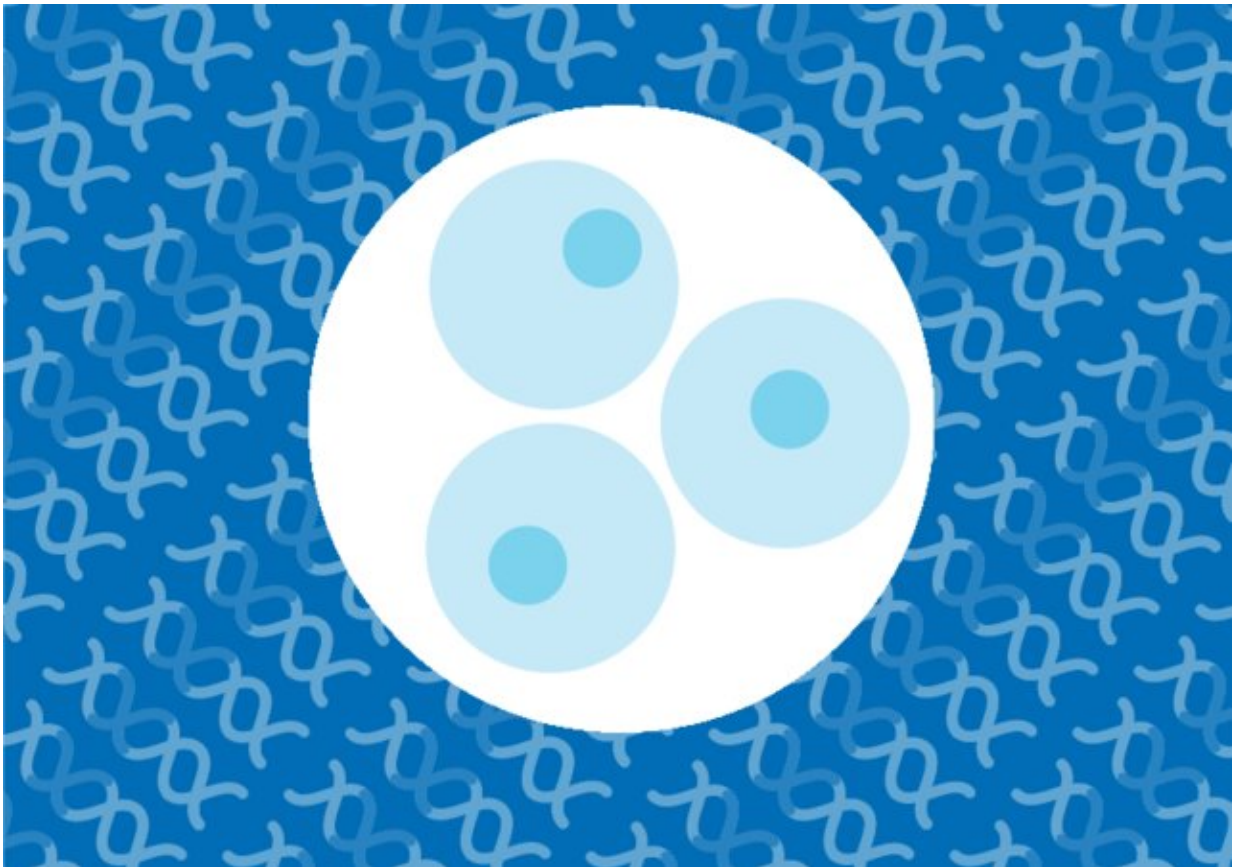


Gene expression signatures indicate loss of function by master regulators of the genome

April 10 2023, by Rob Levy



Credit: Broad Communications

Second only to the notorious TP53 gene, the genes for assemblages known as mSWI/SNF protein complexes are the most frequently

mutated entities in cancer cells. Made up of 10 to 15 subunits, the complexes are built from the activity of 29 individual genes.

The complexes play a key role in modifying chromatin—the twists of DNA and proteins that constitute chromosomes—so that genes become more or less active, switched on or switched off. Mutated forms of the genes responsible for mSWI/SNF complexes are found in more than 20% of [human cancers](#). In some cases, it is the absence or alteration of one or more of the complexes' subunits that causes cancer.

In a new study published in *Molecular Cell*, scientists at Dana-Farber Cancer Institute and the Broad Institute of MIT and Harvard, including Cigall Kadoch, an institute member at Broad and an associate professor at Dana-Farber, used CRISPR-Cas9 technology to systematically stifle the roughly 29 [genes](#) associated with mSWI/SNF complexes, individually and in informative combinations in the context of a cancer cell. They tracked how each shutdown affected the structure and make-up of the complexes.

The researchers then used the data to predict and identify, across thousands of human cancer [gene expression](#) profiles, which tumors harbor a mutation that results in a loss of mSWI/SNF function or which have gene expression patterns that mirror mSWI/SNF mutations. The findings may help doctors determine whether changes in this complex are playing important roles in a patient's cancer. Knowing these signatures, researchers aim to be better able to predict which tumors are likely to respond to the growing array of drug agents that target mSWI/SNF complexes in patients with cancer.

More information: Jordan E. Otto et al, Structural and functional properties of mSWI/SNF chromatin remodeling complexes revealed through single-cell perturbation screens, *Molecular Cell* (2023). [DOI: 10.1016/j.molcel.2023.03.013](https://doi.org/10.1016/j.molcel.2023.03.013)

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