



## Past Research Funded by OMF

To “See A Cure” for eye cancer, investing in ground-breaking research is critical. Since its founding in 2003, OMF has committed over \$550,000 in research grants to some of the leading names in ocular melanoma (OM) research.

Since 2014, OMF has formalized its approach to research funding through a unique partnership with the American Association of Cancer Research (AACR). Working with the AACR and a peer review board of leading OM researchers has allowed OMF to present an annual, peer-reviewed research award to a postdoctoral or clinical research fellow to conduct ocular/uveal melanoma research with a focus on translational and clinical research.

### 2017 Kammerman Family Grant in partnership with Ocular Melanoma Foundation

*Award Amount* \$50,000

*Recipient* Vivian Chua, PhD  
*Institute* Thomas Jefferson University (Philadelphia, PA)  
*Mentor* Andrew Aplin, MD

*Title* **Novel epigenetic targeting approaches in uveal melanoma (UM)**

*Synopsis* BRCA1-associated protein 1 (BAP1) and the bromodomain and extraterminal (BET) proteins regulate gene transcription and tumorigenesis in an epigenetic manner in cancers including UM. Inactivating mutations in BAP1 have been associated with aggressive and metastatic disease in UM whereas inhibition of BET proteins leads to suppression of primary UM growth and effects are associated with suppression of expression of Rad51 and Bcl-xL. After testing of two BET inhibitors, preliminary studies showed that although the BET inhibitors reduce the growth of metastatic UM cell lines, responses to these BET inhibitors suggested that specific conditions in the liver create resistance to BET’s positive effect. This research study aims to (1) investigate the survival mechanisms in uveal melanoma cases where BAP1 is mutated and could be targeted by epigenetic and targeted therapies or in a synthetic lethality approach and (2) analyze reverse phase protein array (RPPA) data to identify mechanisms mediating FGF2 in altering BET inhibitor effects in UM cells, and whether targeting of the FGF2/FGFR pathway increases sensitization of UM cells to BET inhibition. The goal is to determine new epigenetic targeting approaches for metastatic uveal melanoma.





## 2016 AACR-Ocular Melanoma Foundation Fellowship in honor of Robert C. Allen, MD

*Award Amount* \$50,000

*Recipient* Jessica Teh, MD  
*Institute* Sidney Kimmel Cancer Center, Thomas Jefferson University (Philadelphia, PA)  
*Mentor* Andrew Aplin, MD

*Title* **Utility of CDK4/6 inhibitors in uveal melanoma**

*Synopsis* After treatment of primary uveal melanoma tumors, 50% of patients will develop macro-metastases and currently there are no FDA-approved targeted inhibitor treatments for metastatic UM. MEK-ERK1/2 signaling is activated frequently in uveal melanoma due to driver mutations in either GNAQ or GNA11. While MEK inhibitors are FDA-approved in cutaneous melanoma, they provide a 14% response rate and modestly improve progression-free survival in uveal melanoma. Dr. Teh's proposal aims to utilize an in vivo reporter model to monitor the effects of the combination of MEK and CDK4/6 inhibitors and to identify optimal dosing schemes for this combination. Additionally, she will work on determining the effect of BAP1 status in the modulation of response to the combination leveraging new metastatic uveal melanoma cell lines, a new in vivo metastatic colonization model, and uveal melanoma patient samples from clinical trials. Dr. Teh hopes to ultimately provide the pre-clinical basis for targeted inhibitor combinations in late-stage uveal melanoma.





## 2015 AACR-Ocular Melanoma Foundation Fellowship in honor of Robert C. Allen, MD

*Award Amount* \$50,000

*Recipient* Stefan Kurtenbach, MD  
*Institute* Miller School of Medicine of the University of Miami (Miami, FL)  
*Mentor* Bill Harbour, MD

*Title* **BAP1 loss deregulates neural crest guidance cue signaling in uveal melanoma**

*Synopsis* Dr. Kurtenbach's work with Dr. William Harbour at Miami University has involved the classification of uveal melanomas into two significant subgroups: Class 1 tumors associated with low metastatic risk and Class 2 tumors with high metastatic risk. This test, commercialized by Castle Biosciences (the GEP test), is now widely used as a routine clinical test and is the gold standard for precision medicine in this cancer. Dr. Kurtenbach's JIA grant-funded work takes this to the next level, deepening our understanding of Class 2 tumors and their association with inactivating mutations in the tumor suppressor gene BAP1. A better understanding of the link between loss of BAP1 and liver metastasis may be the key to identifying new, targeted therapies to treat ocular melanoma. His research investigates the possibility of gene function restoration and the identification of protein treatment options to prevent metastasis. In addition, his study looks for biomarkers in the Class 1 tumors to predict the small percentage that results in metastasis.

*Findings* Although Dr. Kurtenbach's research is ongoing, initial results found PRAME mRNA as the most significant predictor for metastasis in Class 1 tumors. These results have been published in "Clinical Cancer Research."  
(<http://clincancerres.aacrjournals.org/content/22/5/1234>).





## 2014 AACR-Ocular Melanoma Foundation Fellowship

*Award Amount* \$50,000

*Recipient* Alexander Shoushtari, MD  
*Institute* Sloan-Kettering Institute for Cancer Research (New York, NY)  
*Mentor* Richard Carvajal, MD

*Title* **Overcoming Resistance to MEK Inhibition in Advanced Uveal Melanoma**

*Synopsis* Dr. Shoushtari helped coordinate a randomized, multicenter trial combining a MEK inhibitor called trametinib with/without an AKT inhibitor called GSK2141795. This represented a novel approach to treating ocular melanoma and tested the scientific hypothesis that combined MEK and AKT inhibition is better than MEK inhibition alone.

As part of the clinical trial, tumor biopsies were taken before and during treatment. Dr. Shoushtari and colleagues analyzed the genetic changes during treatment in the biopsy specimens and compared patients whose tumors responded to therapy with those whose tumors did not respond to therapy. Comparing these tumors will help shed light on how uveal melanomas rely on MAPK, AKT, or other growth signaling pathways to grow. The results of the research are being applied to help plan new approaches to treating uveal melanoma, and will be generalizable to other types of tumors that rely on these growth pathways.

*Findings* Two benefits of the study were the amassing of the largest annotated biorepository of uveal melanoma and cultivating the research across multiple centers in the United States and Europe. In Shoushtari's words, "The fact that we were able to accrue rapidly across multiple centers shows unequivocally that multicenter trials in this rare disease can be conducted efficiently." Dr. Shoushtari is now a board-certified medical oncologist. He works at Memorial Sloan Kettering Cancer Center in NYC. His clinical expertise is uveal melanoma.





## Other Research Awards

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| 2016 | <b>\$40,000</b> - Takami Sato, MD, PhD (Jefferson University Hospital) <ul style="list-style-type: none"><li>• <i>Patient-derived xenograft (PDX) mouse model development</i></li><li>• <i>Cancer vaccine targeting mutated GNAQ/GNA11</i></li><li>• <i>Uveal melanoma patient registry and cluster analysis</i></li></ul> |
| 2013 | <b>\$10,000</b> - Bill Harbour, MD, PhD (Bascom Palmer Eye Institute, University of Miami)   |
| 2012 | <b>\$10,000</b> - Takami Sato, MD, PhD (Jefferson University Hospital)<br><b>\$12,500</b> - Melanoma Know More Junior Investigator Grant   |

## About OMF

The Ocular Melanoma Foundation (OMF) is the leading research and patient support organization focused on eye cancer. OMF was established by Dr. Robert Allen, a renowned eye surgeon who was diagnosed with ocular melanoma (OM), a rare eye cancer diagnosed in 2,000 adults in the U.S. annually. Today, OMF is the #1 destination for uveal melanoma information online and a leading provider of patient education and support programs, including novel assistance programs for patient travel and ocular prosthetics. The 'Eye Am Not Alone' patient retreat is the largest gathering of OM patients and caregivers in the world and OMF has raised over a million dollars towards the fight against eye cancer while partnering closely with the American Association for Cancer Research (AACR) and the Rare Cancer Research Foundation (RCRF) to fund groundbreaking cancer research.

Learn more at [ocularmelanoma.org](http://ocularmelanoma.org).

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