

The fourth WG meeting has been organized in Faculty of Pharmacy at Ege University on 5-6th March 2020. It started with the introduction of the local organizer Prof. Gunay YETIK-ANACAK (MC member for Turkey). Prof. Stefano ALCARO, the Chair of the COST Action, mentioned the purpose of the meeting and put into words about how sad he was about not being able to attend the meeting because of COVID-19 in his video talk. Prof. Ayfer YALCIN, the Dean of the Faculty, welcomed the attendees and congratulated the local organizers as this scientific meeting was held in Faculty of Pharmacy at Ege University.

Due to the COVID-19 emergency the meeting schedule was reorganized on site, trying as much as possible to maintain the original program.

Anthony BURKE was moderator of the first session ‘Multi-targeting agents against cancer and infections’. The moderator briefly summed up whether the conversations in the first session will be made as a skype call, as a video talk or as a live presentation. Due to the COVID-19, Alessandra MONTALBANO, Sheraz GUL and Danijel KIKELJ could attend the meeting through virtual joining. The first speaker was Filipa RAMÍLO GOMES from Portugal with her ‘Epigenetic Multitargeting in Cancer: Design, Synthesis And Biological Evaluation of Novel Inhibitors’ named presentation. The second speaker was Alessandra MONTALBANO from Italy. ‘Repositioning of [1,6] Naphthyridines as Antiviral Agents on HSV-1’ named video from Montalbano was watched. Florence MCCARTHY, MC member for Ireland, presented his work named ‘Indolocarbazole maleimides with dual inhibition of kinases and topoisomerase I’. Then ‘The effect of New Synthesized Resveratrol Derivate H1 on angiogenesis’ named research was presented by Emine Nur ÖZBEK, from Turkey. Miguel Ángel MEDINA, from Spain, presented ‘A Comparative Study of The Antiangiogenic Activity of Hydroxytyrosyl Alkyl Ethers as Multitargeted Bioactive Compounds’. ‘Multitarget Covalent Inhibitory Property of Klavuzons’ named research was presented by Ali ÇAĞIR, from Turkey. Then Sheraz GUL, MC substitute for Germany, reported his ‘High throughput in-vitro early toxicity and off-target liability assays to rapidly identify limitations of novel thyromimetics’ presentation via skype. This session was closed by WG1 leader Danijel KIKELJ’s video that named ‘Toward Multitarget DNA Gyrase Inhibitors Possessing Antibacterial Activity’.

Fernanda BORGES as a moderator of ‘Reports of the WG leaders’ part talked about the leaders presentations that were shown as video talks. Danijel KIKELJ, WG1 leader, mentioned that the aim of WG1 was to supply Chemotheca with new chemicals and synthesize the multi-target ligands designed in WG 4. He reported that the outputs of WG1 were to optimize synthetic routes and extraction protocols to obtain compounds and to initiate a chemical catalog program. He emphasized the importance of scientific interactions with biologists and computational chemists belonging to other WGs. Eugenio GAUDIO, WG2 leader, pointed out the productive collaborations provided by COST action. As WG2, they evaluate target obtained by in silico simulation method. He mentioned that besides the traditional targets for diseases, the important thing is to develop small molecules for multi-targeting effects. He talked about the importance of multi target molecules in obtaining patents by giving dual effective molecules examples. He ended his speech by thanking the COST action for opportunities for collaborations. Sharon Bryant, WG3 leader, could not attend the meeting. Hanoch SENDEROWITZ, WG4 leader, mentioned new computational tools to develop for the discovery of multi-target ligands as an aim of WG4’s. Selecting and testing the best protocol for virtual screening simulations was a part of this. He talked about the numbers of members, published papers, activities (training schools) related to WG4 and collaboration with other working groups. He said that the interacting with WG3 is important because of Chemotheca database. He explained strategies for solving multi objective optimizing problem (MOOP) such as the balance between pharmacokinetic (ADME) and potency of drug. He ended his speech by taking attention the importance of further developing Chemotheca. With this respect, the Chair highlighted, also informing all MuTaLig community by email, that a consistent number of novel compounds were inserted in the Chemotheca, now reached more than 60000 compounds that can be searched and downloaded for virtual screening purposes by means of its searching facilities.

The second session ‘Multi-targeting agents against neurodegenerations’ was moderated by Fernanda BORGES. This session started with ‘Natural Product Hybrids are Potent Neuroprotectants in Vitro

And in Vivo: Multi-Target Ligands with Unknown Targets?’ presented by Michael DECKER, from Germany. Second speaker was Anthony BURKE from Portugal, talked about ‘Targeting Alzheimer’s Disease with 4-Aminochromane Derivatives’. ‘Combination of Adenosine Antagonism with Additional H3R Antagonism for the Treatment of Parkinson’s Disease’ named research was reported by Holger STARK, MC member for Germany. Then, Wiesława Agnieszka FOGEL, MC member Poland, presented ‘Histamine H3 receptor antagonism as a valuable component for multitarget directed ligands (MTDL)’ named study. Then, ‘Repurposing Compounds Designed to Treat Mental Diseases as Potential Drugs Against Neurodegenerative Diseases’ was presented by Agnieszka A. KACZOR, from Poland. The last speaker was Francesco MESITI, from Italy. He reported the presentation named ‘Mapping the chromone-3- phenylcarboxamides pharmacophore: structure-activity-toxicity and efflux transport studies’.

Florence MCCARTHY was moderator for the third session ‘Multi-targeting agents against vascular diseases or oxidative stress’. First speaker of this session was Marcelino MANEIRO, from Spain. He talked about ‘Interplay between superoxide dismutase, catalase and peroxidase activities for salen-manganese complexes’. ‘Mitochondriotropic Cinnamic Acid Antioxidant Improves Cellular Resistance to Stress’ named research presented by second speaker Ricardo AMORIM, from Portugal. Then, Deniz KALELİ DURMAN, from Turkey, reported her ‘Vascular effects of pioglitazone related to perivascular adipose tissue (PVAT)’ named study. ‘The journey from ethnobotanical studies to pharmacological target: The effect of imperatorin and isoimperatorin on penile relaxation’ was presented by Nazlıcan BELEN, from Turkey. The last speaker of this session and this day was Yeşim KAYA YAŞAR, from Turkey. She reported ‘A Potential Repositioning of Trimetazidine for the Treatment of Bladder Dysfunction: Effects on Mouse Detrusor Contractility and Cytprotection’ named research.

End of the third session, participants who wanted to attend the gala dinner were taken to the gala dinner by buses. Body percussion dance show with mortar and pestle ‘A multi-targeting pharmacist: Galen from Aegean land’ was performed by Prof. Gunay YETİK-ANACAK, PhD and undergraduate students of the Faculty of Pharmacy at Ege University. Participants enjoyed dancing with the live music. Beside a folkloric dance of the region called Zeybek was presented in a traditional outfit by a professional dancer. Due to last period of the COST action a cake with the MuTaLig Logo was cut by Fernanda BORGES and Gunay YETİK-ANACAK.

The second day started with the fourth session “New methods in Drug Discovery, in silico pharmacology and drug repurposing”. The moderator was Holger STARK. Two speakers of this session David C. MAGRI and Rita GUEDES did not attend the meeting for the COVID emergency. The first speaker Marie Louise JUNG, from France, presented ‘New screening libraries arising from the Prestwick Chemical Drug Library’ named research of her. Second speaker was Diego Liberati from National Research Council of Italy. He reported ‘Drug design in silico: dream, (next) future or even coming reality?’ named presentation via Skype. ‘Lead to Target: A Computational Approach to Identify Possible Protein Targets of Molecules with Known Experimental Biological Activity’ named research presented by Sérgio F. SOUSA, from Portugal. Then MC member for Estonia and communication manager Alfonso T. GARCÍA-SOSA talked about ‘Multi-Target Ligand Design is Ripe for New Methods’. Onur SERÇİNOĞLU, from Turkey, reported ‘New Inhibitors of the BmrA Pump Identified Through Virtual Screening’ named research of him.

In conclusion, 24 oral communications were presented in consecutive sessions in two days. The oral presentations of Alessandra MONTALBANO and Danijel KIKELJ were shown as videos. Sheraz GUL and Diego Liberati preferred presented their oral communications via skype. As usual, a poster session was organized during this meeting especially for young researchers. 27 posters were presented. Abstracts of oral communications and posters could be found at book of abstracts WG Izmir in <http://www.mutalig.eu/>.

The meeting was concluded by a round table. The round table meeting was held with the participation of present participants, videos of Stefano ALCARO and Antonio LUPIA and via Skype participation of Maria Laura BOLOGNESI, Stefano ALCARO and Daniel KIKELJ. As 4th WG meeting is the last meeting of MuTaLig, follow up projects were discussed. Follow up application of MuTaLig and a new COST

Action application were considered. Therefore, two applications may be better than one. Considering that, the deadline for the next COST Action application is 22nd of April 2020, the new ideas and the possible core group of the new action were considered. Several ideas were proposed by the participants and MuTaLig core group. Cardiovascular diseases, aging, infectious diseases, chronicle diseases and neurodegenerative diseases were the main areas proposed. Among these ideas, based on the expertise of the existing MuTaLig group and the results obtained in this COST Action, targeting neurodegenerative field was found to be the most rational option. For sure, it is important to add new aspects to the field. On the other hand, Chemotheca would serve as a beneficial tool in the next proposal. Finally, it is noted that the participation of everybody is another key point therefore, we would find a way in the new action to include all. Additionally, contribution of the companies must be considered and urged for better covering areas and inclusiveness. In the light of these proposals, a group of delegates from 7 different countries were selected for the further discussion.

The awarding ceremony was performed by the organizing committee. Three oral communications awards were given to Francesco MESITI (1st), Ricardo AMORIM (2nd) and Wieslawa Agnieszka FOGEL (3th). Three awards for posters went to #17 Pedro SOARES (1st), #4 Daniel CHAVARRIA (2nd) and #31 Zeynep YILMAZ SERÇİNOĞLU (3th).

After the scientific program ended, the social program continued with those who wanted to participate. 40 persons joined the trip started in Yesilova Hoyuk, the oldest settlement area in Izmir. First Zafer Derin gave a presentation about Yesilova Hoyuk. After visiting Yesilova Hoyuk social activities continued with an Izmir City Tour that 28 persons joined. The city tour started at Konak (Izmir City Center) with the Clock Tower which is a symbol of Izmir. After The Clock Tower the trip continued by walking around the Kemeraltı Bazaar, the most popular shopping center of Izmir. Participants of city tour tasted Turkish coffee in Kızlarağası Hanı, a favorite spot for locals and tourists to drink the best Turkish coffee in Izmir.

As a part of social events, Ephesus, House of Virgin Mary and Sirince Daily tour was held on 7th March Saturday with a limited number of participants. The tour was started from Ephesus by tour guide. House of Virgin Mary was visited after Ephesus. Last place was old Orthodox village Sirince.

All the participants presented their glad to join the meeting on leaving. This report was gently prepared by the local organizer Prof. Gunay YETİK-ANACAK (MC member for Turkey) and young researchers Elif ALAN and Dr. Gülşah BAYRAKTAR. The organising committee did a great job to face with the difficulties encountered last minute to the COVID emergency. Especially young researchers Dr. Gülşah BAYRAKTAR, Elif ALAN, Merve SAYLAM, Emine Nur ÖZBEK and Nazlıcan BELEN was very active to organize virtual participations through skype and video calls. A special thank goes to her and her team.

All additional updates will be posted in the MuTaLig web www.mutalig.eu as soon as possible.

Catanzaro, April 14th 2020

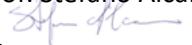
Prof. Stefano Alcaro

Chair of COST Action CA15135

Photo gallery of the 4th WG meeting



Entrance meeting venue at the Faculty of Pharmacy of the Ege University of Izmir (Turkey)



Greetings from the Dean of the Faculty of Pharmacy of the Ege University of Izmir (Turkey)



Mutalig participants in front of the Galen bust in the garden of the Faculty of Pharmacy of the Ege University of Izmir (Turkey)



Registration desk in the morning of the first day



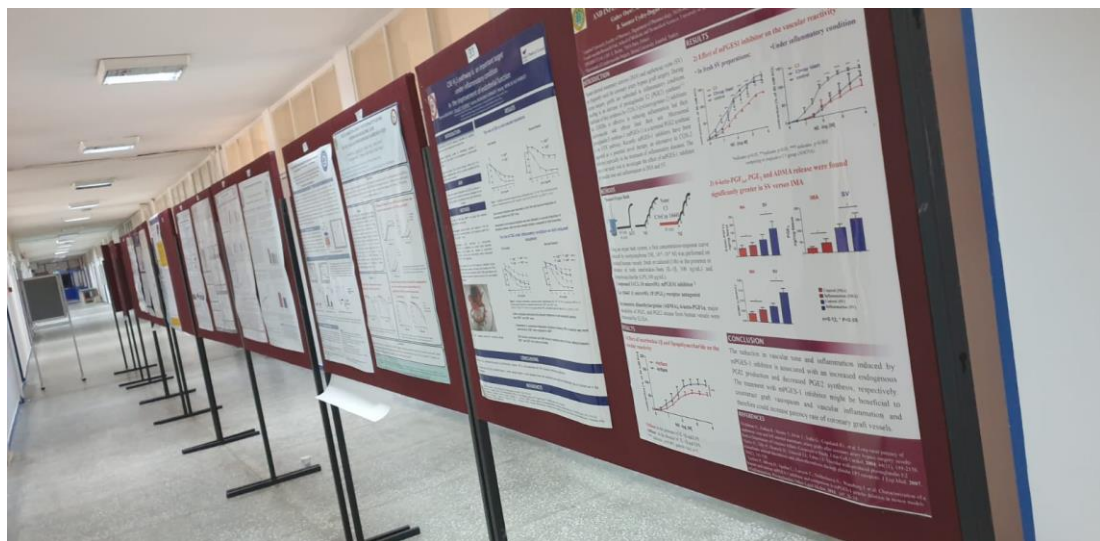
Coffee Breaks of the meeting in the conference hall



Coffee Breaks of the meeting in the conference hall



Beginning of the first day-Conference Room





Poster area



COST ACTION CA15135
Final status of WG activities
within the MuTaLig COST Action

**Ege University, Faculty of Pharmacy,
Bornova, İzmir, Pearl of the Aegean**
March 5th - 6th 2020

Stefano Alcaro, Chair CA15135 MuTaLig COST Action
video recorded at Università Magna Graecia di Catanzaro (Italy)







Introduction of the MuTaLig COST Action Chair Stefano Alcaro by video talk



WG1 Development of new chemical entities

WG1 Leader
Danijel Kikelj – Faculty of Pharmacy University of Ljubljana Askerceva 71000 Ljubljana (Slovenia) – danijel.kikelj@ffa.uni-lj.si

WG1 Objectives
This Working Group will provide to Chemoteca **new chemical entities**, i.e. small organic molecules, preferably based on privileged scaffolds, obtained by means of **synthetic traditional and advanced methods** or by **extraction from natural sources**, such as plants, functional foods and microorganisms. This WG will also synthesize the multi-target ligands designed in WG 4.

WG1 Tasks

- up-to-dating synthetic routes applied to drug discovery programs;
- optimizing protocols for easy extractions of essential oils and nutraceuticals;
- synthesis, purification and physico-chemical characterization of bioactive compounds.

WG1 Milestones

- compiling the list of “in-house” chemical entities;
- updating during the Action the list with new synthetic and/or extracted bioactive compounds;
- scaling up fine-tuning the decoration of scaffolds, extraction in function of the predicted and/or experimentally determined activities toward multiple targets.

WG1 Deliverables

- reviewing and optimizing synthetic routes and extraction protocols to obtain compounds of interest;
- starting a chemical catalog program;
- providing with new chemical entities guided by **scientific interactions with biologists and computational chemists belonging to other WGs.**

The WG1 leader of the MuTaLig COST Action Danijel Kikelj by video recorded talk



Report of the WG2 leader of the MuTaLig COST Action Eugenio Gaudio by video recorded talk

Status of WG activities of the MuTaLig COST Action


WG4: Development of Computational methods for multiple ligand design and discovery

Hanoch Senderowitz, Bar-Ilan University, Israel


4th work group meeting, Izmir, Turkey, March 2020


The WG4 leader of the MuTaLig COST Action Hanoch Senderowitz by video recorded talk

00:00:05




MuTaLig COST ACTION CA15135
Annual meeting 2020 -
Izmir (Turkey), March 5th-6th 2020







**REPOSITIONING OF [1,6] NAPHTHYRIDINES
 AS ANTIVIRAL AGENTS ON HSV-1**



DIPARTIMENTO DI SCIENZE E TECNOLOGIE
 BIOLOGICHE CHIMICHE E FARMACEUTICHE (STERICHE)

Alessandra Montalbano
 University of Palermo
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Video talk of the contribution by Alessandra Montalbano, University of Palermo (Italy)

COST ACTION CA15135
 Final status of WG activities
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**Ege University, Faculty of Pharmacy,
 Bornova, İzmir, Pearl of the Aegean**
March 5th - 6th 2020

Stefano Albano, Chair CA15135 MuTaLig COST Action
 video recorded at Università Magna Graecia di Catanzaro (Italy)



ROUND TABLE March 6th 2020






Best wishes




Round table conclusion video talk by the Chair of CA15135



Thanks to Local organisation team by Gunay Yetik Anacak



Best oral presentation award is given to Francesco Messiti



Group photo in the conference room at the end of the meeting



MuTaLig cake at the gala dinner



Group photo at the social tour during the visit of Neolithic archeological site



Visit of Neolithic archeological site

