



ABSTRACT BOOK

**COST Action 17104 (STRATAGEM) WG3
Meeting - International Online Symposium on
“New Therapeutic Tools Against Preclinical
Models of Multidrug Resistant Tumors”
4th November 2020**



COST is supported by the EU Framework Programme
Horizon 2020

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Nuray Erin – WG3 Vice-Leader (Turkey)

Chiara Riganti – Chair (Italy)

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STRATAGEM Action Summary

This Action will build the first multidisciplinary network, including academic laboratories, research institutes, small and medium enterprises (SMEs), with a wide range of excellent and non-overlapping expertise, aiming at improving at the same time the diagnosis and therapy of multidrug resistant (MDR) solid tumors. Until now, there are fragmented knowledge on biomarkers and therapeutic tools used against MDR tumors; there are not algorithms predictive/diagnostic of MDR tumors ex ante; all the past therapies against MDR tumors failed. The key challenge of this Action is to fill these gaps, by producing a comprehensive, open and user-friendly platform of knowledge on MDR tumors, identifying new diagnostic/predictive biomarkers, producing new and safe compounds applicable to personalized treatments of MDR tumors. Up to 70% of solid tumors are resistant at the diagnosis: this means poor life quality and poor prognosis for patients, high management costs for the European healthcare systems. This Action is working to improve diagnosis and treatment of patients with MDR tumors and reduce the costs for their management. Second, by creating fruitful collaborations between basic and industrial research, we will give impulse to the creation of new Start-up and SMEs in Europe. Finally, the Action aims at raising the level of European research on MDR, reducing the disparity in the research quality between EU countries and ITC, providing the necessary training for European early stage researchers (ESRs) to grow as future independent research leaders, regardless of location, age or gender.

Action website: <https://stratagem-cost.eu/>

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COST is a unique means for European researchers, engineers and scholars to jointly develop their own ideas and new initiatives across all fields of science and technology through trans-European networking of nationally funded research activities.

Website: <http://www.cost.eu/>

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Dear Friends,

Welcome to the third WG3 online Meeting. Given the current pandemic restrictions, we decided to extend the WG3 Meeting into a small Symposium, to allow us to better know each other and exchange scientific ideas. As you know, the WG3 aims to explore and validate the efficacy of new therapeutic tools against pre-clinical models of MDR tumors. However, this event is open to members from all WGs of STRATAGEM, with complementary scientific aims.

This one-day online Symposium includes two outstanding plenary lectures given by Prof. Elisa Giovannetti and Prof. Godefridus J. Peters, on topics highly relevant to our objectives. We have eight excellent selected oral presentations given by young scientists/students from different member's laboratories, from various parts of the world.

Twenty posters are available at our webpage (following login) and will be shortly presented during the Symposium, in the form of 5-minute "Speed-talks". At the end of the Meeting/Symposium, we will award prizes for the best presentations. These will be selected by the Prizes Selection Committee, consisting of members of the Scientific Committee who will attend sessions.

The WG3 members Meeting itself, will take place at the end of the morning session, during which an update on relevant topics will be made. We wish that this online Meeting/Symposium enhances the scientific knowledge of all participating scientists and students, providing a valuable experience and new opportunities for future collaborations.

Finally, and most importantly, we hope you enjoy this scientific day!

Novel class of P-glycoprotein inhibitors from *Plectranthus* spp.

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Multidrug resistance (MDR) is one of the main challenges in cancer treatment, in which overexpression of P-glycoprotein (P-gp) plays an important role. Therefore, there is an urgent need to identify new compounds that can exert anticancer effects and at the same time revert MDR. In this context, *Plectranthus* genus (Lamiaceae) is a great source of cytotoxic compounds that could be used as lead molecules for drug development, such as 6,7-dehydroroyleanone (**1**) (*P. madagascariensis* (Pers.) Benth. essential oil) and 7 α -acetoxy-6 β -hydroxyroyleanone (**2**) (*P. grandidentatus* Gürke) [1].

The aim of this work was to prepare a small library of new 12-O-substituted derivatives with potential P-gp inhibitory effect by exploring the reactivity of the natural royleanones **1** and **2**. In this study, we identified a new derivative that exhibited a P-gp inhibitory activity higher than the natural diterpenes **1** and **2**, and comparable to Dexverapamil. Furthermore, this compound showed the ability to sensitize the resistant cell line NCI-H460/R to doxorubicin. This activity was evaluated in the human non-small cell lung carcinoma (NCI-H460) cell line and its MDR counterpart NCI-H460/R with the P-gp overexpression by using the MTT and Rhodamine 123 accumulation assays. Further derivatizations and quantitative structure–activity relationship analysis are ongoing to discover new derivatives with improved activity.

References: [1] Isca VMS et al. (2020). ACS Med Chem Lett. 11 (5): 839-845.

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