Department of Biological Sciences

Graduate Seminar

Speaker – **Swati Swagatika** Advisor – **Dr. R. S. Tomar**
Date/Time – **17 Apr. 2017, at 10:00 AM** Venue – **L11, LHC**

Mechanistic insights into the effect of Cantharidin on epigenome using *Saccharomyces cerevisiae* as a model organism

Abstract:

Cantharidin, a terpenoid compound, is found in Spanish fly, *Cantharis vesicatoria*. It has been widely studied as an anticancer molecule because of its cytotoxic effects on several human cancer cell lines [1, 2]. The anticancer properties of this compound are accredited to its ability to induce cell death through G2/M cell cycle arrest, DNA damage and apoptosis [1, 2]. Additionally, it is known to suppress cancer metastasis [3]. Cantharidin has also been shown to be a potent inhibitor of protein phosphatase 2A (PP2A), a positive regulator of cell growth and division [4]. Although several studies on cantharidin have brought ample knowledge about its potential genetic targets and usage as an anticancer molecule, the epigenetic targets of this compound are largely unknown. In the present study, we used cantharidin as a small molecule to understand its effect on epigenome using budding yeast as a model organism. Our initial screening with H3/H4 deletion library revealed few histone tail truncation/substitution mutants to be sensitive upon cantharidin treatment. Furthermore, we found down regulation of *CRG1* (Cantharidin Resistance Gene; that confers resistance to cantharidin) expression in few sensitive strains. Taken together, our study is aimed at unraveling the potential epigenetic targets of cantharidin.

References:

1. Li, W., Xie, L., Chen, Z., Zhu, Y., Sun, Y., Miao, Y., Xu, Z. & Han, X. (2010) Cantharidin, a potent and selective PP2A inhibitor, induces an oxidative stress-independent growth inhibition of pancreatic cancer cells through G2/M cell-cycle arrest and apoptosis, *Cancer science.* **101**, 1226-33.
2. Hsia, T. C., Lin, J. H., Hsu, S. C., Tang, N. Y., Lu, H. F., Wu, S. H., Lin, J. G. & Chung, J. G. (2015) Cantharidin induces DNA damage and inhibits DNA repair-associated protein levels in NCI-H460 human lung cancer cells, *Environmental toxicology.* **30**, 1135-43.
3. Shen, M., Wu, M. Y., Chen, L. P., Zhi, Q., Gong, F. R., Chen, K., Li, D. M., Wu, Y., Tao, M. & Li, W. (2015) Cantharidin represses invasion of pancreatic cancer cells through accelerated degradation of MMP2 mRNA, *Scientific reports.* **5**, 11836.
4. Honkanen, R. E. (1993) Cantharidin, another natural toxin that inhibits the activity of serine/threonine protein phosphatases types 1 and 2A, *FEBS letters.* **330**, 283-6.