

“Fire in the Smoke: Battling Brain Tumors” with Michael Lim

Transcript of Cerebrum Podcast



Guest: Michael Lim, M.D., is director of the Brain Tumor Immunotherapy Program and a professor of neurosurgery, oncology, otolaryngology, and radiation oncology at Johns Hopkins. Lim’s research laboratory is focused on understanding the mechanisms of immune evasion by primary brain tumors. Lim obtained his M.D. from the Johns Hopkins University School of Medicine and completed his residency in neurosurgery at Stanford University Hospital. In addition to running a laboratory, he also directs the immunotherapy clinical trials program at Johns Hopkins. He currently serves as the principal investigator of several large brain tumor immunotherapy clinical trials based on findings from his laboratory.

Host: Bill Glovin serves as editor of *Cerebrum* and the *Cerebrum Anthology: Emerging Issues in Brain Science*. He is also executive editor of the Dana Press and *Brain in the News*. Prior to joining the Dana Foundation, Mr. Glovin was senior editor of *Rutgers Magazine* and editor of *Rutgers Focus*. He has served as managing editor of *New Jersey Success*, editor of *New Jersey Business* magazine, and as a staff writer at *The Record* newspaper in Hackensack, NJ. Mr. Glovin has won 20 writing awards from the Society of Professional Journalists of New Jersey and the Council for Advancement and Support of Education. He has a B.A. in Journalism from George Washington University.

Bill Glovin: Senator John McCain has been diagnosed with glioblastoma, a fast-growing, aggressive type of central nervous system brain tumor that killed Senator Edward Kennedy and Bo Biden, the son of former Vice President Joe Biden.

Welcome to the *Cerebrum* Podcast. Hi, I’m *Cerebrum* Editor, Bill Glovin, and on the phone with us today is Dr. Michael Lim, director of the Brain Tumor Immunotherapy Program at Johns Hopkins University School of Medicine in Baltimore. He’s also a Professor of Neurosurgery and a bunch of other stuff, too numerous to mention. Dr. Lim was kind enough to co-write our latest *Cerebrum* article, [“Fire in the Smoke: Battling Brain Tumors,”](#) which you can read at dana.org. The article focuses mainly on glioblastoma, which is the most common grade IV brain cancer. Let me mention that the only time Dr. Lim had time to do this was 8 a.m. on a Saturday morning, which speaks to what a busy man he is.

Welcome to the podcast, Dr. Lim. With so many titles, which suggest enormous responsibility, take us through a typical day for you.

Michael Lim: There is no typical day. You know, there are days when I’m operating a lot and then I go into my lab after I operate and go late, or other days I have clinic and I

go into my lab. I always go to my lab, I mean, I try to do what I call my academic work. It's either meeting with my lab or going over data.

You know, in terms of a typical day, I'd say on certain days I operate, on certain days I see clinic, and on certain days I try to do research.

It varies upon the week. It's not like one tumor comes a day. It's not like a widget where you just make it once a day. There could be weeks where there's just a lot of patients with tumors and then there'll be weeks when it's quieter and I can spend more time doing research stuff.

Bill Glovin: Tell me a little bit about your background; where you're from and how long you've been at Hopkins.

Michael Lim: In terms of where I'm from, I grew up mainly in New Hampshire and Minnesota, but New Hampshire. I did my undergraduate work at the University of New Hampshire and my medical school at Hopkins and then I lived in California for seven years. I went to medical school at Hopkins for five years. I did a research here called the Howard Hoosier and then I went to California for seven years and then came back to Hopkins and have been here, I think, this is my 12th year, now.

Bill Glovin: Tell me, or tell people the difference between glioblastoma and other brain cancers.

Michael Lim: Glioblastoma is basically a type of brain tumor that arises from the brain and they are within a family of tumors called gliomas. These gliomas can be graded from one to four, with four being the most aggressive and glioblastoma is Grade IV. Does that make sense?

Bill Glovin: Is it the way it spreads—or possibly no?

Michael Lim: No, basically when you look at it under a microscope there are certain features to a tumor that suggests whether it behaves more aggressively than not. These criteria is the way the cells look. They call it nuclear atypia. Basically, cancer cells have a nucleus that looks abnormal. That usually signifies that the DNA has been altered in a way. You can't see that with a microscope, but the nucleus of a cell you can make out is different. They call it mitosis. You can actually see cells dividing under the microscope. If you see cells start dividing under the microscope that usually means that tumor is growing quickly. Endothelial hyperplasia, which basically means it's very vascular, and necrosis, areas of necrotic. Necrosis in the tumor. Those are all characteristics that suggest that the tumor is going to be really aggressive. When you have three of those four features, that becomes a glioblastoma.

Bill Glovin: Now, there's 100 different forms of brain cancers. Is glioblastoma the most common?

- Michael Lim: It is the most common.
- Bill Glovin: Any reason why? Do we know why?
- Michael Lim: We don't really know but, you know, these entities that we've created are sometime the spectrum of tumors on a time scale. We think a lot of these Grade II tumors and Grade III tumors have actually become a glioblastoma if they're given enough time. Does that make sense?
- Bill Glovin: The survival rate is approximately 20 months, yet in the article you use an example of someone who has actually survived glioblastoma. Would we know why somebody would survive it?
- Michael Lim: That patient is a very rare patient. There are case reports of patients like him that basically got an infection and then for some reason survived. Many people believe that infection caused an immune response to basically kill off somebody's cancer. Does that make sense?
- Bill Glovin: Well, I noticed that three years ago, injections of viruses associated with the common cold were used which showed some positive signs. Has there been progress there or was that a false alarm?
- Michael Lim: That's a different ... I guess to complete the story with the bacterial infection, that's very different than a viral infection. Most of the cases of people who have lived a long time are from viruses are from bacteria, not viruses.
- Now, in terms of the viral infection story, we think it's promising, but we just don't know the results of that yet. We have to follow those patients and they have to be processed, but in general, many people are excited about the viruses.
- Bill Glovin: It's still being explored. It's an avenue you're still going down?
- Michael Lim: Mm-hmm (affirmative) and we think there's been some promising results.
- Bill Glovin: Great. Two years ago, Dr. Chris Duma did a Ted Talk on glioblastoma and talked about inventing the Gamma Knife which is a machine which gives radiation to the front of the tumor or where it's going rather than where it is. Has this made any difference?
- Michael Lim: I think it's an interesting approach, it's just I haven't seen any data on that.
- Bill Glovin: Okay. It's still too new to be an accepted practice I would assume.
- Michael Lim: We have to do a lot more rigorous clinical trials. I mean, even with the viral story, it's taking a while.

Bill Glovin: There's been so much progress made in treating, let's say, bone cancer and even other types of cancer, yet glioblastoma has proved so difficult to treat. Why is that?

Michael Lim: Well, I think most of us in the field believe that because it's basically a different tumor in terms of ... I think most of the progress that's been made is with immunotherapy. With the immunotherapy, we think that ... I mean there's been an incredible amount of FDA approvals. I don't know if you've noticed, on the announcements and newspaper articles for different cancers. But there are some set of tumors that are not responding and they're basically called cold tumors. Tumors that respond are being called hot tumors, and cold tumors that are not responding are being called cold tumor. Does that make sense?

Glioblastomas look like they're a cold tumor. With them being a cold tumor, and they're not the only tumor, that's cold. Pancreatic cancer and prostate cancer have also been disappointing. It just looks like they arise different, the cells, the way they suppress the immune system is different than a melanoma. We think that the strategy of using an inhibitor is not working because it's a different mechanism of immunosuppression and we're still actively looking at figuring out how to reverse that and we're still hopeful, we just know it's a different way.

Bill Glovin: Is there any evidence that glioblastoma can be passed down?

Michael Lim: There are some genetics, I mean we do see them in families so there is evidence that certain types of ... We think that, first of all, glioblastomas are still a heterogeneous group of tumors. It's not just one entity and we're learning that through molecular analysis and as we're studying the molecular analysis we do find that there are some that appear to be genetically passed on. Genetically it increases your predisposition. Does that make sense? Basically, some are passed on but not all.

Bill Glovin: Does gene modification hold any promise?

Michael Lim: In short, yeah. Gene modification is facing the same problems. Glioblastoma is facing the same problems as other tumors, you've got to be able to gene modify every tumor cell. We don't have something that efficiently modifies every tumor cell, yet.

Bill Glovin: Since we haven't made much progress in treating glioblastoma, do you know if there are patients who are seeking homeopathic treatments in other countries?

Michael Lim: Basically, I guess to a bigger point we are throwing the kitchen sink at it and so people are looking at homeopathic stuff.

Bill Glovin: Has anything showed any promise?

Michael Lim: Not that I'm aware of.

- Bill Glovin: At the end of your article you write “the negative results of clinical trials to date represent a call to action.” What kind of action are you referring to?
- Michael Lim: I think that it suggests that we are rethinking our strategies. Sometimes our problem with a current strategy is that ... I mean, it enlightens us to rethink our strategy, right? First of all, we have applied a lot of immunotherapies that worked in other cancers to glioblastoma and have had disappointing results, as an example. I think it just means that more research is needed in understanding how the glioblastoma surpassed the immune system, as an example. I think we also meant to say we need to rise up to this challenge because it's a very daunting tumor. It's a very hard tumor to cure. It's kind of rah, rah—like we need to rise up to this challenge.
- It's like, you know, playing in a league and you played the Golden State Warriors and they're a really hard team so sometimes some teams get really psyched up to blame them, you know?
- Bill Glovin: Yeah, when Kawai Leonard comes to the Knicks, that's going to help us. I noticed that neuroimaging has been pretty amazing in showing pictures of the brain and has that been helpful or can that still be improved?
- Michael Lim: Oh, I think that's always going to improve. Neuroimaging, basically, works as we get better with computer technology, right?
- Bill Glovin: Yeah. Anything else that I've left out that you think is important to mention?
- Michael Lim: I'd say from a personal standpoint, because of what I do in my research and what my lab is like, we are still hopeful that we'll come up with therapies for glioblastoma. We have seen case reports of people responding to immunotherapies, like check point inhibitors and car t-cells. We are seeing hints of responses, I just think that I'm very optimistic that we're going to hopefully find some key findings and maybe help with some novel therapies. That's kind of how I would leave it in that sense, that I'm still very optimistic
- You know, our patients, it's really an honor to take care of our patients. As you said, my whole life is focused around trying to take care of patients with brain tumors. If I'm not operating on them and trying to understand clinically, we're in the lab operating and trying to figure that out. I'm not unique in that, I think there are many people in the world that are doing this. I guess the way I would leave it on an optimistic note is that there are some positive, there have been case reports of people responding to immunotherapy. There's a lot of people who are dedicated to doing this and we're constantly getting new people and new ideas, and so I'm optimistic in that respect.
- Bill Glovin: Would you say maybe we're five years away from real progress? Ten years away? Is this going to happen in our lifetimes, or we just don't know?

Michael Lim: I guess the way I would say it is we feel optimistic that we're going to find something. I think when it happens it'll be sudden, but we don't know when it'll happen.

Bill Glovin: I think that's a good place to end. Thanks again, to Dr. Michael Lim, one of the country's foremost experts on brain cancer. Just as a short aside, Dr. Lim was telling me that when he was an undergraduate at the University of New Hampshire, he studied starfish and clams in trying to understand cell pathways, leukemia, and cell division. As co-writer on the *Cerebrum* article, Dr. Chris Jackson, a chief resident, majored in English. Now they are both in the Glioblastoma world.

Anyway, you can find the article a dana.org and as always, thanks for listening. I'm *Cerebrum* Editor, Bill Glovin at the Dana Foundation. Have a great day.