Andrei L Gartel, J Drug Metab Toxicol 2015, 6:4
http://dx.doi.org/10.4172/2157-7609.C1.002

OMICS International
conferenceseries.com

World Congress and Exhibition on
Antibiotics
September 14-16, 2015 Las Vegas, USA

Thiazole antibiotics against cancer

Andrei L Gartel
University of Illinois, USA

The oncogenic transcription factor forkhead box M1 (FOXM1) is overexpressed in human cancer, while its expression is turned off in terminally differentiated cells. For this reason, FOXM1 is an attractive target for anticancer drugs. Using a high-throughput, cell-based assay system, we screened for and isolated the antibiotic thiazole compound Siomycin Aas FOXM1 inhibitor. Next, we found that structurally similar thiazole antibiotic, thiostrepton also inhibits the transcriptional activity and expression of FOXM1. The thiazole antibiotics efficiently inhibited the growth and induced strong apoptosis in human cancer cell lines of different origin. It turned out that Siomycin A and thiostrepton act as proteasome inhibitors in mammalian cells. In addition, we showed that thiostrepton, when formulated into nanoparticles, is highly suited for delivery to tumors. We decided to examine whether other known thiazole antibiotics such as berninamycin, micrococcin P1 and P2, thiocillin and YM-266183 (lacking the quinaldic acid ring B) also have this activity. Several thiazole antibiotics have a macrocyclic loop connecting thiazole rings at position 2 and 3 described as ring A, while thiostrepton and Siomycin A have in addition a quinaldic acid macrocycle also connected to thiazole on position 2 described as ring B. We found that berninamycin, micrococcin P1 and P2, thiocillin and YM-266183 do not act as proteasome inhibitors. Moreover, structural modification of thiostrepton to thiostrepton methyl ester (with open B ring) also did not show this activity. These data suggest that A and B rings are required for the proteasome inhibitory activity of these drugs.

Biography

Andrei L Gartel, PhD is an Associate Professor in Department of Medicine at the University of Illinois at Chicago, and the academic editor of PLOS ONE. He is the author of 86 peer-review publications with more than 8500 citations and with H-index 35. His scientific interests are cancer, cell cycle, transcriptional gene regulation, cyclin-dependent kinase inhibitors including p21, regulation of oncogenic transcription factors FOXM1 and c-Myc. He showed that thiazole antibiotic thio-strepton targets FOXM1 and could be delivered in nanoparticles to cancer cells to suppress FOXM1.

agartel@uic.edu

Notes: