[MUSIC PLAYING]

JOON H UHM: Molecular testing or DNA testing on tumors now in the 21st century needs to be considered for the great majority, if not all, brain tumor patients.

ROBERT B JENKINS: We need to use molecular genetic tools to help improve the classification of gliomas, to determine a patient's prognosis, and to determine the kind of therapy that they should receive.

DANIEL HONORE LACHANCE: Brain tumors actually occur as a result of a large number of genetic alterations.

JOON H UHM: What the researchers here at Mayo Clinic and across at other institutions have found is that looking into the DNA you can classify brain tumors far more precisely than simply by looking how pink they are, how many cells are dividing.

ROBERT B JENKINS: We can use that genetic information to more solidly place these tumors into specific types that might respond to specific kinds of therapy.

IAN F PARNEY: Patients with certain molecular classifications that do really well with one treatment but not with another. And as we have this established is a way that we can look at this information, we're really going to be able to tailor our treatments much better, and find new treatments better for patients that may be underserved by what we had before.

ROBERT B JENKINS: We discovered that the short arms of chromosome one and the long arm of chromosome 19 were co-deleted in a particular kind of glioma.

JOON H UHM: What we call 1P19Q deletion, this is when two pieces of DNA in the human chromosomes basically disappear. And we don't really know why that's a good thing for the patient, but when those two pieces of DNA are missing, that patient's brain tumor is actually forecasted to grow up more slowly, but very importantly, be more sensitive to radiation and to certain category of chemotherapies.

ROBERT B JENKINS: Some brain tumors have 1P19Q co-deletion. Some brain tumors have IDH mutation. Some brain tumors have TERT promoter mutation, some tumors have all three of those. Some tumors have none of those. Some tumors have one or two of those. So we thought, well, if we can test the tumors for those three alterations, we could put them into molecular genetic

groups.

DANIEL HONORE LACHANCE: By just using three key genetic mutations, gliomas could be classified into five groups that had in common certain important characteristic, such as the age of presentation.

ROBERT B JENKINS: Those five molecular groups can predict a patient's prognosis, meaning how long they can expect to live. And at least two of the groups determine what kind of therapy the patient will get. So for example, a person that has what we call a triple positive glioma, meaning they have 1P19Q co-deletion, IDH mutation, and TERT promoter mutation, those patients should be getting chemotherapy and radiation therapy regimen specifically designed for that tumor, and that tumor type only.

JOON H UHM: If a person tumor is missing 1P19Q, there's no doubt that we should give that patient chemotherapy, either with or after the radiation. And that actually doubles the life expectancy with radiation alone from about eight years to about 15, 16 years, or more.

DANIEL HONORE LACHANCE: The patient that has the combination, say, of all three mutations, the co deletion, IDH mutation, and the TERT promoter mutation, we know that those patients have an oncology's peak median survivals of greater than 15 years and with some patients that are truly long term survivors. If we treated those patients too aggressively at the onset, when they live 15 and 20 years, they may suffer the long term consequences of our therapies and be neurologically impaired because of the treatments, when if perhaps we could come up with a different approach for those patients that we know are going to do well, they might end up having a better longer term quality of life.

JOON H UHM: IDH mutation and telomerase mutation, and they also have a very good prognosis. The next one down is IDH mutation only. And then you have what's called triple negative. And when you have none of these three, good, genetic characteristics, that patient, it's not a guarantee that he or she would do poorly, but it doesn't look well.

ROBERT B JENKINS: If they have one of the mutations, meaning if they have a TERT promoter mutation, that group of tumors is what we used to call primary glioblastoma, the most common brain tumor and the tumor of the worst prognosis. If a tumor falls into that group, they get a different chemotherapy and a different radiation therapy.

IAN F PARNEY: We're able to use the molecular findings to help augment the information that we get from the MRI scan to take the best surgical approach for an individual patient. If that particular tumor

has an IDH mutation in it, then there's a very strong association with improved survival and outcome if we take out all of the area that we can safely take out. So what we always want to do in any brain tumor surgery is we want to take out the most tumor that we can safely take out to get the best outcome and survival.

DANIEL HONORE LACHANCE: Each person's tumor is different, and therefore in the end, each person needs an individualized approach to treating their tumor. And it's only by having this kind of detailed information available that we can begin to understand the different patterns of patients' different tumor types.

JOON H UHM: We now have five molecular categories of glioma. We're absolutely certain it goes far beyond five, it'd be 50, 500, who knows? There are thus far 40,000 known human genes. 40,000. And we now five types of human brain tumors based upon genetics, so really, I think the sky's the limit.