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Andrei L Gartel

University of Illinois at Chicago, USA

FOX(M1) and cancer

FOXM1 is an oncogenic transcription factor that is overexpressed in the majority of human cancers and is a potential target for anticancer drugs. We identified proteasome inhibitors as the first type of drugs that target FOXM1 in cancer cells. Moreover, we found that HSP90 inhibitor PF-4942847 that does not act as proteasome inhibitor also suppresses FOXM1. Chaperone HSP70 is induced after treatment with both proteasome/HSP90 inhibitors and after heat-shock stress and we identified this chaperone as a novel negative regulator of FOXM1 after proteotoxic stress. We showed that FOXM1 and HSP70 interact in cancer cells following proteotoxic stress and FOXM1/HSP70 interaction led to inhibition of FOXM1. We have previously shown that FOXM1 interacts with nucleophosmin (NPM) in cancer cells and NPM determines the cellular localization of FOXM1. Mutations in NPM1 result in cytoplasmic re-localization of NPM (NPM1mut) and favorable outcome for the patients. We found the evidence that improved outcomes in the subset of NPM1mut AML may be partially explained by the cytoplasmic re-localization and consequent functional inactivation of FOXM1. First, we confirmed the co-localization of FOXM1 and NPMmut in the cytoplasm of AML patients bone marrow biopsies and determined a strong cytoplasmic expression of FOXM1 only in NPM1mut AML cells. We also showed an important role of FOXM1 in chemo-resistance in leukemia cell lines with nuclear, but not cytoplasmic FOXM1. These data imply that suppressing of FOXM1 in AML could increase sensitivity to standard chemotherapy.

Biography

Andrei L Gartel, PhD, is an Associate 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 25 reviews. He has more than 11,000 citations and his h-index is 41. His scientific interests include cancer, regulation of oncogenic transcription factors FOXM1, protein-protein interactions; cell cycle and regulation of CDK inhibitor p21. Specifically, his lab is interested in the identification of new FOXM1 inhibitors. He received his funding from NIH, DOD and private companies/foundations.

agartel@uic.edu

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