

Rowan University

Rowan Digital Works

School of Osteopathic Medicine Faculty
Scholarship

School of Osteopathic Medicine

12-15-2017

Targeting Ribosome Assembly Factors Selectively Protects p53 Positive Cells from Chemotherapeutic Agents

Russell T. Sapio
Rowan University


Anastasiya Nezdur
Rowan University

Matthew Krevetski
Rowan University

Leonid Anikin
Rowan University

Vincent J. Manna

Follow this and additional works at: https://rdw.rowan.edu/som_facpub

 Part of the [Biological Phenomena, Cell Phenomena, and Immunity Commons](#), [Cancer Biology Commons](#), [Cell Biology Commons](#), [Chemical and Pharmacologic Phenomena Commons](#), [Medical Toxicology Commons](#), [Medicinal Chemistry and Pharmaceutics Commons](#), [Neoplasms Commons](#), [Pharmaceutical Preparations Commons](#), and the [Physiological Processes Commons](#)

See next page for additional authors

Let us know how access to this document benefits you - share your thoughts on our feedback form.

Recommended Citation

Sapio RT, Nezdur AN, Krevetski M, Anikin L, Manna VJ, Minkovsky N, Pestov D. Targeting ribosome assembly factors selectively protects p53 positive cells from chemotherapeutic agents [Conference Abstract P1305]. *Molecular Biology of the Cell*. 2017 Dec 15;28(26):3727. doi: 10.1091/mbc.E17-10-0618. PMID: 29237772. PMCID: PMC5739290.

This Poster is brought to you for free and open access by the School of Osteopathic Medicine at Rowan Digital Works. It has been accepted for inclusion in School of Osteopathic Medicine Faculty Scholarship by an authorized administrator of Rowan Digital Works. For more information, please contact brush@rowan.edu.

Authors

Russell T. Sapio, Anastasiya Nezdyur, Matthew Krevetski, Leonid Anikin, Vincent J. Manna, N. Minkovsky, and Dimitri G Pestov

P1305

Board Number: B312

Targeting Ribosome Assembly Factors Selectively Protects p53 Positive Cells from Chemotherapeutic Agents.

R.T. Sapio¹, A.N. Nezdyur², M. Krevetski³, L. Anikin¹, V.J. Manna⁴, N. Minkovsky³, D. Pestov¹;

¹Cell Biology and Neuroscience, Graduate School of Biomedical Sciences, Rowan University, Stratford, NJ,

²Chemistry and Biochemistry, Rowan University, Glassboro, NJ, ³Biological Sciences, Rowan University, Glassboro, NJ, ⁴Molecular Biology, Graduate School of Biomedical Sciences, Rowan University, Stratford, NJ

Many chemotherapeutic agents act in a nondiscriminatory fashion, targeting both cancerous and noncancerous cells in S phase and M phase. One approach to reduce the toxic side effects in normal tissue is to exploit the differences in p53 functionality between cancerous and noncancerous cells. For example, activating p53 signaling by nongenotoxic means can transiently arrest noncancerous p53 positive cells in G1 phase and protect them from the cytotoxic effects of chemotherapeutic drugs. However, since most cancerous cells have faulty p53 signaling, they will proceed to cycle, and continue to be affected by the drug. In this study we asked if this G1-phase arrest and cytoprotection can be achieved by targeting ribosome biogenesis. Through the expression of a dominant negative mutant ribosome assembly factor Bop1, we were able to transiently inhibit rRNA maturation. Using this genetic model, we have shown that inhibition of rRNA maturation protects 3T3 cells from chemotherapeutic agents camptothecin and methotrexate. This cytoprotection is associated with a transient arrest of cells in G1 phase, and is p53 dependent. We have also shown that the depletion of ribosomal protein Rps19 via shRNA arrests cells in G1 phase and protects them from camptothecin. However, this G1 arrest and cytoprotection was not achieved in shRNA-mediated depletion of several other tested ribosomal proteins, indicating distinct cellular responses to different targets in ribosome biogenesis. Using a mixed population of isogenic p53 positive and p53 negative cell lines, we have further shown that camptothecin in combination with the inhibition of ribosome biogenesis selectively kills p53 negative cells. We propose that the inhibition of select post-transcriptional ribosome assembly steps can enhance the efficiency of existing chemotherapeutic treatments.