Focus on Faculty #21 Nada Jabado



Dr. Nada Jabado is a Professor of Pediatrics and staff physician in the Department of Hematology and Oncology at the Montreal Children's Hospital. She completed her residency in pediatrics with a specialization in hemato-oncology, obtained a PhD in Immunology in Paris and followed that by a postdoctoral fellowship in biochemistry at McGill. She began her career as an independent investigator at The Research Institute of the McGill University Health Centre in 2003, pioneering a research program in pediatric brain tumours which is now unparalleled. Her group uncovered that pediatric high-grade astrocytomas (HGA) are molecularly and genetically distinct from adult tumours. More importantly, they identified a new molecular mechanism driving pediatric HGA, namely recurrent somatic driver mutations in the tail of histone 3 variants (H3.3 and H3.1) at amino acid positions K27 (Lysine to Methionine, K27M) and G34 (Glycine to Valine or Arginine, G34V/R).

Dr. Jabado's ground-breaking work has created a paradigm shift in cancer with the identification of histone mutations in human disease for the first time. This finding has revolutionized the field, as the epigenome was a previously unsuspected hallmark of oncogenesis, thus linking development and what we now know are epigenetic-driven cancers. This work and other publications in the subject are considered landmark papers (over 3000 citations since 2012). Dr. Jabado has over 150 peer-reviewed publications to her credit, with an impressive number of senior-author, high-impact publications in such prominent journals as *Nature Genetics*, *Nature, Science* and *Cancer Cell*, to name a few. She established the ICHANGE (International CHildhood Astrocytoma Novel Genomic and Epigenomic) Consortium which groups researchers from 17 countries. This is a unique set of resources which enables the scientific community to explore pediatric brain tumors in depth with the ultimate aim of offering better therapeutic options by providing datasets, international collaborations and access to technology to all members of participating countries. Dr. Jabado is an international leader in the field of neuro-oncology and cancer, honored by invitations as Keynote and Guest Speaker at top ranked symposia and universities. She has received numerous national and international accolades while garnering prestigious awards throughout her career. She is one of the best-funded investigators at McGill, with grants from CIHR, FRSQ, Genome Canada, NIH, a Large Scale Genomic grant

from Genome Canada as well as funding from philanthropic organizations. She was recently inducted as a Fellow to the Royal Society of Canada.

Dr. Jabado is part of a rare breed of physicians that can actively link research to the bedside, a true clinician scientist. Her dedication to scientific research in pediatric brain tumours and her passion for the patients in her care are inspiring and infectious to colleagues and trainees alike. Her coworkers describe her as The Tasmanian Devil, a moving force of nature that can uproot entire schools of thought with gale-force winds. Anyone who has witnessed her speak in public will also attest to this phenomenon. Legend has it that she lives on coffee and chocolates. Dr. Jabado considers downtime as time spent racing the ski slopes with her physician husband and three teenage children who are a family of avid skiers.

We asked Dr. Nada Jabado to choose a few of her most prominent articles which was not unlike asking her to pick a favorite child:

Schwartzentruber J, Korshunov A, Liu XY, Jones DT, Pfaff E, Jacob K, Sturm D, Fontebasso AM, Quang DA, Tonjes M, Hovestadt V, Albrecht S, Kool M, Nantel A, Konermann C, Lindroth A, Jager N, Rausch T, Ryzhova M, Korbel JO, Hielscher T, Hauser P, Garami M, Klekner A, Bognar L, Ebinger M, Schuhmann MU, Scheurlen W, Pekrun A, Fruhwald MC, Roggendorf W, Kramm C, Durken M, Atkinson J, Lepage P, Montpetit A, Zakrzewska M, Zakrzewski K, Liberski PP, Dong Z, Siegel P, Kulozik AE, Zapatka M, Guha A, Malkin D, Felsberg J, Reifenberger G, von Deimling A, Ichimura K, Collins V P, Witt H, Milde T, Witt O, Zhang C, Castelo-Branco P, Lichter P, Faury D, Tabori U, Plass C, Majewski J*, Pfister SM* and Jabado N* (2012). Driver mutations in histone H3.3 and chromatin remodelling genes in paediatric glioblastoma. Nature 482(7384): 226-231. (*co-senior and co-corresponding authors)

Fontebasso AM, Papillon-Cavanagh S, Schwartzentruber J, Nikbakht H, Gerges N, Fiset P O, Bechet D, Faury D, De Jay N, Ramkissoon LA, Corcoran A, Jones DT, Sturm D, Johann P, Tomita T, Goldman S, Nagib M, Bendel A, Goumnerova L, Bowers DC, Leonard JR, Rubin J B, Alden T, Browd S, Geyer JR, Leary S, Jallo G, Cohen K, Gupta N, Prados M D, Carret A S, Ellezam B, Crevier L, Klekner A, Bognar L, Hauser P, Garami M, Myseros J, Dong Z, Siegel PM, Malkin H, Ligon AH, Albrecht S, Pfister SM, Ligon KL, Majewski J*, **Jabado N*** and Kieran MW* (2014). Recurrent somatic mutations in ACVR1 in pediatric midline high-grade astrocytoma. **Nat Genet** 46(5): 462-466. (*co-senior and co-corresponding authors)

Kleinman CL, Gerges N, Papillon-Cavanagh S, Sin-Chan P, Pramatarova A, Khuong-Quang DA, Adoue V, Busche S, Caron M, Djambazian H, Bemmo A, Fontebasso AM, Spence T, Schwartzentruber J, Albrecht S, Hauser P, Garami M, Klekner A, Bognar L, Montes JL, Staffa A, Montpetit A, Berube P, Zakrzewska M, Zakrzewski K, Liberski PP, Dong Z, Siegel PM, Duchaine T, Perotti C, Fleming A, Faury D, Remke M, Gallo M, Dirks P, Taylor MD, Sladek R, Pastinen T, Chan JA, Huang A, Majewski J* and **Jabado N*** (2014). Fusion of TTYH1 with the C19MC microRNA cluster drives expression of a brain-specific DNMT3B isoform in the embryonal brain tumor ETMR. **Nat Genet** 46(1): 39-44. (*co-senior and co-corresponding authors)

Lu C, Jain SU, Hoelper D, Bechet D, Molden RC, Ran L, Murphy D, Venneti S, Hameed M, Pawel BR, Wunder JS, Dickson BC, Lundgren SM, Jani KS, De Jay N, Papillon-Cavanagh S, Andrulis IL, Sawyer SL, Grynspan D, Turcotte RE, Nadaf J, Fahiminiyah S, Muir TW, Majewski J, Thompson CB, Chi P, Garcia BA, Allis CD*, **Jabado N***, Lewis PW* (2016). Histone H3K36 mutations impair mesenchymal differentiation and promote sarcomagenesis. **Science** 352(6276):844-849. (*co-senior and co-corresponding authors)