# Research

## Chromatin Therapeutics

We have identified in several cancer types novel frequent mutations in chromatin enzymes. The latter include 1) histone modifiers such as*UTX*,*MLL3*,*SETD2*; 2) subunits of the SWI-SNF complex including*ARID1A*and*PBRM1*; and 3) subunit of MEDIATOR complex such as*MED12*. Athough all these genes are involved in gene regulation, the functional relevance of these mutations in tumorigenesis remains largely unknown. To date, we have established patient-derived cancer cell lines and xenografts harboring these mutations. By combining molecular and structural studies, our laboratory will focus on the studies of novel chromatin drugs to help elucidate the roles of these enzymes and their dysregulation in tumorigenesis. Our ultimate goal is to bring this new interesting group of drugs, either as monotherapy or combination therapy, to clinical use.

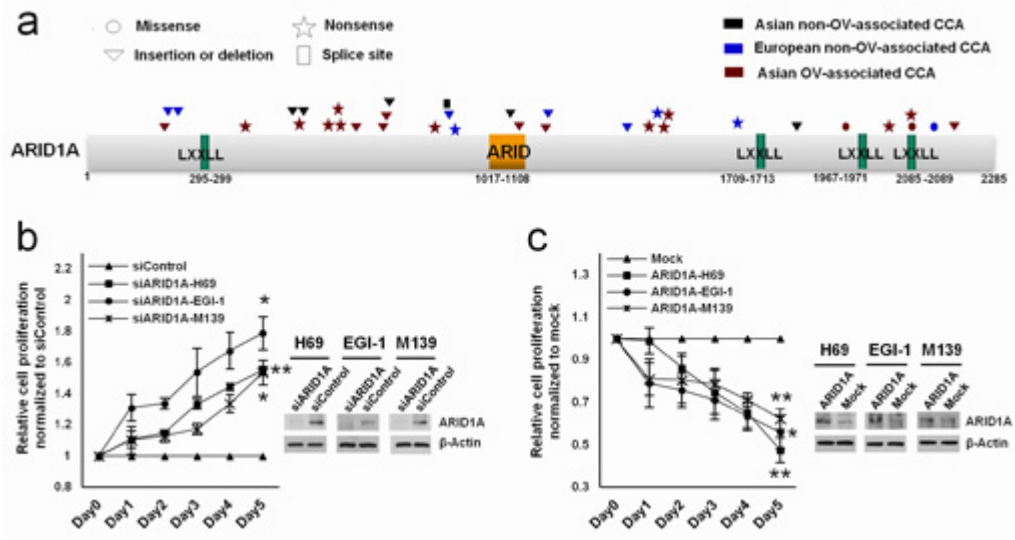


**Figure Legend:** Somatic mutations in*ARID1A*and the suppressive role of*ARID1A*in cholangiocarcinoma cell proliferation.**(a)**Distribution of*ARID1A*mutations identified in all cohorts of samples. ARID, AT-rich interactive domain; LXXLL, C-terminal leucine-rich LXXLL motif.**(b)**Relative proliferation of cell lines H69, EGI-1 and M139 (wild-type*ARID1A*) depleted of endogenous*ARID1A*using*ARID1A*-specific (siARID1A_3) compared to control siRNA.**(c)**Relative proliferation of the same cell lines exogenously transfected with vector expressing wild-type*ARID1A*(pCGT-*ARID1A*) or empty vector (mock).