Critique-Acetylation of p53 Activates Transcription through Recruitment of

Coactivators/Histone Acetyltransferases

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P53 is a tumor suppressor that works and functions in the cell cycle arrest. One of the significant suppressor p53 in individuals is predominantly involved in stopping and restricting the production of tumors. Different studies have shown that persons receiving only one copy of p53 from their parents are susceptible to malignancies and tumors. The reversible cycle that is acetylation of p53 resulted because of DNA damage. This study observed that the acetylation of p53 affects the action and roles of p53. The acetylation declines the p53-dependent transcription and it also declines G1 cell cycle arrest[[1]](#footnote-1). The study identifies that endogenous p21 promoter have been perceived to intensify its association and bond with p53 by the examination of chromatin immunoprecipitation. CBP, acetylated histones and TRRAP are the coactivators that increase association with p21. This study significantly evaluated the acetylation of p53, it's working, function, and role in the activity of p53[[2]](#footnote-2). It was suggested that the acetylation of p53 is not to improve the binding of DNA but is to endorse the recruitment of coactivator and histone acetylation. In this paper, acetylation of p53 activates transcription through recruitment of coactivators/histone acetyltransferases conducted by Nickolai and the colleagues in the year 2001 was analyzed and assessed.

**Article Summary**

The damage to cellular DNA resulted in the activation of suppressors particularly tumor suppressors. One of the important suppressor p53 in humans works by stopping and restricting the production of tumors. The acetylation of p53 is a reversible process that happens because of damage to DNA. The acetylation of p53 affects the activity and functions of p53. The acetylation decreases p53-dependent transcription and it also decreases G1 cell cycle arrest[[3]](#footnote-3). The endogenous p21 promoter has been observed to amplify its association and link with p53 by the analysis of chromatin immunoprecipitation. CBP, acetylated histones and TRRAP are the coactivators that are also have amplified association with p21[[4]](#footnote-4). The major function of the acetylation of p53 is not to upsurge the binding of DNA but is to endorse the recruitment of coactivator and histone acetylation. In this article, the acetylation of p53 and the recruitment of coactivators is significant for the functioning of p53 was observed.

P53 is important for cell proliferation and to halt the cell division before replication. It is also important for monitoring DNA damage. If the repair is not recovered, cellular apoptotic death occurs which is also encouraged by p53. p53 action is controlled from side to side numerous posttranslational alterations that mainly arise in the amino side of the protein and also in the carboxyl-terminal areas. With the consequences of DNA impairment reaction, p53 converts into strongly phosphorylated. Numerous kinases counting Chk2 and Cdk-stimulated kinase phosphorylated in the amino portion of the protein and resulted in p53 stabilization. The stabilization also needs CAK, ATR, and the phosphoinositol 3 kinase-related members ATM. The carboxyl-terminal also required phosphorylation and it stimulates binding of DNA in vitro. The outcomes existing in the study specify that acetylation is a precarious alteration of p53 required significantly for its working in vivo. It is required for p53's working in stimulating transcription. Acetylation is required for the endogenous gene p21. It is also important for p53 active reporter plasmid. Significantly, the major role of acetylation of p53 was in p53-mediated detention of the cell cycle at G1. It requires p53 associated with multiple transcription genes. This study significantly recognizes an acknowledged mechanism that is responsible for the acetylation. That mechanism is the coactivators or HATs recruitment by physical communication[[5]](#footnote-5). The initiator and essential element in the acetylation progression was histone acetyltransferase.

**Article Critique**

The study has identified that p53 acetylation is important for the physiological functions of p53. These functions involve the cell cycle arrest when there is an occurrence of DNA damage[[6]](#footnote-6). The acetylation of the p53 strongly activates the coactivators which are involved in the association of phosphorylation. The study evaluated that a large number of activators are acetylated for the transcription process. It is required for the DNA sequence-specific elements that is the coactivator's recruitment. The study approach to identify how the acetylation process creates transmission of signals to represent mechanisms for the activation of transcription was significant[[7]](#footnote-7). The other covalent alteration processes were identified successfully particularly in p53 that occurs in acetylation as posttranslational. This posttranslational modification resulted in the reaction of damage to DNA. P53 is acetylated in the regions of carboxyl-terminal specifically in the areas where regulatory tetramerization domain is located[[8]](#footnote-8). P53 acetylation is assumed to be required for the regulatory functions of p53. In the case of histone deacetylase-linked protein, p53 deacetylation conceded in its capability to encourage cell cycle detention and apoptosis[[9]](#footnote-9). The study conducted competently and experimentally proven as elaborate in the study, the function of acetylation of p53 was observed in vivo. Acetylation places in p53 were replaced, and histones bound to the p21 promoter in cells. To observe the function and status of p53, chromatin immunoprecipitation was castoff. The study indicated that acetylation is important for the functioning of p53. It was also observed that coactivators were recruited to promote p53 genes.

The outcomes showed in the study specify that acetylation is an unjustified alteration of p53 compulsory meaningfully for its working in vivo[[10]](#footnote-10). It is required for p53's functioning in stimulating transcription. Acetylation is mandatory for the endogenous gene p21. It is also significant for p53 active reporter plasmid. Suggestively, the major role of acetylation was observed in the study. It is suggested that the function of p53 was in p53-mediated detention of the cell cycle at G1. It needs p53 related to multiple transcription genes. This research significantly recognizes an acknowledged mechanism that is accountable for the acetylation. The mechanism is the coactivators or HATs recruitment by physical interrelation[[11]](#footnote-11). The research showed that acetylation transpires in the cells and also the p53 acetylation causes acetylation of histones. Examination identifies that an acetylation cascade exists in cells, where acetylation of p53 may lead to acetylation of histones. The major and essential element in the acetylation mechanism is histone acetyltransferase.

The study was performed experimentally, a methodology chosen was effective in identifying the role of acetylation of p53. The expression and purification of p53 was performed by utilizing amino-terminal 6His-tagged p53 and transformed BL21 E. coli was grown induced by 1mM isopropyl-D-thiogalactopyranoside at OD600 of 0.8[[12]](#footnote-12). The gel filtration and binding analysis was performed by utilizing superdex 200 HR10/30 column. Acetylation of the p53 was observed by taking equal amounts of purified wild type p53 and mutant p53 (acetylation site was substituted). Other experimental methods such as protein-protein interactions, PCR and indirect immunofluorescence were performed according to prescribed procedures. The acetylation of p53 where arginine substituted by lysine residues were performed. All these substituted processes in p53 showed that it does not affect structural reliability. Modern studies have indicated that effective binding of DNA does not need acetylation on longer binding sites in vitro. However, this study indicates that acetylation of p53 is not mandatory for the transcription in vitro but activates transcription[[13]](#footnote-13). This study was also performed on chromatin templates. In vivo, it may be required because of overcoming actions of DNA linked repressors which usually overlap p53 binding sites. Previous studies have suggested that p53 acetylation is involved in the actions of apoptosis and controlling the growth[[14]](#footnote-14). However, acetylation is a significant event for the upregulation of p53 functions.

**Conclusion**

The acetylation of p53 is essential for the activities and functioning of p53. It is significantly evaluated by the study that the acetylation of p53 is involved in the activation of the transcription process. The transcription was activated by the recruitment of coactivators. These coactivators were essentially required by the acetylation of p53[[15]](#footnote-15). The DNA damage causes acetylation of p53 and ultimately it affects the transcription. Certain coactivators and their immense phosphorylation processes with the help of histone acetyltransferases activates the transcriptional process in the cells. The research conducted experimentally proved and elaborate on the function and role of acetylation of p53. Experimentally, acetylation placed in p53 was substituted, and histones bound to the p21 promoter in the cells. To detect the function and status of p53, chromatin immunoprecipitation was utilized. After analysis, it was indicated that acetylation is important for the functioning and activities of p53. It was successfully suggested that coactivators were recruited to promote p53 genes[[16]](#footnote-16). The results presented in the research by Nickolai and the colleagues stipulate that acetylation is a compulsory modification of p53 required significantly for its working in vivo that is activation of transcription by recruitment of coactivators.

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