
4th Annual Conference
New diagnostic and therapeutic tools against multidrug resistant tumours
Prague, Czechia
6-8 September 2021
STRATAGEM
CA17104
cost
EUROPEAN COOPERATION
IN SCIENCE & TECHNOLOGY
Funded by the Horizon 2020
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Local Organizing Committee:

Ing. Jitka Viktorová, Ph.D.
Ing. Denisa Kučerová
Ing. Simona Dobiasová
Assoc. prof. Ing. Jan Lipov, Ph.D.

Venue:

Vienna House Diplomat Prague
Evropská 370/15, 160 41 Prague 6
Czech Republic

Date of Event:

6th-8th September 2021

Funded by the Horizon 2020 Framework Programme of the European Union

Welcome to the Annual Meeting 2021!

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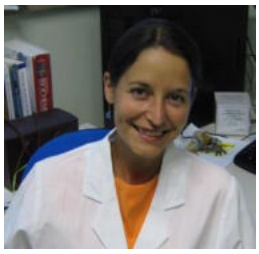
Before 2018, there were no European consortia that simultaneously studied the diagnostic, therapeutic and toxicological challenges related to the diagnosis and treatment of multidrug resistance (MDR) in tumours. Since April 2018, COST Action STRATAGEM – "New Diagnostic and Therapeutic Tools against Multidrug Resistant Tumours" has aimed to fill this gap. STRATAGEM currently includes more than 200 researchers, from across Europe and neighboring countries, who are focused on improving the diagnosis and treatment of MDR tumours.

The coordinated use of multiple tools – including high throughput bioinformatics analysis, a range of "OMICS" technologies, *ad-hoc in-vitro*, *ex-vivo* and *in-vivo* biochemical and pharmacological assays, rational design and the formulation of synthetic anti-cancer drugs, and the rational choice of natural compounds – has allowed STRATAGEM to create an integrated platform for the identification of new diagnostic/predictive biomarkers and therapeutic targets in MDR tumors, with consequent benefits for oncological patients.

Our 4th Annual Conference in Prague provides us with the unique opportunity to bring together a wide range of expertise, from academic and research institutions to private companies, to facilitate the exchange of know-how and the construction of new exciting and interdisciplinary collaborations. Excellent key-note speakers will give lectures on several aspects of tumor biology. Specific sessions will be dedicated to networking and to young researchers, who will have the possibility to present their work and receive precious feedback and advice, with the aim of establishing a network of high-level young European researchers in the MDR field. Last, but not least, social events and prizes for the best oral communications and posters will round off the meeting!

Immense THANKS go to to Jitka, Denisa and the entire local organizer committee. Without their considerable effort, this meeting would not be possible. Many many THANKS go also to the Core Group, which managed many aspects of this meeting, and to Javier and Dale for their irreplaceable support.

My best wishes for a productive and fruitful meeting: it will be a success without any doubt!



Chiara Riganti
Chair CA17104
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Sclareol, a fragrant natural compound, suppresses P-glycoprotein activity and sensitizes resistant cancer cells to doxorubicin

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Abstract: Multidrug resistance (MDR) is one of the major obstacles to successful cancer treatment. How to overcome cancer MDR is still an unsolved issue in clinical practice although several generations of MDR transporters' inhibitors have been developed and widely investigated so far. Nature is an important source of potential anticancer agents capable to suppress the activity of membrane transporters implicated in MDR such as P-glycoprotein (P-gp). In this study, we evaluated the effects of sclareol (SC), a naturally occurring labdane type diterpene, on the P-gp activity and its potential to sensitize different human cancer cell lines to doxorubicin (DOX). To that end, we used several human cancer cell lines (colorectal carcinoma, DLD1, and its MDR variant DLD1-TxR, non-small cell lung carcinoma NCI-H460, and its MDR variant NCI-H460/R, glioblastoma U251, U87, and its MDR variant U87-TxR) and normal human embryonic lung fibroblasts (MRC-5). The effects of SC alone and in combination with DOX on cell viability were assessed by MTT, while the effects on DOX and rhodamine 123 (Rho 123) accumulation as determinants of P-gp activity were assessed by flow cytometry. The efficient concentrations of SC that significantly decreased cell viability (IC50 values) ranged between 20 μM for DLD1 and 60 μM for MRC-5. The presence of MDR phenotype did not diminish the SC effect on cell viability, even more, SC was more potent in U87-TxR than in U87 cells. The effects of 72 h simultaneous treatment of SC (10 and 20 μM) with DOX (20, 50, 100, 200 and 500 nM) demonstrated the considerable potential of SC to sensitize DLD1, DLD1-TxR, NCI-H460/R, U87-TxR and U251 cells to DOX. However, the observed sensitization was not due to the P-gp inhibition in all MDR cancer cell lines. Only in NCI-H460/R the obvious suppression of P-gp was observed due to the significant increase in the accumulation of both P-gp substrates (DOX and Rho 123). SC did not affect the P-gp activity in DLD1 and DLD1-TxR cells. On the contrary, DOX and Rho123 accumulation increased in U87 and U87-TxR albeit the fact that U87 cells do not express P-gp. Results obtained in this study showed a considerable potential of SC to sensitize cancer cells to DOX. However, the effects of SC are cancer type-specific and not solely dependent on the suppression of P-gp activity. Further investigations are envisioned to determine molecular mechanisms of SC in different cancer cell types.

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