncology Consortium. *Int J Cancer.* 2019 Oct 1;145(7):1889-1901. doi: 10.1002/ijc.32258. Epub 2019 Apr 3. PMID: 30861105. <https://pubmed.ncbi.nlm.nih.gov/30861105/>
- An S, Camarillo JM, Huang TY, Li D, Morris JA, Zoltek MA, Qi J, Behbahani M, Kambhampati M, Kelleher NL, Nazarian J, Thomas PM, Saratsis AM. Histone tail analysis reveals H3K36me2 and H4K16ac as epigenetic signatures of diffuse intrinsic pontine glioma. *J Exp Clin Cancer Res.* 2020 Nov 25;39(1):261. doi: 10.1186/s13046-020-01773-x. PMID: 33239043; PMCID: PMC7687710. <https://pubmed.ncbi.nlm.nih.gov/33239043/>
- Hoeman CM, Cordero FJ, Hu G, Misuraca K, Romero MM, Cardona HJ, Nazarian J, Hashizume R, McLendon R, Yu P, Procissi D, Gadd S, Becher OJ. ACVR1 R206H cooperates with H3.1K27M in promoting diffuse intrinsic pontine glioma pathogenesis. *Nat Commun.* 2019 Mar 4;10(1):1023. doi: 10.1038/s41467-019-08823-9. PMID: 30833574; PMCID: PMC6399349. <https://pubmed.ncbi.nlm.nih.gov/30833574/>
- Panditharatna E, Kilburn LB, Aboian MS, Kambhampati M, Gordish-Dressman H, Magge SN, Gupta N, Myseros JS, Hwang EI, Kline C, Crawford JR, Warren KE, Cha S, Liang WS, Berens ME, Packer RJ, Resnick AC, Prados M, Mueller S, Nazarian J. Clinically Relevant and Minimally Invasive Tumor Surveillance of Pediatric Diffuse Midline Gliomas Using Patient-Derived Liquid Biopsy. *Clin Cancer Res.* 2018 Dec 1;24(23):5850-5859. doi: 10.1158/1078-0432.CCR-18-1345. Epub 2018 Oct 15. PMID: 30322880; PMCID: PMC6279526. <https://pubmed.ncbi.nlm.nih.gov/30322880/>
- Lee S, Kambhampati M, Yadavilli S, Gordish-Dressman H, Santi M, Cruz CR, Packer RJ, Almira-Suarez MI, Hwang EI, Nazarian J. Differential Expression of Wilms' Tumor Protein in Diffuse Intrinsic Pontine Glioma. *J Neuropathol Exp Neurol.* 2019 May 1;78(5):380-388. doi: 10.1093/jnen/nlz021. PubMed PMID:30990879; PubMed Central PMCID: PMC6467196.