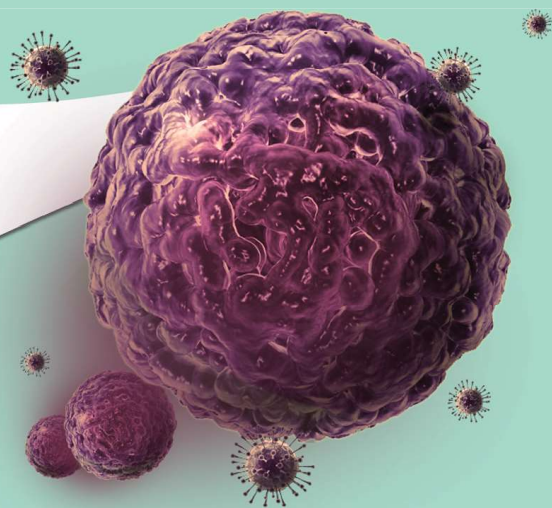
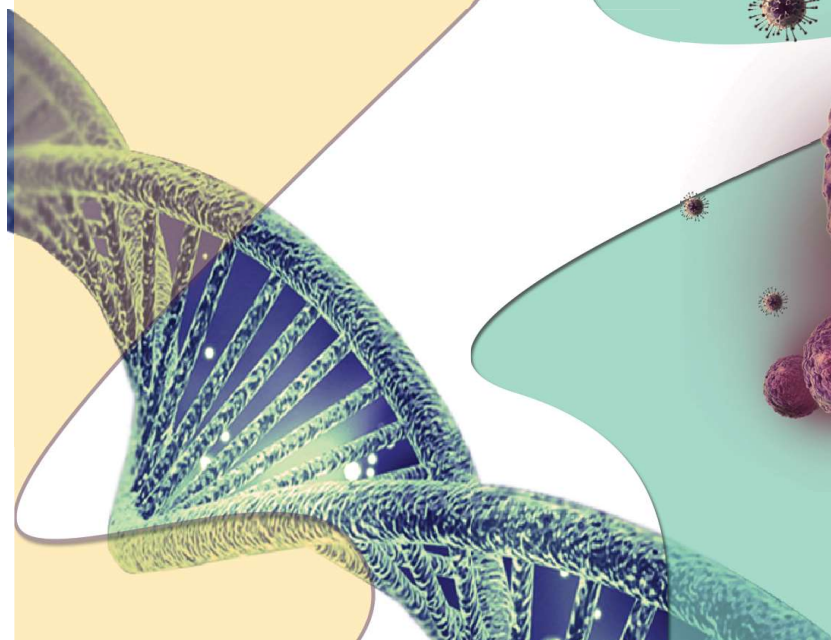


SERBIAN ASSOCIATION FOR CANCER RESEARCH

**4<sup>TH</sup> CONGRESS OF SDIR:  
BRINGING SCIENCE TO ONCOLOGY  
PRACTICE: WHERE IS SERBIA?**

**ABSTRACT  
BOOK**



**BELGRADE  
3 - 5 OCTOBER**

**2019**

4<sup>TH</sup> CONGRESS OF THE SERBIAN ASSOCIATION FOR CANCER RESEARCH  
WITH INTERNATIONAL PARTICIPATION

**ABSTRACT**

**BOOK**

“BRINGING SCIENCE TO ONCOLOGY PRACTICE:  
WHERE IS SERBIA?”

**SDIR-4**

**Belgrade, 3 - 5 October 2019**

## THE FOURTH CONGRESS OF THE SERBIAN ASSOCIATION FOR CANCER RESEARCH

with international participation

“BRINGING SCIENCE TO ONCOLOGY PRACTICE: WHERE IS SERBIA?”

SDIR-4

3-5 October 2019, Hotel “M”, Bulevar oslobođenja 56a, Belgrade, Serbia

Serbian Association for Cancer Research (SDIR) is a member of the European Association for Cancer Research (EACR).

President of SDIR-4 Congress

*dr sc. med.* Mirjana Branković-Magić

THE FOURTH CONGRESS OF THE SERBIAN ASSOCIATION FOR CANCER RESEARCH  
with international participation “Bringing Science to Oncology Practice: Where is Serbia?”

Belgrade, 3-5 October 2019

Publisher: Srpsko društvo istraživača raka, 11000 Beograd

Year: 2019.

Editors: *dr sc.* Ivana Matić, *dr sc.* Marija Đorđić Crnogorac

Print: DOSIJE STUDIO, Beograd

Number of copies: 120

ISBN: 978-86-919183-2-3

CIP - Каталогизacija у публикацији - Народна библиотека Србије,  
Београд

616-006(048)

SERBIAN Association for Cancer Research. Congress (4 ; 2019 ; Beograd)  
Bringing Science to Oncology Practice: Where is Serbia? : abstract book  
/ 4th Congress of the Serbian Association for Cancer Research with  
International Participation SDIR-4, Belgrade, 3 - 5 October 2019 ; [editors  
Ivana Matić, Marija Đorđić Crnogorac]. - Beograd : Srpsko društvo  
istraživača raka,, 2019 (Beograd : Dosije studio). - 57 str. ; 23 cm

Tiraž 120. - Registar.

ISBN 978-86-919183-2-3

a) Онкологија - Апстракти

COBISS.SR-ID 279690764

## P29 - O

## c-Src inhibitors pyrozolo[3,4-d]pyrimidines, Si306 and pro-Si306, evade multidrug resistant phenotype and suppress invasion in glioblastoma

Marija Nešović<sup>1</sup>, Ana Podolski-Renić<sup>1</sup>, Tijana Stanković<sup>1</sup>, Aleksandra Divac Rankov<sup>2</sup>, Igor Nikolić<sup>3,4</sup>, Goran Tasić<sup>3,4</sup>, Maurizio Botta<sup>5</sup>, Milica Pešić<sup>1</sup>, Jelena Dinić<sup>1</sup>

<sup>1</sup>Department of Neurobiology, Institute for Biological Research "Siniša Stanković", University of Belgrade, Belgrade, Serbia

<sup>2</sup>Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Belgrade, Serbia

<sup>3</sup>Clinic for Neurosurgery, Clinical Center of Serbia, Belgrade, Serbia

<sup>4</sup>School of Medicine, University of Belgrade, Belgrade, Serbia

<sup>5</sup>Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Siena, Italy

**Background:** Glioblastoma multiforme (GBM) are the most frequent and aggressive (WHO grade IV) brain tumors in adults. GBM have high expression of c-Src tyrosine kinase involved in survival, migration and invasiveness of tumor cells. Thus, c-Src emerged as a potential target for GBM therapy. **Materials and methods:** Antiproliferative effect of c-Src inhibitors pyrozolo[3,4-d]pyrimidines, Si306 and its prodrug pro-Si306, was assessed in human GBM cell line U87, multidrug resistant (MDR) U87-TxR, and primary GBM cells by MTT assay. Anti-migratory and anti-invasive effects of c-Src inhibitors were evaluated by gelatin degradation and transwell invasion assays. Their effect on c-Src, extracellular signal-related kinase (ERK), and focal adhesion kinase (FAK) expression was analyzed by western-blot and flow-cytometry. Zebrafish model was used to evaluate anti-invasive potential of pro-Si306 in U87 xenografts *in vivo*. **Results and conclusions:** c-Src inhibitors were more efficient in cell growth inhibition compared to dasatinib, a well-known tyrosine kinase inhibitor. The potency of Si306 and pro-Si306 was not affected by the MDR phenotype. Migratory potential of U87, U87-TxR, and primary GBM cells was significantly decreased by both inhibitors. Si306 and pro-Si306 also compromised cells' ability to degrade the matrix and invade through basement membrane. Both compounds reduced phosphorylation of c-Src, and its downstream signaling components, ERK and FAK, in GBM cell lines. *In vivo*, pro-Si306 showed anti-invasive effect against U87 xenografts in zebrafish model. Considering their ability to suppress migration and invasion and overcome MDR, Si306 and pro-Si306 could be considered in GBM treatment alone or in combination with other chemotherapeutics. **Keywords:** glioblastoma, multidrug resistance, primary cells, invasion, migration