

11<sup>th</sup> International Conference and Exhibition on

# Pharmacology and Ethnopharmacology & International Conference on **Pharmaceutical Oncology**

July 18-19, 2018 | Atlanta, USA



## *Andrei L Gartel*

*University of Illinois, USA*

### **The role of Forkhead box protein M1 in cancer**

Forkhead box protein M1 (FOXO1) is overexpressed in the majority of human cancers and its expression correlates with unfavorable prognosis. Since the FOXO1 regulatory network is a major predictor of adverse outcomes in human cancers, inactivation of FOXO1 by the FOXO1 inhibitors an attractive treatment strategy. Nucleophosmin (NPM) belongs to the nucleophosmin/nucleoplasmin family of chaperones, which are ubiquitously expressed in mammalian cells. FOXO1 interacts with NPM in human cancer cells and NPM knockdown in human cancer cells led to significant down-regulation of FOXO1. Our data suggest that in human cancer cells NPM interacts with FOXO1 and their interaction is required for sustaining the level and localization of FOXO1. In some cases of AML mutant NPM re-localizes to the cytoplasm. We found that improved outcome for AML patients with mutant NPM1 is linked to the cytoplasmic localization and consequent functional inactivation of FOXO1 that driven by mutant NPM to the cytoplasm. This premise suggests that nuclear FOXO1 is one of the drivers for AML development. We identified two compounds that inhibit NPM/FOXO1 interaction and suppress FOXO1 expression in human cancer cell lines. In addition, these compounds synergize with different chemotherapeutic drugs. The compounds are predicted to bind at two sites on NPM homo-oligomerization domain and they would likely block NPM oligomerization. Therefore, by disrupting monomer-monomer interactions, they are also precluding binding of NPM and FOXO1. In addition, we found that honokiol and HSP70 bind to FOXO1 and inhibit its activity and expression. We hypothesize that since FOXO1 contributes to the progression and metastasis of human cancer, targeting FOXO1 with small molecules will improve treatment outcomes for cancer patients.

### **Biography**

Andrei L Gartel, PhD, is a Professor in the Department of Medicine at the University of Illinois at Chicago, and is the academic editor of PLOS ONE. He is the author of 90 peer-review publications that include more than 20 reviews. He has more than 11,000 citations and his h-index is 41. His scientific interests include cancer, cell cycle, protein-protein interactions, regulation of CDK inhibitor p21 and regulation of oncogenic transcription factor FOXO1. Currently, his lab is interested in identification of new FOXO1 inhibitors. He received his funding from NIH, DOD and private companies/foundations.

[agartel@uic.edu](mailto:agartel@uic.edu)

### **Notes:**