STRATAGEM
CA17104

ABSTRACT BOOK

COST Action 17104 (STRATAGEM)
WG2 Meeting and International Online Symposium on "Synthesis and nanodelivery strategies for new therapeutic tools against Multidrug Resistant Tumours"

cost
EUROPEAN COOPERATION
IN SCIENCE AND TECHNOLOGY

COST is supported by the EU Framework Programme
Horizon 2020

PROGRAM

9h30 Welcome

9h40 - 13h – MORNING SESSION

9h40 **Keynote Lecture I – Prof. Romano Silvestri (Sapienza University of Rome, Italy):** *New anti-Cancer Agents through an Interaction with Tubulin.*

10h30 **Anne Vessières (Sorbonne Université, France)**: *Biological activity of ferrocifens on human PDCLs of glioblastoma (GBMs). A step toward personalized medicine.*

10h50 **Kateřina Valentová (Czech Academy of Sciences, Czech Republic):** *Selectively halogenated flavonoids: Preparation, biophysical properties, and multidrug resistance modulation.*

11h10 **Arasu Ganesan (University of East Anglia, United Kingdom)**: *Multitargeting epi-epi drugs for multidrug resistance.*

11h30 **Alfonso T. Garcia-Sosa (University of Tartu, Estonia):** *Predicted Protein Kinase C isoform interactions and experimental inhibition of breast cancer stem cell-inducing spheres.*

11h50 Coffee break

12h - 13h WG2 member meeting (for WG2 members)

13h - 14h – INTERVAL (LUNCH BREAK)

14h - 18h – AFTERNOON SESSION

14h Keynote Lecture II – Prof. Fabiana Quaglia (Naples University, Italy): *Biodegradable nanoparticles delivering therapeutic combinations in MDR cancer.*

14h50 **Cristina Del Plato (Istituto Italiano di Tecnologia, Italy)**: *Design and synthesis of piperazine-based compounds conjugated to Humanized ferritin as delivery system of siRNA in cancer cells.*

15h10 **Veronica Bastos (University of Aveiro, Portugal)**: *UCNPs nanocapsules for doxorubicin targeting delivery in melanoma cell lines.*

15h30 **Denitsa Aluani (Medical University of Sofia, Bulgaria)**: *Micellar Encapsulation of Doxorubicin with CAPE Enhance its Cytotoxicity Against Lymphoma L5178 MDR1 cells*.

15h50 **Christina N. Banti (University of Loannina, Greece)**: *Novel silver glycinate metallodrug; A non toxic antiproliferative agent induces apoptosis on human breast cancer cells.*

16h10 Coffee break

16h20 Speed-talks of poster presentations

16h20 **Silvia Cammarone (Sapienza University of Rome, Italy)**: *Chalcones and Chalcone-mimetic Derivatives as Notch blocking agents in T-cell acute lymphoblastic leukemia.*

16h25 **Pierre Idlas (University of Angers, France)**: *Formulation of ferrocifen loaded lipid nanocapsules against multidrug resistant ovarian adenocarcinoma.*

16h30 **Florence O. McCarthy (University College Cork, Ireland)**: *Novel 11-substituted ellipticines as potent anticancer agents with divergent activity against cancer cells.*

16h35 **Francesca Picarazzi (University of Siena, Italy)**: *Structural elucidation of novel Imidazo[1,2-a]pyridine inhibitors of Aldehyde Dehydrogenase 1A Family.*

16h40 **Vera M. S. Isca (Universidade Lusófona de Humanidades e Tecnologias, Lisboa, Portugal)**: *Innovative nanosystems with natural cytotoxic royleanone diterpenes from Plectranthus spp.*

16h45 **Oscar Briz (University of Salamanca, Spain)**: *Transportome manipulation by gene therapy to sensitize liver and gastrointestinal tumors to chemotherapy.*

16h50 **Valeria Vergine (Sapienza University of Rome, Italy)**: *$mPEG_{5kDa}$-cholane/Glabrescione B delivery system as promising tool for the treatment of Hh-dependent tumors.*

16h55 **Nicolas Clere (University of Angers, France)**: *p722 ferrocifen loaded lipid nanocapsules improve survival of murine xenografted-melanoma via a potentiation of apoptosis and an activation of $CD8^+$ T lymphocytes.*

17h00 **Bruno M. F. Gonçalves (University of Lisbon, Portugal)**: *Exploring the efflux and modulation mechanisms of Human ABCG2 through Molecular Dynamics Simulations.*

17h05 **Arif Kivrak (Van Yüzüncü Yil University, Turkey)**: *Synthesis of Novel Artemisinin-Benzothiophene Hybrid Molecules.*

17h10 **Wolfgang Link (Instituto de Investigaciones Biomédicas "Alberto Sols", Spain)**: *Harmine and Piperlongumine revert TRIB2-mediated drug resistance.*

17h15 **Mariacristina Failla (University of Turin, Italy)**: *NO release regulated by doxorubicin as the green light-harvesting antenna.*

17h20 **Sundus Erbas-Cakmak (Konya Food and Agriculture University, Turkey)**: *Activatable Photodynamic Therapy Agents for Use in Multi-Drug Resistant Tumors.*

17h25 **Enrique Domínguez-Álvarez (Consejo Superior de Investigaciones Científicas, Spain)**: *Selenocompounds: a novel approach to fight cancer resistance.*

17h30 **Isabella Romeo (Istituto Italiano di Tecnologia, Italy)**: *Synergistic inhibition of the Hedgehog pathway by newly designed Smo and Gli antagonists bearing the isoflavone scaffold.*

17h35 **David S. P. Cardoso (University of Lisbon, Portugal)**: *Generation of a library of indole alkaloid derivatives as ABCB1 inhibitors in resistant cancer cells.*

17h40 **Philippe Bertrand (University of Poitiers, France)**: *Simplified tetraethylene oxide-mediated synthesis of gold nanoparticles and their internalization by cancer and neuronal cells.*

17h45 **Michela Puxeddu (Sapienza University of Rome, Italy)**: *New 1,1'-Biphenyl-4-sulfonamides as Potent and Selective Human Carbonic Anhydrase inhibitors.*

17h50 **Sarah Le Saux (University of Montpellier, France)**: *Stability, cellular interactions and post production modification of murine mesenchymal stem cells (mMSC) derived Extracellular Vesicles.*

17h55 **Florence O. McCarthy (University College Cork, Ireland)**: *Isoquinolinequinone N-oxides as anticancer agents effective against drug resistant cell lines.*

18h00 **Niamh M. O'Boyle (Trinity College Dublin, Ireland)**: *Combretazets: Enantiomeric β-Lactams for the Treatment of Breast Cancer.*

18h05 **Hulya Ayar Kayali (Izmir Biomedicine and Genome Center, Turkey)**: *Synthesis and Characterization of Therapeutic Antibody-drug Conjugates against Multidrug Resistant Ovarian Cancer Therapy.*

18h10 Prizes for best presentations and closing remarks

Abstracts - Oral presentations

The abstracts presented herein are organised as per the event programme

Novel silver glycinate metallodrug; A non toxic antiproliferative agent induces apoptosis on human breast cancer cells.

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Background: Silver(I) metallodrugs exhibit significant *in vitro* antiproliferative activity against many cancerous cell lines, including adenocarcinoma cells [1]. The antiproliferative activity of silver ion is due to its binding to the DNA bases, on its binding to thiol groups of the protein and on its interaction with mitochondrion, which activates the mitochondrial apoptotic pathway of the cells [1]. Amino acids, on the other hand, as biocompatible ligands can deliver the metal ion to its biological target preventing its reduction under physiological conditions [2-3]. Metal complexes with amino acids can be more selective toward the abnormal cells in respect to the normal ones [3]. This is due to the over-expression of the amino acids receptors of the abnormal cells [1].
Aims: The combination of a biocompatible agent with a metal ion enhances its activity because of the easy penetration of the agent into cytoplasm and its delivery to intracellular biological targets, selectively [1].
Methodology and results: The new covalent polymeric silver(I) complex with glycine (GlyH), $[Ag_3(Gly)_2NO_3]_n$ (AGGLY) was synthesized and was characterized by spectroscopic techniques and single crystal X-ray crystallography. The *in vitro* cytotoxic activity of AGGLY was tested against human breast adenocarcinoma cancer cell lines: MCF-7 and MDA-MB-231. The *in vitro* and *in vivo* genotoxicity was evaluated by micronucleus assay and Allium cepa model. The mechanism of action was studied by cell morphology, cell cycle arrest, AO/EB Staining, and permeabilization of the mitochondrial membrane test. The molecular mechanism of it was studied by the binding affinity towards the calf thymus DNA
Conclusion: AGGLY is a non toxic antiproliferative agent which induces apoptosis on human breast cancer cells though mitochondrion pathway

References

[1] Banti C.N. and Hadjikakou S.K.. (2013) Metallomics, 5: 569-596; *ibid* (2014) Dalton Trans. 43: 6848-6863; *ibid* (2016) Inorg. Chem. 55: 8681–8696; *ibid* (2019) J. Inorg. Biochem. 194: 7–18; *ibid* (2018) Eur. J. Med. Chem.143: 1687-1701
[2] Peacock A.F.A. et al (2012) J. Inorg. Biochem. 117: 298–305
[3] Andrejevic T.P. et al. (2020) Chemistry 2: 203–218

Acknowledgements:

(i) C.N.B. has been financially supported by the State Scholarships Foundation (IKY) (Project No. 2019-050-0503-17816), through the Operational Programme "Human Resources Development, Education and Lifelong Learning" in the context of the project "Reinforcement of Postdoctoral Researchers - 2nd Cycle" (MIS-5033021), which is co financed by Greece and the European Union (European Social Fund- ESF). (ii) S.K.H. acknowledges the Oncology Department of Novartis Hellas S.A.C.I. for the financial support (Project No. 82819). (iii) C.N.B. and S.K.H. are thankful to the COST Action CA17104 "New diagnostic and therapeutic tools against multidrug resistant tumors" members for the stimulating discussions, (iv) This research has been co-financed by the European Union and Greek national funds through the Operational Program Competitiveness, Entrepreneurship and Innovation, under the call RESEARCH – CREATE – INNOVATE (project code:T1EDK-02990).