BIOGRAPHICAL SKETCH

Provide the following information for each individual included in the Research & Related Senior/Key Person Profile (Expanded) Form.

NAME:
HUANG, ANNIE

POSITION TITLE:
Senior Scientist, Professor, Tier 1 Canada Research Chair, Hospital for Sick Children, University of Toronto

EDUCATION/TRAINING

INSTITUTION AND LOCATION	Degree(If Applicable)	YEAR (s)	FIELD OF STUDY
University of Toronto, Canada	PhD	1993	Medical Molecular Genetics
University of Toronto, Canada	MD	1995	Medicine
SickKids Hospital, Toronto, Canada	Residency	1998	Clinical Genetics,
SickKids Hospital, Toronto, Canada	Clinical Fellowship	2000	Pediatrics
Ontario Cancer Institute, Toronto, Canada	Research Fellowship	2002	Haematology / Oncology
			Molecular and Cell Biology

A. Personal Statement

Dr. Huang is a clinician-scientist at the Labatt Brain Tumor Research Center, Cell Biology Program, Hospital for Sick Children/University of Toronto, who has focused on basic science and translational research for rare embryonal brain tumors that primarily affect younger children. She established the global collaborative Rare Brain Tumor Consortium (rarebraintumorconsortium.ca), now one of the largest clinical registry and biorepository for rare cancers, that has played an important role in advancing clinical and biological understanding of these orphan cancers. Her laboratory was one of the first to define the molecular landscape and develop novel diagnostic and subtyping tools for rare CNS cancers including ATRTs, ETMR and Pineoblastoma. Current and future work in the Huang lab is aimed at deeper mechanistic understanding, development of disease models and informing innovative therapeutics for these rare cancers.

B. Positions and Honors

Positions

2002 – Present Neuro-Oncologist, Division of Hematology/Oncology, Dept. of Pediatrics, SickKids Hospital
2006 – Present Principal Investigator, Labatt Brain Tumor Research Centre, SickKids Research Institute
2013 – Present Senior Scientist, Cell Biology Program, Research Institute, SickKids Hospital
2017 – Present Professor, Departments of Pediatrics, Medical Biophysics, Lab Medicine and Pathobiology, University of Toronto
2020 – Present Associate Chair of Research, Department of Paediatrics, SickKids Research Institute

Honours:

2019 Tier 1 Canada Research Chair in Rare Childhood Brain Tumours

2019 –2026	Awarded: Canada Research Chair Tier 1; Rare Pediatric Brain Tumors.
2019	Nominee: Mentorship Award. Children's Oncology Group Young Investigators Committee.

Leadership and Committee contributions:

2004 – Present	Founder/lead investigator, Rare Brain Tumour Consortium:(http://rarebraintumorconsortium)
2012 – Present	PNET Biology Studies Lead, Head Start Childhood Brain Tumor Clinical Trials Consortium
2016 – Present	Biology co-chair, Head start 4 for Newly diagnosed children (less than 10 years old) with medulloblastoma and other central nervous system primitive neuro-ectodermal tumors
2016 – Present	Embryonal Brain Tumour Committee, Children's Oncology Group (COG)
2016 – Present	CNS Tumors Leadership Committee, Children's Oncology Trial Group (COG)
2016 – Present	Chair, CNS Tumors Biology Studies Committee, Children s Oncology Trial Group (COG)
2017 – Present	Site Lead, Canadian Child Health Clinician Scientist Program, University of Toronto
2017 – Present	College of Reviewers, Canadian Institute of Health Research (CIHR)
2017 – Present	Institutional Co-PI, Pacific Pediatric Neuro-Oncology Consortium (PNOC)
2018 – Present	Associate Editor, Neuro-Oncology
2018 – Present	Steering Committee, Collaborative Network for Neuro-Oncology Clinical Trials (CONNECT)
2018 – Present	CNS Lead, Solid Malignancy Translational Research Committee, Children's Oncology Group (COG)
2018 – Present	Permanent member, CAMP study section, NIH
2019 – Present	Co-lead ATRT Working group, Pacific Pediatric Neuro-Oncology Consortium (PNOC)
2019 – Present	Associate Editor, Neuro-Oncology Advances
2020 – Present	Lead, Pediatric Track, Society of Neuro-Oncology

C. Contributions to Science

1. Rare Brain Tumour Consortium (RBTC; rarebraintumorconsortium.ca):

Dr Huang established the RBTC, an international collaborative consortium of >146 centres with a clinical registry and linked biorepository of >3000 rare pediatric brain tumours to provide a much needed resource for studies of these orphan diseases. Since its inception, the RBTCs unique reagents and data sets have been used in multiple landmark discovery and clinical publications, and to inform evaluation of prospective trial cohorts.

Capper D, et al. DNA methylation-based classification of human central nervous system tumors. *Nature. 2018 Mar 22; 555 (7697):469-474.*

Johann PD, et al. Atypical Teratoid/Rhabdoid Tumors Are Comprised of Three Epigenetic Subgroups with Distinct Enhancer Landscapes. *Cancer Cell. 2016 Mar 14; 29(3):379-93.*

Lambo S, et al. The molecular landscape of ETMR at diagnosis and relapse. *Nature. 2019 Dec 04; 576(7786):274-280.*
Reddy A, et al. Efficacy of High-Dose Chemotherapy and Three-Dimensional Conformal Radiation for Atypical Teratoid/Rhabdoid Tumor: A Report from the Children's Oncology Group Trial ACNS0333. *Journal of Clinical Oncology. 2020 Feb 27*

2. Molecular categories and prognosticators in rare embryonal brain tumours:
Dr Huang's lab has generated some of the first molecular data on rare embryonal brain tumours previously called "CNS-PNETs", which enabled discovery of new diagnostic markers and disease categories including identification of the novel C19MC oncogene in ETMRs, molecular sub-classes of ATRTs and pineoblastoma. These discoveries are informing diagnostic schemas and have been incorporated into the WHO diagnostic classification for brain tumours.

Picard D, Miller S, Hawkins CE, Huang A. Markers of survival and metastatic potential in childhood CNS primitive neuro-ectodermal brain tumors: an integrative genomic analysis. *Lancet Oncology. 2012; 13(8):838-48.*

Spence T, et al. CNS-PNETs with C19MC amplification and/or LIN28 expression comprise a distinct histo-genetic diagnostic and therapeutic entity. *Acta Neuropathol. 2014 Aug; 128(2):291-303*

Torchia J, et al. Molecular subgroups of atypical teratoid rhabdoid tumours in children: an integrated genomic and clinicopathological analysis. *The Lancet Oncology. 2015 May;16(5):569-82.*

Li BK, et al. Pineoblastoma segregates into molecular sub-groups with distinct clinico-pathologic features: A Rare Brain Tumor Consortium registry study. *Acta Neuropathologica. 2020 Feb;139(2):223-241.*

Liu A, et al. Clinical and molecular heterogeneity of pineal parenchymal tumors: a consensus study. *Acta Neuropathol. 2021 Feb 22. doi: 10.1007/s00401-021-02284-5. Epub ahead of print. PMID: 33619588.*

3. Novel oncogenic mechanisms and therapeutic targets in rare EBTs:

The Huang lab has leveraged conventional and functional genomic tools to gain insights into oncogenic mechanisms underlying rare embryonal tumors including ETMRs and ATRTs. They have demonstrated that both of these infant brain tumors are primarily driven by epigenetic mechanisms. For ETMRs, they discovered the large polycistronic C19MC miRNA locus is activated by entrapped hybrid enhancers to drive a multiple oncogene dependency in ETMRs. Their work also showed that ATRTs comprise therapeutically distinct molecular classes, driven primarily by epigenetic mechanisms due to defective SWI/SNF functions.

Li M, et al. Frequent amplification of a chr19q13.41 microRNA polycistron in aggressive primitive neuroectodermal brain tumors. *Cancer Cell. 2009 Dec 8; 16(6):533-46*

Spence T, et al. A novel C19MC amplified cell line links Lin28/let-7 to mTOR signaling in embryonal tumor with multilayered rosettes. *Neuro Oncol. 2014 Jan;16(1):62-71. doi: 10.1093/neuonc/not162. Epub 2013 Dec 4*

Kleinman CL, et al. Fusion of TTYH1 with the C19MC microRNA cluster drives expression of a brain specific DNMT3B isoform in the embryonal brain tumor ETMR. *Nat Genet. 2014 Jan; 46(1):39-44. Epub 2013 Dec 8.*

Torchia J, et al. Integrated (epi) Genomic Analyses Identify Subgroup – Specific Therapeutic Targets in CNS Rhabdoid Tumors. *Cancer Cell. 2016 Dec 12; 30(6):891-908.*

Li H, et al. HERC3-mediated SMAD7 ubiquitination degradation promotes autophagy-induced EMT and chemoresistance in glioblastoma. *Clinic Cancer Research. 2019 Jun 15;25(12):3602-3616*

Sin-Chan P, et al. A C19MC-MYCN-LIN28A oncogenic circuit driven by hijacked super-enhancers represents a distinct therapeutic vulnerability in ETMRs. *Cancer Cell. 2019 Jul 8;36(1):51-67.e7.*

Published Work Link: https://pubmed.ncbi.nlm.nih.gov/?term=annie+huang&sort=date

Book Chapters Published

1. Li BK, Khan S, Mumal I, Raguram N, Lafay-Cousin L, **Huang A**. *Embryonal Brain Tumors*. In: Pediatric Neuro-Oncology, 2nd Edition. (Scheinemann K, Bouffet E, ed). Springer Publishing. 2021: 127-138.

2. Habeler C, Kool M, Hasselblatt M, **Huang A,** Judkins A, Wesseling P. *Atypical Rhabdoid Teratoid Tumours*. Chapter 4.2.0.2. In: WHO Classification of Tumors: Central Nervous System Tumours. 5th Edition. IARC Publications. 2021: 221-225

3. Wesseling P, Korshunov A, Kool M, Strum D, **Huang A,** von Hoff K. *Embryonal Tumors with Multi-layered Rosettes.* Chapter 4.2.0.4. In: WHO Classification of Tumours: Central Nervous System Tumors. 5th Edition. IARC Publications. 2021: 228-231.

4. Wesseling P, Korshunov A, Strum D, Kool M, Strum D, **Huang A,** von Hoff K, Haberler C. *CNS Embryonal Tumour.* Chapter 4.2.0.6. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 220-238.

5. Wesseling P, Korshunov A, Kool M, Strum D, **Huang A,** von Hoff K, Solomon D. *CNS Tumour with BCOR internal tandem duplication.* Chapter 4.2.0.7. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 235-237.

6. Hasselblatt, M, Orr BA, Jones DTW, **Huang A**, Sunerl M, Vasiljevic A. *Pineocytoma*. Chapter 5.0.0.1. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 243-245.

7. Hasselblatt, M, Orr BA, Jones DTW, **Huang A**, Sunerl M, Vasiljevic A. *Pineal Parenchymal Tumours of Intermediate Differentiation*. Chapter 5.0.0.1. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 246-248.

8. Hasselblatt, M, Orr BA, Jones DTW, **Huang A**, Sunerl M, Vasiljevic A. *Pineoblastoma.* Chapter 5.0.0.1. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 249-252.

9. Hasselblatt, M, Orr BA, Jones DTW, **Huang A**, Sunerl M, Vasiljevic A. *Papillary Tumour of the Pineal Region.* Chapter 5.0.0.1. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 253-255.

10. Hasselblatt, M, Orr BA, Jones DTW, **Huang A**, Sunerl M, Vasiljevic A. *Desmoplastic myxoid tumour, SMARCB1 mutant,* Chapter 5.0.0.1. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 256-258.

11. Solomon DA, Alexandrescu S, Pfister S, von Diemling A, Kolsche C, Brent DA, Strum D, **Huang A**, von Hoff K, Haberler C, Foulkes W. *Primary intracranial sarcoma, DICER1-mutant*. Chapter 8.2.0.2. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 323-325.

12. Judkins A, Wesseling P, Biegel JA, Eberhart C, **Huang A**, Kool M. *Rhabdoid Tumour Pre-disposition Syndrome*. Chapter 14.0.012. In: WHO Classification of CNS Tumours 5th Edition. IARC Publications. 2021: 460-461.

13. **Huang A**, Holly L, Poussaint T, Adesina A, Pollack I, Bouffet E, Chinatagumpala M. *Tumors of the Central Nervous System Tumors A Embryonal and Pineal Region*. In: Principles and Practice of Pediatric Oncology 8th Edition. (Blaney S, Helman L, Adamson P, ed). Wolters Kluwer. 2021: 624-637.

14. Holly L, **Huang A**, *Chapter 34: Atypical Teratoid Rhaboid Tumors*. In: Oncology of CNS Tumors 3rd edition. (Tonn JC, Reardon D, Rutka JT, Westphal M, ed). Springer Nature Switzerland AG. 2019: 615-629

Current Research Funding Grants

1.

Pediatric Brain Tumor Foundation USA. *Defining Therapeutic Vulnerabilities in Infant Pineoblastoma* ($100, 000 2022-2023). **PI: A. Huang**

2. Canadian Institute of Health Research: (CIHR), CIHR Operating Grant- *New mouse models and targeted therapies for aggressive forms of germline and sporadic Pineoblastoma (*$1.25 million 2021-2026). P.I: Zacksenhaus E; **Co-investigator: Huang A**

3. Canadian Institute of Health Research: (CIHR), CIHR Operating Grant- *Delineating mechanisms of cellular and phenotypic heterogeneity in ETMRs, (*$967,726 2021-2026). **P.I: Huang A.**

4. Cure Search Foundation Operating grant – *Immunomodulatory therapies for ultra-high risk pediatric brain tumors* (1 million USD 2020-2022) PI: Fouladi M, **Co-I: Huang A**, Drissi R.

5. Stand Up to Cancer Pediatric Catalyst Grant: April. Immunomodulation to treat poor- prognosis pediatric brain tumors. ($400,000 USD, 2018-2020 to Dr. Huang's lab) P.I. Fouladi M, Co-P.I. Olson J, **Huang A**, Jabado N

6. Hudson Monash Paediatric Precision Medicine Program: Phase 2 ($4,864,000 3 years, Sept. 1, 2019, to Aug 31, 2022). P.I. Firestein R Co-P.I. Cain J, Downie P, Gough D, Williams B, **Huang A**, Reddel R, Wood P, Algar E, Resnick A, Hansford J, Rosenbluh J, Daly R.

7. Canadian Institute of Health Research (CIHR) Project Grant: Molecular Basis of Clinical Heterogeneity in Rhabdoid Brain Tumours ($1,023,190 5 years, January 2019 to December 2024 **P.I. Huang A.**

8. Canadian Cancer Society Research Institute Impact Team Grant: *Advancing Biology Based Therapies for Rhabdoid Brain Tumors.* ($250,000/annum, 2017 - 2022). **P.I. Huang A,** Co-PI: DeCarvalho D, Bouffet E, Rutka J and Arrowsmith C. No cost extension to 2023 due to COVID.

9. Canadian Institute of Health Research: (CIHR), CIHR Operating Grant- *Delineating transforming pathways in primitive neuro-ectodermal brain tumors.* ($1.0M 2015 - 2020). **P.I. Huang A.**