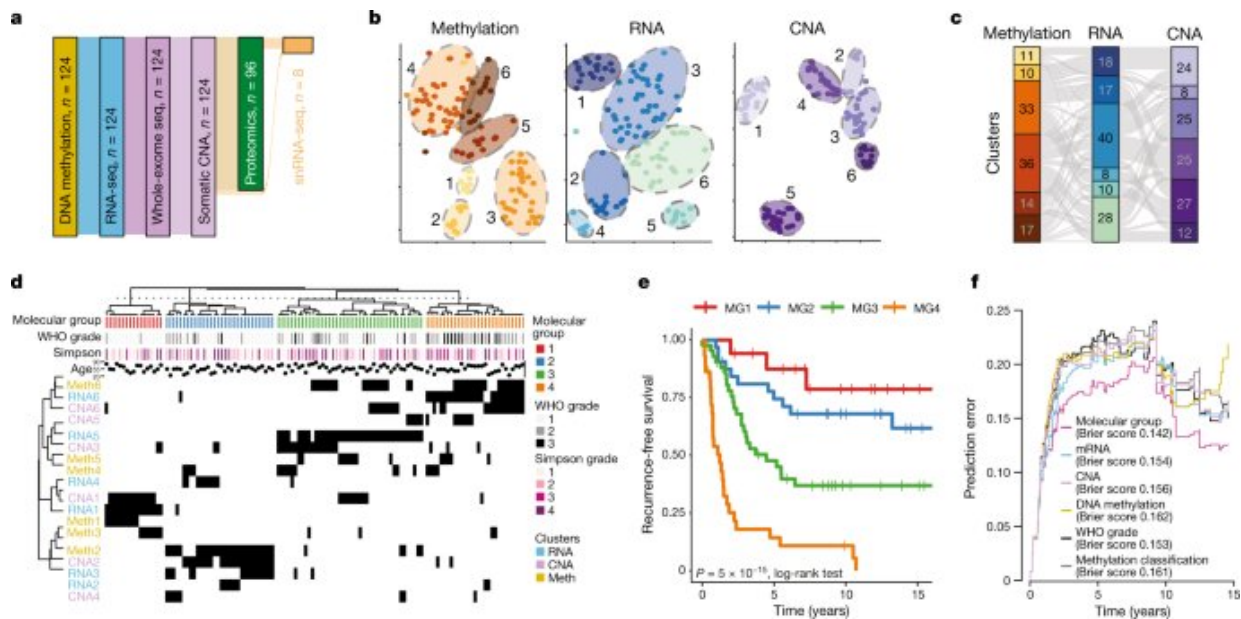# Expanding understanding of brain tumor biology to unlock new treatment options

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Credit: DOI: 10.1038/s41586-021-03850-3

Princess Margaret Cancer Centre researchers have made new findings which provide a deeper understanding of the most common—but highly under-studied—type of brain tumor, opening a new treatment pathway for patients.

Research conducted by Senior Scientist Dr. Gelareh Zadeh's lab at the Macfeeters-Hamilton Neuro-Oncology Program offers expanded insight

into the biology of meningiomas, the most common form of [brain](link) tumor. Even though meningiomas are the most common brain tumor, they have been highly understudied. In fact, knowledge about meningiomas and their current three-stage classification—known as the World Health Organization grade—has changed little in 30 years.

Treatment options have largely been limited to surgery and some use of radiation therapy. The new findings from the PM team show that there are in fact four distinct subtypes of meningiomas based on integrated genomic and epigenomic characteristics of the tumors.

The study has identified unique tumor characteristics which have led to other viable medical [treatment options](link) for the first time, based on the biological drivers of these tumors.

"This is really a transformation in our understanding of meningiomas," Dr. Zadeh says. "For many years, patients have often needed to have multiple rounds of surgery and radiation, with very limited lasting effects.

"Having the option of a medical treatment changes the landscape for our patients."

Dr. Zadeh, who also serves as Medical Director of the Krembil Brain Institute at UHN, Head of Division of Neurosurgery at UHN and Chair of Neurosurgery at the University of Toronto, is senior author of the study, which was published in *Nature* on Aug. 25. Dr. Farshad Nassiri, Vanier Canada Graduate Scholar and chief neurosurgery resident in Toronto, is first author of the study.

"The classification that we've discovered, for the first time gives insight into the biology of the full spectrum of meningiomas," Dr. Nassiri says. "Before, no one really knew how these tumors became aggressive.

"Biology is very closely associated with treatment sensitivity and personalized medicine. This gives us the first real look at more tailored therapeutics as opposed to a catch-all type treatment for patients."

Dr. Zadeh says her team took the findings on the new tumor classifications and moved them toward clinically usable tests with the help of fellow Princess Margaret Senior Scientists Drs. Thomas Kislinger, Daniel de Carvalho and Gary Bader, as well as Dr. Ken Aldape from the National Cancer Institute.

"We found that each group of meningioma expressed very specific proteins, and that these proteins could be assayed using conventional techniques that are already available in neuropathology laboratories," says Dr. Zadeh, who holds both the Dan Family Chair in Neurosurgery and the Wilkins Family Chair in Neurological Brain Tumor Research. "This means that this classification can be immediately used in almost all cancer centers around the world."

The group has also for the first time found new treatment options based on a biological rationale for meningiomas.

"We noticed that the most aggressive group of meningiomas—that we called proliferative meningiomas—may be treated using a drug that is already FDA approved for other cancers," Dr. Nassiri says.

Dr. Nassiri says the work was made possible by UHN's expansive brain tumor bio-bank of more than 5,000 brain tumor samples with matching clinical data, together with the strength of the meningioma consortium that he and Dr. Zadeh lead.

"This is where The Princess Margaret really distinguishes itself, having this invaluable resource for this very under-studied orphan disease," he says.

Dr. Zadeh says "this study is truly a reflection of the strength of the Princess Margaret and UHN environment where we can bring the talent and expertise together."

Co-second authors, Drs Jeff Lui, Vikas Patil and Mamatjan Yasin from the Zadeh lab, worked closely with Drs Nassiri and Zadeh to make these genomic datasets and this body of work serves as an invaluable resource, made publicly available for the scientific community to use and build on the current discoveries.

"Creating a tool similar to The Cancer Genome Atlas for meningiomas will place us on the map of brain tumor discoveries" says Dr. Nassiri.

More information: Farshad Nassiri et al, A clinically applicable integrative molecular classification of meningiomas, *Nature* (2021). DOI: 10.1038/s41586-021-03850-3

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