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Large scale cancer genome studies have revealed a prominent role for epigenetic dysregulation in cancers. In particular, inactivating mutations in multiple subunits of the mSWI/SNF chromatin remodeling complexes, such as SNF5, ARID1A, ARID1B, ARID2, and PBRM1 among others, have uncovered their potent roles as tumor suppressors. The mSWI/SNF complexes are among several ATP-dependent complexes that utilize the energy of ATP hydrolysis to mobilize nucleosomes and therefore impact chromatin assembly, transcription, DNA repair and recombination. The mechanisms by which loss of these chromatin regulators contributes to tumorigenesis are poorly understood. Investigating such mechanisms should provide insight into therapeutically targeting cancers with such mutations. As several mutations within this complex can be found either alone or in combination with one another in distinct cancer types (e.g., BRG1 in lung cancers, PBRM1 in renal cell carcinoma), it will be important to understand how mutations in each of these subunits specifically contributes to tumorigenesis, or whether certain common consequences occur as a result of such deficiencies. We are therefore using a combination of genomic, proteomic, and functional RNAi approaches in order to further understand the role of this complex in cancers in order to provide novel avenues for targeted therapeutics.

Selected Publications

ARID1B is a specific vulnerability in ARID1A-mutant cancers. [2]
Helming KC, Wang, X, Wilson BG, Vazquez F, Haswell JR, Manchester HE, Kim Y, Kryukov GV, Ghandi M, Aguirre AJ, Jagani Z, Wang Z, Garraway L, Hahn WC, and Roberts CWM.
Nature Medicine. 2014 March; 20(3):251-4.

Residual complexes containing SMARCA2/BRM underlie the oncogenic drive of SMARCA4/BRG1 mutation. [3]
Wilson BG, Helming KC, Wang X, Kim Y, Vazquez F, Jagani Z, Hahn WC, Roberts CW.
Mol Cell Biol. 2014 Mar; 34(6):1136-44.

Functional epigenetics approach identifies BRM/SMARCA2 as a critical synthetic lethal target in BRG1-deficient cancers. [4]
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 B, Meyer MJ, Saenz-Vash V, Zhai H, Myer VE, Porter JA, Keen N, McLaughlin ME, Mickanin C, Roberts CWM, Stegmeier F, and Jagani Z.
Proc Natl Acad Sci U S A. 2014 Feb 25; 111(8):3128-33.

Click here [5] for additional publications.

Links
[1] https://www.novartis.com/our-science/postdoc-program/research-themes/cancer-biology/zainab-jagani-phd
[2] https://www.ncbi.nlm.nih.gov/pubmed/24562383
[3] https://www.ncbi.nlm.nih.gov/pubmed/24421395
[4] https://www.ncbi.nlm.nih.gov/pubmed/24520176
[5] http://www.ncbi.nlm.nih.gov/pubmed/?term=Jagani+Z