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My lab focuses on discovering novel targeted therapies for cancer treatment. We are involved in every aspect of the drug discovery process, from target validation (Will erasing this target stop cancer cells from growing uncontrollably? What cells/cancer subtypes will respond if we erase this target?), to discovering chemical matter that modulates the activity of the target (How do we inhibit / disrupt / destruct this target?), to translation of lab findings into clinical success (Which patients would benefit from this treatment? How can we make the therapy more effective?) . As such, our work entails the combination of many different expertises (biology, pharmacology, chemistry, biochemistry, bioinformatics, etc) resulting in a highly stimulating, multi-disciplinary teamwork environment.

We are currently interested in therapies targeting the MAPK pathway, which have been developed to treat RAS- or RAF-mutant tumors with high constitutive MAPK signaling. While effective in inducing temporary tumor regression, tumors eventually grow resistant to the single-agent targeted therapeutics. To overcome these challenges, targeted therapies have been combined in the clinic, including the combination of dabrafenib (BRAFi) and trametinib

(MEKi) in BRAF+ melanoma and, more recently, in BRAF+ lung cancer. Identifying further effective therapeutic combinations for MAPK agents will be critical to progress in cancer treatment. Yet, systematically finding the ideal combination regimen remains a difficult task. A priori it is not clear which approach is likely to be more effective or what indication would be more susceptible to a given combination and empirically testing all possible combinations is impractical.

We propose to build computational models, which take into account the state of the tumor cell (i.e. its gene expression profile) to accurately predict synergistic combination partners for MAPK inhibitors.

# Selected Publications

Hyperactivation of MAPK Signaling Is Deleterious to RAS/RAF-mutant Melanoma. [2]
Leung GP, Feng T, Sigoillot FD, Geyer FC, Shirley MD, Ruddy DA, Rakiec DP, Freeman AK, Engelman JA, Jaskelioff M*, Stuart DD*.
*Mol Cancer Res. 2019 Jan 1;17(1):199-211.*

Functional epigenetics approach identifies BRM/SMARCA2 as a critical synthetic lethal target in BRG1-deficient cancers. [3]
Hoffman GR, Rahal R, Buxton F, Xiang K, McAllister G, Frias E, Bagdasarian L, Huber J, Lindeman A, Chen D, Romero R, Ramadan N, Phadke T, Haas K, Jaskelioff M, Wilson BG, Meyer MJ, Saenz-Vash V, Zhai H, Myer VE, Porter JA, Keen N, McLaughlin ME, Mickanin C, Roberts CW, Stegmeier F, Jagani Z.
*Proc Natl Acad Sci U S A. 2014 Feb 25;111(8):3128-33.*

Click here [4] for additional publications.

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**Links**
[1] https://www.novartis.com/our-science/postdoc-program/research-themes/cancer-biology/mariela-jaskelioff-phd
[2] https://www.ncbi.nlm.nih.gov/pubmed/30201825
[3] https://www.ncbi.nlm.nih.gov/pubmed/24520176
[4] https://www.ncbi.nlm.nih.gov/pubmed/?term=jaskelioff