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Researchers and colleagues identify PHF20, a regulator of gene P53

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Researchers at Moffitt Cancer Center and colleagues have identified PHF20, a novel transcriptional factor, and clarified its role in maintaining the stability and transcription of p53, a gene that allows for both normal cell growth and tumor suppression. PHF20, the researchers found, plays a previously unknown and unique role in regulating p53.

When p53 is activated, it can mend DNA damage and eliminate cancer cells by binding to DNA. How p53 maintains its basal level and becomes activated remain elusive, but identifying transcription factor PHF20 and understanding its interaction with p53 and its induction of p53 protein stability and transcription has provided a clue.

Results of their research appeared in a recent issue of *Nature Structural & Molecular Biology* and also in The *Journal of Biological Chemistry*.

"When a cell undergoes alterations that predispose it to become cancerous, p53 is activated to either mend the DNA damage or eliminate the affected cells, thereby preventing the development of tumors," said Jin Q. Cheng, Ph.D., M.D., a senior member of the Molecular Oncology Department and Molecular Oncology and Drug Discovery Program at Moffitt. "A number of mechanisms normally keep a regulatory strong check on p53 and allow for rapid activation. Still much is unknown about the mechanism of p53 regulation."

After identifying PHF20 as a novel transcriptional factor, the researchers set out in subsequent studies to probe the function of human

PHF20 and its effect on p53. They found that PHF20 not only transcriptionally induces p53 but also directly interacts with and stabilizes p53. Akt negatively regulates these processes by interaction and phosphorylation of PHF20.

To determine whether the absence of PHF20 might regulate stress-induced p53 expression, the researchers "knocked down" PHF20. In doing so, they demonstrated that in the absence of PHF20, p53 was reduced. These findings established the role of PHF20 as a key regulator of p53 and additional link between Akt and p53.

According to Cheng, the identification of PHF20 as a regulator of p53 is significant because PHF20 "participates in simultaneous multiple interactions with other proteins and DNA" and serves to stabilize and induce p53.

"Regulation of p53 is critical to allow both normal cell growth and tumor suppression," explained Cheng. "However, further investigation is required to understand PHF20 tumor suppressor function and its possible involvement in human malignancy."

Provided by H. Lee Moffitt Cancer Center & Research Institute