



New Diagnostic and Therapeutic Tools against
Multidrug Resistant Tumours

ABSTRACT BOOK

STRATAGEM CA17104
Annual Conference
3rd MC meeting and 4th WGs meeting
Belgrade, Serbia
27th - 28th February, 2020

Welcome to Belgrade

The COST Action CA17104 STRATAGEM Annual Conference – 3rd MC meeting and 4th WGs meetings will take place in Belgrade, at the 88 Rooms Hotel in Belgrade, from 27th to 28th February, 2020. In line with the Action title “New diagnostic and therapeutic tools against multidrug resistant tumours”, this meeting will provide an excellent scientific program led by international experts. Invited speakers with different expertise in cancer research, therapy, chemistry, toxicology, and bioinformatics will widen our knowledge from tumor microenvironment to tumor therapy. A talk dedicated to the memory of our honorable colleague Prof. Maurizio Botta will remind us of his work and achievements. His work inspired fruitful collaborations within our COST Action. Besides, special attention will be given to the education of young scientists through the round tables “Meet the invited speakers”, “MDR research towards therapy” and “MDR research towards diagnostics”. Information on how to apply for the STSM and ITCCG will also be provided during our Annual Conference. ECIs will be given a chance to present their successful STSM stories and compete for the Best Poster Award.

Belgrade – a historic capital full of beauty, history of destruction and reconstruction, famous for its traditional hospitality, food and the best time in Europe – is the perfect place to go for new ideas and collaborations.

We look forward to welcoming you at the STRATAGEM Meeting!

Scientific Committee

Dr. Chiara Riganti – Action Chair (Italy)
Prof. Roberta Fruttero – Former Action Chair (Italy)
Dr. Javier De Las Rivas – Action Vice Chair (Spain)
Mr. Thomas Mohr – WG 1 Leader (Austria)
Prof. Catherine Passirani – WG 2 Leader (France)
Prof. M. Helena Vasconcelos – WG 3 Leader (Portugal)
Dr. Simona Saponara – WG 4 Leader (Italy)
Dr. José M. Padrón - Science Communications Manager (Spain)
Dr. Milica Pešić - STSM Coordinator (Serbia)
Dr. Jitka Viktorova – ITC CG Coordinator (Czech Republic)

Local Organizing Committee

Department of Neurobiology
Institute for Biological Research “Siniša Stanković” - National Institute
of Republic of Serbia
University of Belgrade

Dr. Milica Pešić
Dr. Jelena Dinić
Dr. Tijana Stanković
Dr. Ana Podolski-Renić
Dr. Miodrag Dragoj
Dr. Sofija Jovanović Stojanov
Mirna Jovanović
Ana Kostić

Pyrazolo[3,4-d]pyrimidine derivatives, Si306 and pro-Si306, inhibit the growth of sensitive and multidrug resistant glioblastoma

Jelena Dinic^a, Ana Podolski-Renic^a, Marija Nesovic^a, Ana Kostic^a, Aleksandra Divac Rankov^b, Miodrag Dragoj^a, Igor Nikolic^{cd}, Goran Tasic^{cd}, Milica Pesic^a

^aDepartment of Neurobiology, Institute for Biological Research "Sinisa Stankovic" -National Institute of Republic of Serbia, University of Belgrade, Serbia ^bInstitute of Molecular Genetics and Genetic Engineering, University of Belgrade, Serbia ^cClinic for Neurosurgery, Clinical Center of Serbia, Belgrade, Serbia ^dSchool of Medicine, University of Belgrade, Serbia
E-mail: jelena.dinic@ibiss.bg.ac.rs

Glioblastoma (GBM) is the most frequent and aggressive brain tumor in adults. Main characteristics of GBM include high proliferation rate, infiltrating nature, and resistance to chemotherapy and radiation. GBM have high expression of c-Src tyrosine kinase which has a key role in regulating survival, proliferation, angiogenesis and invasiveness of tumor cells. Thus, c-Src emerged as a potential target for GBM therapy. Anticancer properties of c-Src tyrosine kinase inhibitors Si306 and its prodrug pro-Si306, pyrazolo[3,4-d]pyrimidines were assessed in human GBM cell line U87, its multidrug resistant (MDR) counterpart U87-TxR, and human primary GBM culture. Si306 and pro-Si306 triggered ROS generation and DNA damage in sensitive and MDR GBM cell lines, as well as primary GBM cells. Both compounds induced a prominent cell death in primary GBM culture, while the effect on GBM cell lines was predominantly antiproliferative, characterized by decrease in Ki-67 expression and cell cycle disturbance. Moreover, the investigated compounds made primary GBM culture more prone to anoikis. In addition, Si306 and pro-Si306 showed strong antiproliferative effect in U87 xenografts in zebrafish embryo model. The antiglioblastoma effects of investigated c-Src inhibitors were more prominent when compared to dasatinib, a well-known tyrosine kinase inhibitor. The presence of the MDR phenotype did not diminish the activity of the compounds. The investigated pyrazolo[3,4-d]pyrimidines displayed significant anticancer potential in GBM which makes them good candidates for further development regarding treatment of this cancer type.