



**SPRING 2021**

**Biochemistry and Molecular Biology  
Brown Bag Series**

**Akshay Hira**

Ph.D. Student

***“TIP60 mediated regulation of  $\Delta$ Np63 $\alpha$  is associated with cisplatin resistance”***

Tuesday, January 19, 2021

11:00 AM

**Please contact x3249 if you would like to attend but  
did not receive an emailed link.**

Lab: Madhavi Kadakia, Ph.D.

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

## Abstract

### **TIP60 mediated regulation of $\Delta$ Np63 $\alpha$ is associated with cisplatin resistance**

$\Delta$ Np63 $\alpha$ , 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  $\Delta$ Np63 $\alpha$  and increases its protein stability. Since  $\Delta$ Np63 $\alpha$  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  $\Delta$ Np63 $\alpha$  levels in multiple SCC cell lines including acquired Platinum resistant A431 Pt cells and naturally cisplatin resistant JHU006 cell line. Knockdown of TIP60 and  $\Delta$ Np63 $\alpha$  sensitizes cells to cisplatin and induces cell death. Moreover, pharmacological inhibition of TIP60 reduces acetylation of  $\Delta$ Np63 $\alpha$  in cisplatin resistant cells and thus sensitize the cells to cisplatin. To further determine the role of TIP60 and  $\Delta$ Np63 $\alpha$  in promoting cisplatin resistance, we examined the change in the transcript levels of 62 DDR genes in cisplatin sensitive and resistant cell line. Taken together, our data suggests that increased TIP60 in cisplatin resistance cells protects  $\Delta$ Np63 $\alpha$  levels from degradation, thereby promoting cisplatin resistance in SCCs.