A Simple, Effective Approach to Screen and Identify H2A-H2B Binding Proteins

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Histone binding proteins regulate histone metabolism and play important roles in multiple biological processes that are linked to human diseases. Here we developed an in-silico approach to screen and identified human histone H2A-H2B binding proteins. Target proteins are selected from the protein database and screened based on protein characteristics, which include specific histone binding motifs, protein folding tendency, and overall charges. Then, the binding between H2A-H2B and selected proteins is predicted by AlphaFold2, a computational protein structure prediction method, and further validated by pulldown experiments. Using this approach, we screened the DNA replication-associated proteins and demonstrated that NP1L1, CHD1, TCAB1, and H3BQ83 are H2A-H2B binding proteins. Collectively, this study reports a simple yet effective approach to identifying novel H2A-H2B binding proteins.

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