SPRING 2022

Biochemistry and Molecular Biology Brown Bag Series

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" TIP60 mediated regulation of ΔNp63α is associated with cisplatin resistance"

Tuesday, January 25, 2022

11:00 AM

Location 135 Oelman Hall

Lab: Madhavi Kadakia, Ph.D.

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

TIP60 mediated regulation of ΔNp63α is associated with cisplatin resistance

ΔNp63α, member of the p53 family of transcription factor, is overexpressed in squamous cell carcinomas (SCCs) including cutaneous SCC and Head and Neck SCC where it induces cell survival and inhibits cell apoptosis and invasion. TIP60 is a histone acetyltransferase (HAT) which mediates cellular processes such as transcription and DNA damage response (DDR). Previous studies from our lab have shown that TIP60 acetylates ΔNp63α and increases its protein stability. Since ΔNp63α is known to transcriptionally regulate several DDR genes, its stabilization by TIP60 may contribute to the failure of platinum-based drugs in SCC. TIP60 positively regulates ΔNp63α levels in multiple SCC cell lines including acquired Platinum resistant A431 Pt cells and naturally cisplatin resistant JHU006 cell line. Knockdown of TIP60 and ΔNp63α sensitizes cells to cisplatin and induces cell death. Moreover, pharmacological inhibition of TIP60 reduces acetylation of ΔNp63α in cisplatin resistant cells and thus sensitize the cells to cisplatin. To further determine the role of TIP60 and ΔNp63α in promoting cisplatin resistance, we examined the change in the transcript levels of DDR gene panel in cisplatin sensitive and resistant cell line. Taken together, our data suggests that increased TIP60 in cisplatin resistance cells protects ΔNp63α levels from degradation, thereby promoting cisplatin resistance in SCCs.