ACCELERATE
THE CAMPAIGN for UW MEDICINE

November 26, 2018

Dear Friends of Merkel cell carcinoma research,

Greetings! As we enter this season of celebration, I would like to express my gratitude for your support of our Merkel cell carcinoma program. I am proud to outline some of the developments that have taken place in the past year, many of which were made possible through your generosity.

The Success of Immunotherapy
Our team's efforts in various immunotherapy trials for Merkel cell carcinoma (we have led over five such trials) have resulted in the rapid adoption, since 2016, of immunotherapy as the standard of care for advanced MCC. For decades, chemotherapy had been the only option to treat patients with advanced MCC. Multiple studies have shown that although MCC often initially responds to chemotherapy, responses are generally short-lived, typically lasting only about 90 days from the start of chemotherapy. In contrast, among patients who initially respond to immunotherapy, about 80% continue to benefit for well over one year (and counting!) after starting immunotherapy. Results from our trials thus led to the inclusion of these new immunotherapy agents (avelumab, pembrolizumab, and nivolumab) in the 2018 National Comprehensive Cancer Network (NCCN) guidelines as preferred treatment options for patients with advanced MCC. Chemotherapy is now only indicated in patients who are not eligible for immunotherapy. Based on recent findings from one of our clinical trials, we are hopeful for an additional FDA approval (pembrolizumab, Keytruda) for patients with advanced MCC by the end of 2018.

Merkel Antibody Test
In 2010, our team developed the Merkel cell polyomavirus antibody test. This blood test is performed in a clinical laboratory at UW, currently the only institution in the country that offers this service. This test reliably detects recurrences of MCC in patients that produce these antibodies. When performed at diagnosis, this test helps all patients whether or not they make these antibodies. For patients who make these antibodies, we have a way to detect early recurrence that requires fewer scans. For patients who do not make these antibodies, we know they have a 40% higher risk of MCC recurrence, and we will need to follow them closely with scans. Excitingly, in 2018, this test was recommended in the official NCCN guidelines for routine use in managing MCC. With over 1,000 unique MCC patients who have used this test, the impact of this program is significant and anticipated to grow further.

A Program Project Grant
Your philanthropy has provided the necessary support for our Merkel cell carcinoma team to rapidly advance research even as we passed through a challenging funding transition. Over the past three years, we shifted our focus from traditional National Institutes of Health (NIH) "R01" grants in order to apply for a much bigger NIH Program Project Grant, "P01." Your support has helped during this period by providing unrestricted money for MCC research as our earlier grants ended. In 2017, the first submission of our Program Project Grant scored well but not quite favorably enough to be funded. I am happy to report that our 2018 submission received a

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superb score and is extremely likely to be funded in early 2019. This Program Project Grant would replace funding from the prior R01 grants and also provide support for other excellent research groups in and beyond Seattle to collaborate with us as we make further progress against this aggressive skin cancer.

American Academy of Dermatology Award
Our MCC-focused research has been selected to receive the American Academy of Dermatology's 2019 Eugene J. Van Scott Award for Innovative Therapy of the Skin. At the March 3rd 2019 plenary session of the AAD meeting in Washington, DC, I will deliver the Phillip Frost Leadership Lecture. This award represents one of the highest honors in dermatology. It is being given in recognition of our multi-disciplinary work on Merkel cell carcinoma that has led to profound changes in the management of patients with early stage and advanced MCC.

Our Future Goals
Even with recent advances in treatment for MCC, there is still much work to be done. Roughly 50% of patients have ongoing benefit from currently available immunotherapies, leaving 50% who never respond or only respond temporarily.

<u>Increasing the Percentage of Patients who Respond to Immunotherapy</u>
We believe a key reason that some patients do not respond to immunotherapy is that they likely lack effective immune cells (killer T cells) that target MCC. In early 2019, as part of our Program Project Grant, Drs. Kelly Paulson and Aude Chapuis are set to lead a clinical trial that aims to improve the efficacy of immune checkpoint inhibitors by engineering a patient's T cells to better fight and recognize the Merkel cell polyomavirus. In addition to these "engineered T cells," patients will also receive avelumab (broadly stimulates the immune response) as well as radiation to the largest tumors (lowers the tumor volume and improves the ability of the immune system to "see" the cancer).

<u>Create brand new treatments, such as therapeutic vaccines for MCC</u>
Because 80% of all MCC tumors are driven by a virus, we hope to create a therapeutic vaccine that will target a specific portion of the virus that is required for the cancer to grow. For 20% of patients whose tumors are "virus negative" we may be able to generate personalized vaccines based on their cancer's unique mutation signature, something that can now be determined within a few days, for less than $2,000. A custom vaccine could then be quickly made to try to teach the immune system to see the unique mutations present in the tumor but nowhere else in the patient's body.

Personal Updates
2018 was a big year for my family for several reasons. My wife Stephanie and I sent our older son, Alex, off to Harvey Mudd College where he is studying computer science and playing violin in the orchestra. Our younger son, Max, is in 8th grade. He also plays the violin, ultimate frisbee, and enjoys gaming with his friends.

Thank You
My colleagues and I are grateful for your support of our work in Merkel cell carcinoma research. If you are interested in supporting MCC research, please go to: https://merkelcell.org/join-thefight/donate/. If you have any questions about our work, please contact me or my advancement colleague, Christine Chan Anderson at ccanders@uw.edu or 206.221.3286. Have a wonderful holiday season and a joyful new year.

Sincerely,

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