Alexei G Basnakian et al., J Clinic Toxicol 2016, 6:5(Suppl)
http://dx.doi.org/10.4172/2161-0495.C1.018

Identification of cell death endonuclease inhibitors as potential anti-toxicity drugs

Alexei G Basnakian, Dae Song Jang, Tariq Fahmi, Narsimha R Penthala and Peter A Crooks
[1]University of Arkansas for Medical Sciences, USA
[2]Central Arkansas Veterans Healthcare System, USA

Apoptotic endonucleases are the enzymes that universally induce irreversible cell death by fragmenting DNA in response to cell injury. While most of the DNase/endonuclease activity is used after cell death, the latest studies showed that genetic inactivation of some endonucleases provide protection of cells and tissues against DNA breaks induced by cytotoxic stimuli. These data suggest that DNases act before the "point of no return" in cell death, and display a possibility for new therapeutics aimed to inhibit endonucleases for tissue protection. However, inhibitors of apoptotic endonucleases are not available. We have developed several high throughput screening assays based on a proprietary fluorescent probe. This assays applied in solution allowed the identification of several new inhibitors of two apoptotic DNases, deoxyribonuclease I (DNase I) and endonucleases G (EndoG). The DNase inhibitors were able to partially protect kidney cells and mice from cisplatin toxicity. These or similar assays have a great promise as tools for new drug discovery.

Biography

Alexei G Basnakian received his PhD and DSc degrees from the Russian Academy of Medical Science, both in the field of DNA endonucleases. He had Post-doctoral trainings in Molecular Biology at the Harvard Medical School and in Toxicology/Cancer Research at the National Center for Toxicological Research. He is Professor in the Department of Pharmacology and Toxicology, and Director of the DNA Damage and Toxicology Core Center at the University of Arkansas for Medical Sciences, and Research Career Scientist at the Veteran's Hospital in Little Rock, Arkansas, USA. He is an author of more than 85 peer-reviewed papers and 12 reviews or book chapters. He is an Editorial Board Member of several biomedical journals, and a member of NIH and VA grant study sections. His research interests are in DNA endonucleases and DNA damage associated with toxicity, anti-cancer therapy, cell injury and cell death.

BasnakianAlexeiG@uams.edu

Notes: