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FOX (M1) news-it is cancer

FOX M1 is an oncogenic transcription factor that is overexpressed in majority of human cancers and it is a potential target for anticancer drugs. We identified proteasome inhibitors as the first type of drugs that target FOX M1 in cancer cells. Chaperone HSP70 is induced after treatment with proteasome inhibitors and we identified this chaperone as a novel negative regulator of FOX M1 after proteotoxic stress. We showed that FOX M1 and HSP70 interact in cancer cells following proteotoxic stress and FOX M1/HSP70 interaction led to inhibition of FOX M1. Honokiol is a natural product that inhibits FOX M1-mediated transcription and FOX M1 protein expression. We found that honokiol's inhibitory effect on FOX M1 is a result of direct binding of honokiol to FOX M1. This binding is specific to honokiol, a dimerized allylphenol, and was not observed in compounds that either were monomeric allylphenols or un-substituted dihydroxy phenols. We have previously shown that FOX M1 interacts with nucleophosmin (NPM) in cancer cells and NPM determines cellular localization of FOX M1. Mutations in NPM1 result in cytoplasmic re-localization of NPM (NPM1^{mut}) and favorable outcome for the AML patients. We found the evidence that improved outcomes in the subset of NPM1^{mut} AML may be partially explained by the cytoplasmic re-localization and consequent functional inactivation of FOX M1. We also showed an important role of FOX M1 in chemo-resistance in AML with nuclear, but not cytoplasmic FOX M1. These data imply that suppressing of FOX M1 in AML could increase sensitivity to standard chemotherapy, while overexpression of FOX M1 would increase chemo-resistance of AML cells.

Biography

Andrei L Gartel is working as 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 88 peer-reviewed publications that include more than 25 reviews. He has more than 11,000 citations and his h-index is 38. His scientific interests include cancer, regulation of oncogenic transcription factors FOX M1, protein-protein interactions; cell cycle and regulation of CDK inhibitor p21. Specifically, his lab is interested in identification of new FOX M1 inhibitors. He received his funding from NIH, DOD and private companies/foundations.

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