Ph.D. Seminar I

Department of Chemistry, IIT-Madras

Multi-targeting by small-molecules as a strategy to combat cancer cell proliferation and resistance

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Date: 03.10.19 **Venue: CB310** **Time: 3.00 p.m.**

Cancer is a complex disease with large mortality rates. Estimates show that about 9.6 million people have died of cancer in 2018 alone.[1] Radiation therapy, chemotherapy, immunotherapy *etc.* are some of the common approaches to treat this disease. Chemotherapy using small molecules has shown great promise but resistance development often comes as the bottleneck.[2] This method usually targets the DNA or uses chemical compounds to interfere with metabolic pathways (antimetabolites), kinase function etc. In parallel with this, redox chemotherapy, which employs chemical compounds for perturbing the redox homeostasis in cancer cells is also gaining attention.[3] There are examples of molecules like doxorubicin, mitomycin C, and streptonigrin which operate through both these mechanisms. If good safety profile can be attained, such molecules will face lesser chance of resistance development. In this context, design and development of new chemical compounds which can target more than one target or pathways in cancer cells have high significance. After discussing some of the literature development in this area, the strategies we are following to design new chemical systems will be presented. The proposed doctoral work also aims to understand the cellular effects of small molecules which can release gasotransmitters like H_2S through a biochemical triggering mechanism. This is based on the fact that H_2S releasing molecules were found capable of arresting G2/M phase and reducing cell proliferation in HCT15 model (colon cancer) and MGC803 (gastric cancer) cell lines.[4] Considering wide-spread biochemical roles of H_2S and its involvement in various diseases, new methodologies for its quantification in biological samples will also be discussed.[5]

References:

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3) a) Chen W., Balakrishnan K., Kuang Y., Han Y., Fu M., Gandhi V. and Peng X. *J. Med. Chem.* **2014**, 57, 4498. b) Fleur M. F. and Nathanael S. G. *Nat. Rev. Drug Discov.* **2018**, 17, 353.

4) Ling H., Zhang L. Y., Su Q., Song Y., Luo Z. Y., Zhou X. T., Zeng X., He J., Tan H .and Yuan J. P., *Cell Mol. Biol. Lett.* **2006**, 11,408

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Guide 01-10-19

Seminar Coordinator

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