FALL 2019

Biochemistry and Molecular Biology Brown Bag Series

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Ph.D. Student

"TIP60 regulation of ΔNp63α promotes cellular proliferation"

Tuesday, September 24, 2019

11:00 AM

141 Medical Sciences Building

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http://www.med.wright.edu/bmb

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Abstract

More than 3 million cases of non-melanoma skin cancer (NMSC) are reported in the U.S each year. ΔNp63α, a proto-oncogene in the p53 family of transcription factors, is overexpressed in squamous cell carcinoma (SCC) and associated with poor prognosis and survival. ΔNp63α elicits its tumorigenic effects, in part, by promoting cellular proliferation and cell survival. Despite its importance to SCC, the upstream regulation of ΔNp63α is poorly understood. In this study, we identify TIP60 as a novel upstream regulator of ΔNp63α. Using a combination of overexpression, silencing, and stable expression approaches in multiple cell lines, we showed that TIP60 upregulates ΔNp63α expression. Utilizing a pharmacological inhibitor and cycloheximide treatment, we showed that TIP60 catalytic activity is required for stabilization of ΔNp63α protein levels. We further showed that TIP60 inhibits ΔNp63α ubiquitination and proteasomal degradation by immunoprecipitation of ubiquitinated ΔNp63α with and without TIP60 overexpression. Stabilization of the ΔNp63α protein was further associated with TIP60-mediated acetylation. Finally, we demonstrated that TIP60-mediated regulation of ΔNp63α increases cellular proliferation by promoting G2/M progression by performing MTS assays and flow cytometry. Our findings provide evidence that TIP60 may contribute to SCC progression by increasing ΔNp63α protein levels thereby promoting cellular proliferation.