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# Analyzing the Impacts of Loss of the FANCA Protein on Chromatin State

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## Analyzing the Impacts of Loss of the FANCA Protein on Chromatin State

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Fanconi Anemia (FA) is a rare human genetic disease, which occurs 1 in 160,000 individuals. Patients with FA have a high risk for clinical manifestations such as bone marrow failure, organ malformations, and increased susceptibility to cancer. The median lifespan of FA patients is 29 years; this disease is usually diagnosed during childhood and the treatment options for these patients are limited. Mutations in the FANCA gene are responsible for about 60 percent of all cases of FA. FANCA is an essential protein in the FA core complex which activates two proteins, FANCD2 and FANCI. Previous studies have shown that FANCA associates with BRG1, a subunit of the SWitch/Sucrose Non-Fermentable (SWI/SNF) chromatin remodeling complex. The SWI/SNF complex restructures nucleosomes to make DNA accessible for transcription, translation, and DNA repair. We hypothesize that FANCA may promote the recruitment of this complex to sites of DNA damage to facilitate chromatin remodeling during DNA repair. In this project, we are analyzing the role of FANCA in chromatin plasticity by determining if the absence of FANCA impacts chromatin state. To study the role of FANCA in this process, we immunoprecipitated (IP) BRG1 protein complexes from FA-A patient cells and the same cells complemented with FANCA and performed mass spectrometry (MS) to analyze SWI/SNF proteins in these complexes. Our IP-MS studies were then complemented with immunoblotting experiments using two distinct FA-A cell systems. FA-A patient cells were sent in for Assay for Transposase-Accessible Chromatin with high-throughput sequencing (ATAC-seq) in order to analyze chromatin accessibility across the genome. Our experiments have established that a particular SWI/SNF variant complex - the PBAF complex - is downregulated in the absence of the FANCA. Ongoing experiments aim to establish the functional consequences of downregulated PBAF to the molecular etiology of FA.