MINUTES
THE ONEHEALTHDRUGS MARATHON
COST ACTION CA21111. One Health drugs against parasitic vector borne diseases in Europe and beyond.

ONEHEALTH*DRUGS* FOR ONE HEALTH DAY

Vector-borne parasitic diseases (VBPD) threaten the well-being and health of people and animals across the globe. Because human and veterinary drugs are pivotal in controlling these infections, its widespread use has unintentionally led to their release into the environment, with unpredictable detrimental effects on wildlife and ecosystems. To improve planetary safety and health, we recognise the urgent need for antiparasitic drugs that not only protect humans and animals but also safeguard our ecosystems.

Through the EU COST-Action OneHealth*drugs*, (CA21111) we are committed to innovate drug development, ensuring precise actions, for the early assessment of the drug environmental impact for optimal drug profiles.

To celebrate the One Health Day, we launch the international event, **OneHealthdrugs Marathon** that will take place on 20-23rd Nov.
For information reach out our website www.onehealthdrugs.com"

With this event we would like:

- to invite all network participants to share their research for the first time from the beginning of our Action and to increase our knowledge;
- we also want to generate and transmit a positive feeling of open collaborative atmosphere
- we want to show how new concepts and innovative technologies can be integrated in perspective into all research programs through collaboration, training schools and STSM- COST Action fellowships.

This announcement is coming from the OneHealth*drugs* COST Action CA21111.
Enclosed among the events for the One Health Day at One Health Commission (OHC) webpage (https://onehealthday.com/one/events-overview/y-r-c-s/2023/all/all/all)

Visit OneHealthdrugs Youtube channel https://www.youtube.com/watch?v=OVCziP2HPcI

MEETING LINK (the same for the 4 half days)
https://teams.microsoft.com/dl/launcher/launcher.html?url=%2F_%23%2Fl%2Fmeetup-join%2F19%3AJdu4-YOGoTWvm2EtTXTcbi08m9LpmYFMY_vTAu_mQGU1%40thread.tacv2%2F1700439490058%3Fcontext%3D%257b%2522Tid%2522%253a%2522e787b025-3fc6-4802-874a-9c988768f892%2522%252c%2522Oid%2522%253a%2522ac391189-1971-4664-9abf-5dbf09f2a671%2522%257d%26anon%3Dtrue&type=meetup-join&deeplinkId=e5225420-b3ca-419e-b079-f6743abbb09f&directDl=true&msLaunch=true&enableMobilePage=true&suppressPrompt=true

Structural biology & medchem 20 Nov Monday 2:00-6:00 – DAY 1

Prepared by Ioannis Papanastasious

1. LIST OF ATTENDANTS

Number	Name	Country
1.	See enclosed attendance list	

2. DESCRIPTION OF THE ACTIVITIES

Diverse presentations were delivered, covering the fields of parasitology and nanomedicine. A detailed summary of each speaker's content will be provided.

As it was a face-to-face event, proof of attendance is the signed attendance list.
The first day of OneHealth*drugs* Marathon, focused on the topics of Structural Biology and Medicinal Chemistry. Nine speakers presented their work on relative subjects in the context of the OneHealth umbrella as follows:
Cecilia Pozzi (UNISI) presented their structural biology efforts to decipher the catalytic mechanism of pteridine reductase from Trypanosoma parasites to be employed for the development of new antiparasitic agents.
Ludovica Marotta (UNISI) presented suitable synthetic strategies for the preparation of antimalarial endoperoxides to combat resistance.
Maria Alice Carvalho (U Minho) gave an overview of their synthetic efforts to develop antitrypanosomal and antileishmanial pyrimido[5,4-d]pyrimidines.
Maria Paola Costi (UNIMORE) discussed their strategy to identify broad spectrum low-toxicity antitrypanosomatidic agents based on the Ty-Box library using high-throughput phenotypic screening, chemoinformatics and machine learning methods.
Ivan Bassanini (SCITEC) presented their medicinal chemistry efforts in developing novel derivatives of the triterpene celastrol with antileishmanial activity, targeting an allosteric site of the protozoan heat shock protein Hsp90.
Ioannis Papanastasiou (NKUA) presented their synthetic efforts towards derivatives of the antitubercular drug candidate SQ109, with trypanocidal activity and their interaction with lipid bilayers.
Sandra Gemma (UNISI) showed their results on the design and synthesis of 5-nitrothiophene-2-carboxamides as inhibitors of Leishmania Trypanothione Reductase.
Sara Rossi (UNISI) discussed their green synthetic approach towards a library of chalcones presenting interesting in vitro antileishmanial activity.
Theodora Calogeropoulou (NHRF) presented their approach on the green synthesis of a library of heterocyclic bioisosters of alkylphosphocholines and their *in vitro* biological evaluation against *L. infantum* and *T. brucei*.

Overall, the first day encompassed very interesting presentations and panel discussions towards the discovery of new drugs against neglected diseases taking into account green synthetic approaches and ecotoxicological aspects.

Parasitology & nanomedicine 21 Nov Tuesday 9:30-12:30 - DAY 2

Prepared by Anabela Cordeiro da Silva, Ana Tomás, Luís Cardoso

1. LIST OF ATTENDANTS

Number	Name	Country
	See enclosed attendance list	

2. DESCRIPTION OF THE ACTIVITIES

Diverse presentations were delivered, covering the fields of parasitology and nanomedicine. A detailed summary of each speaker's content will be provided.

Luis Cardoso*: Web sources of information on topics related to Veterinary Parasitology*

The presentation focused on the importance of accurate information in veterinary parasitology, especially considering zoonotic potential. It highlighted various web sources, such as the DPDX laboratory and the CVIBD companion animal vector-borne diseases website, providing valuable insights into diagnostics, treatment, and zoonotic aspects of parasitic diseases. The significance of guidelines from organizations like the World Association for the Advancement of Veterinary Parasitology (WAVP) was emphasized, covering topics like anthelmintic resistance prevention and standardized nomenclature. The need for standardizing disease names, particularly when diseases affect both animals and humans, was underscored for clarity and consistency in communication. Overall, the presentation emphasized the importance of accessing reliable information in the field of veterinary parasitology.

Marlene Lucio*: Rational design of nanotherapeutics bioinspired mimetic models using*

The speaker discussed the potential applications of nanocarriers in enhancing the therapeutic efficacy of anticancer drugs. Through meticulous studies involving self-assembled micelles and liposomes, the encapsulation of anticancer agents demonstrated improvements in drug loading contents, encapsulation efficiencies, and controlled release triggered by pH variations. The research findings suggested promising therapeutic potential for the encapsulated drugs compared to their free counterparts.

A recent undertaking involved the encapsulation of antiparasitic drugs, particularly addressing the low solubility of these drugs. Using cubosomes, the speaker and their team successfully encapsulated an antiparasitic drug, achieving a maximum encapsulation of 80%. The ongoing research aims to further explore and characterize these formulations for potential oral administration, emphasizing factors like shelf stability and particle size.

In essence, the presentation showcased a holistic approach to nanocarrier design, encompassing rational design strategies, biomimetic models, and practical applications. The ongoing research endeavors highlight the commitment to advancing drug delivery systems, particularly in addressing challenges associated with various drug classes, including anticancer and antiparasitic drugs.

Javier Santamaria-Aguirre*: Nanomedicine synergizes Repositioning: Delamanid solid lipid nanoparticles for accessible leishmaniasis treatments*

Javier Santamaría-Aguirre is a pharmaceutical biochemist with a specialty in pharmacy and pharmaceutical technology. His presentation described a study aimed at repurposing approved drugs for an accessible (affordable and available) leishmaniasis treatment applying nanomedicine. Nanomedicine synergizes with

drug repositioning to increase the possibilities of developing safe and effective medicines. Hundreds of millions of people are at risk of being infected with *Leishmania* spp. worldwide. A neglected tropical disease, leishmaniasis is linked with social and economic conditions work, malnutrition, displacement of the of the population, among other conditions. The drugs currently available on the market for the treatment of clinical disease cases (e.g. pentavalent antimonials) can cause adverse effects, and there is also the possibility of resistance by the pathogens, in addition to lengthy and repetitive therapeutic regimens. Repositioning allows reducing costs and development time based on the use of drugs that have other indications. Delamanid was chosen to be incorporated into solid lipid nanoparticles (SLNP). Encapsulated delamanid exhibited greater leishmanicidal activity compared to the free drug in macrophages infected with *Leishmania infantum* amastigotes. The activity of delamanid in SLNP was confirmed *in vivo* murine models of infection with *Leishmania major*. The process of encapsulating drugs offers a promising step towards more accessible and effective leishmaniasis treatments.

Joana Tavares: *Pyrimido [5,4-d] pyrimidine-based compounds as novel antimalarial and antileishmanial drugs*
Joana introduced malaria and leishmaniasis, the importance of drug resistance and failure, and the need for new treatment options for these diseases. She also informed on the tools her lab has available to test drug efficacy *in vivo* against *Plasmodium* and *Leishmania* parasites. Upon this introduction, Joana focused on the topic of her talk, a research involving different laboratories, which aimed at synthesizing and screening novel pyrimido [5,4-d] pyrimidine (PP) derivatives malaria and leishmaniasis therapy. She reported on two PP compounds with *in vitro* nM activity towards *Plasmodium* (chemoresistant and sensitive strains) and selective indexes against eukaryote cell lines 100 to 1000-fold higher. She also referred to a PPs which behaved towards *Leishmania* parasites (in terms of potency and selectivity index) similar to miltefosine. Given the promising data obtained *in vitro*, she plans to test the 3 compounds *in vivo* models of infection.

Nuno Santarem: *Visceral Leishmaniasis in Human Immunodeficiency Virus-Coinfected Patients*
Nuno Santarém from i3S in Porto, Portugal presented a communication on visceral leishmaniasis in HIV-infected adults. These patients are known to be at high risk of developing VL, which frequently courses with high parasite levels and continuous relapses, demanding consecutive courses of therapy. It is though important to understand the reasons underlying Leishmania persistence in such individuals. Nuno described the case of a patient that lived with VL or 9 years and was followed by the research team during a 12 month period. He presented data showing how the serology, parasitaemia and quantification of proinflammatory cytokines upon *in vitro* stimulation with Leishmania antigen changed along the year in analysis, and how this associated with the number of CD4 cells and HIV viraemia. The data, albeit depicting the development of an immune response, suggested that the inability to control the infection may partially stem from an inability to respond to parasite antigens in an effective way. Nuno also reported on the characterization of a *Leishmania* isolate, namely on its decreased susceptibility to miltefosine, which might have contributed to parasite treatment failure. He highlighted the importance of taking the existence of circulating parasites with altered dug sensitivity into consideration when considering the best treatment options, especially in the context of HIV-infected people.

Margarida Duarte: *The essential role of mitochondrial type II NADH dehydrogenase in Leishmania*
this research underscores the pivotal role of type II NADH dehydrogenase (NDH2) in the survival of Leishmania parasites, irrespective of the presence of a functional complex I and fumarate reductase. The study provides detailed insights into NDH2's expression patterns, activity, and subcellular localization in Leishmania infantum, establishing it as an essential component of the respiratory chain throughout the parasite's life cycle.
Genetic deletion experiments confirm the indispensability of NDH2, with parasites only able to survive when a compensatory episomal copy of the gene is introduced. The observed reduction in virulence of NDH2-deleted parasites in mice further highlights the enzyme's critical role in the parasite's pathogenicity.

Contrastingly, fumarate reductase (FRD) was found to be non-essential for in vivo infections, despite its higher expression levels in *L. major*. The decreased virulence of FRD-deleted parasites suggests a limited impact on the parasite's overall fitness in the host.
Overall, these findings position NDH2 as a promising and unique target for the development of leishmanicidal drugs, given its absence in mammalian systems. The study advances our understanding of *Leishmania* bioenergetics, paving the way for more targeted and effective interventions against leishmaniasis.

5. LIST OF ANNEXES

Annex: PDF of the slides presented during the meeting.

Young Researcher and Investigators (YRI)
22 Nov Wednesday 2:00-6:30 - DAY 3

Prepared by Elisa Uliassi, Gulsah Bayraktar and Kayhan Ilbeigi

1. LIST OF ATTENDANTS

Number	Name	Country
	See enclosed attendance list	

2. DESCRIPTION OF THE ACTIVITIES

Diverse presentations were delivered, covering the fields of parasitology and nanomedicine. A detailed summary of each speaker's content will be provided.

The program included several lectures (2 sessions) and is entirely dedicated to Young Researcher Innovators (YRI), who will deliver presentations on miscellaneous OHD-related topics. All speakers were present and able to deliver their talks (with the exception of Ebrahim Abbasi), as described below.

The 1st session was co-chaired by Elisa Uliassi and Gülşah Bayraktar. The 2nd session was co-chaired by Elisa Uliassi and Kayhan Ilbeigi. After each presentation, a short discussion and interaction with the audience allowed all participants interested in the topics to raise questions.

The first lecturer was Rohini Roopnarine, Professor in Veterinary Epidemiology and Veterinary Public Health at St. George's University in Grenada. Rohini's lecture was entitled "Implementing One Health (OH) competencies within the veterinary & medical curricula", where she outlined the interprofessional education (IPE) in veterinary medicine education and veterinary students' for including One Health concepts, and important variants in collaborative and clinical practice.

The second lecture was presented by Bianca Martinengo from the Department of Pharmacy and Biotechnology of the University of Bologna. Bianca's presentation was entitled "Sustainable biocatalytic derivatization of antiparasitic natural lipids and cashew nut-shell liquid (CNSL) derivatives using unspecific peroxygenase (UPOs) enzymes" and focused on her work done during a STSM at Daniele Castagnolo's lab. (Department of Chemistry, University College London). Bianca showed the development of biocatalytic reactions for the derivatization of natural lipids and CNSL derivatives to synthesize a small library of compounds, that will be tested for their antiparasitic potential.

The third lecture was presented by Clara Lima, a Veterinarian and PhD candidate at the Faculty of Pharmacy and i3S, University of Porto. Clara´s presentation was entitled "Comparative study on a multi-parametric serological approach to feline Leishmania infection" and this work was awarded with a ITC conference grant which allowed her to participate a conference in India. During her presentation, Clara reflected on aspects associated to the diagnosis of feline Leishmania infection in different cats in Portugal. Clara also compared some of the major diagnostic tests and analyzed the relative performances.

The fourth lecture was given by Darline Dize, a PhD candidate at the Antimicrobial and Biocontrol Agents Unit (AMBcAU), University of YaoundéI. Darline´s lecture was entitled "Novel antitrypanosomal diaminoquinazoline analogues from repurposing the Medicines for Malaria Venture Open Access Pathogen Box library (MMVPBox)". She presented the Structure Activity Relationship (SAR) study performed on the

parent hit MMV675968, that led to the identification of diaminoquinazolines with good antitrypanosomal activity and cytotoxicity.

The fifth lecture was presented by Gülşah Bayraktar, Research Assistant at the Department of Pharmaceutical Chemistry of Ege University Faculty of Pharmacy. Gülşah ´s lecture was entitled "Design, Synthesis and Biological Evaluation of Antileishmanial Azaheterocyclic Compounds as Inhibitors of the Parasitic Exokinase CK1 (casein kinase 1)" and focused on her work done during a STSM at Pascal Marchand's lab IICiMed of Nantes University – France. She reported on the development of potential anitparasitic inhibitors based on thiazolopyrimidine scaffold against Parasitic Exokinase CK1 (casein kinase 1) and PTR1.

The sixth presentation was lectured by Kayhan Ilbeigi, a PhD Candidate at the Laboratory of Microbiology, Parasitology and Hygiene of the University of Antwerp (BE). Kayhan´s presentation was titled "Evaluation of antiparasitic and (eco)toxicological characteristics of advanced nucleoside-based leads against animal trypanosomiasis" and focused on his work done during a STSM in Prof. Dr. Mirco Bundschuh's lab at the University of Koblenz-Landau, Campus Landau, Germany. During his presentation, Kayhan showed the antiparasitic activity as well as ecotoxicological assessment of 2 nucleoside analogues using *Daphnia magna* and green alga (*Desmodesmus subspicatus*) as test organisms. His preliminary data suggested that the toxicity of these compounds to the tested organisms (*Daphnia* and algae) follows a species-specific pattern.

The seventh lecture was given by Lorenzo Tagliazucchi, a PhD candidate at the Dept of Life Sciences, University of Modena and Reggio Emilia, Italy. Lorenzo´s lecture was entitled "Insights into host-target interaction from the proteome modulation analysis through untargeted LC-MS/MS Proteomics of drug resistant *L. infantum*-THP1 infected cells". He presented the evaluation of drug resistance phenomena in THP- 1 cells with clinical isolates of drug resistant *L. infantum* strain and analyzed by MS based proteomics.

The eighth lecture was given by Marko Jukič, Associate Professor at the University of Primorska (UPR FAMNIT) and at the Faculty of Chemistry and Chemical Technology, University of Maribor (UM FKKT). Marko´s lecture was entitled "Strategic Evolution of SiDOCK@HOME: From COVID-19 Drug Design to a Broad-Spectrum Drug Search". He presented on how SiDOCK@HOME can be applied to drug development: from COVID-19 inhibitors to anti-parasitic drugs.

The nineth lecture was given by Thais Santos, a PhD candidate at the Faculty of Pharmacy, University Paris-Saclay, France. Thais´s lecture was entitled "Liposomes containing amphotericin B: innovative formulation for cutaneous leishmaniasis treatment". She presented on the development and characterization of innovative AmB-PEGylated liposomes (LAmB) for CL therapy.

The tenth lecture was given by Valeria Francesconi, a PhD candidate at the University of Genoa, Department of Pharmacy. Valeria´s lecture was entitled "Guanidino-Containing Derivatives as Promising Agents for Targeting the Folate Enzyme Pathways in Human African Trypanosomiasis". She presented on the development and characterization of guanidino derivatives as dual TbPTR1 and TbDHFR inhibitors, for which crystal structures of both enzymes in complex with selected compounds have been successfully obtained.

The eleventh lecture was presented by Vittoria Monaco from the University of Naples Federico II, Department of Chemical Sciences. Vittoria's presentation was entitled "Activity-based Protein Profiling to investigate the interactome of the antimalarial early lead Plasmodione" and focused on her work done during a STSM at Elisabeth Davioud-Charvet's lab from the *University of Strasbourg*. Vittoria showed the photolabeling of *Plasmodium* protein targets by using photoreactive and 'clickable' PD-derived probes and identify them by mass spectrometry methods.

The twelfth lecture was given by Giulia Malpezzi, a PhD candidate at the Dept of Life Sciences, University of Modena and Reggio Emilia, Italy. Giulia´s lecture was entitled “Preclinical investigation of H80 mechanism of action vs Miltefosine from imaging and MS proteomics for a sustainable lead development and clinical translation”. Giulia presented the evaluation of the mechanism of action and the target of H80 by combining a fluorescence analysis with a mass spectrometry proteomic approach, showing that compound H80 is internalized by the amastigotes through vesicles, via endocytosis, and localizes in the cytoplasm.

Ecotox & One Health. PRICE for YRI

23 Nov Thursday 9:30 am-1:00 pm - DAY 4

Prepared by Elisa Uliassi and Clara Lima

1. LIST OF ATTENDANTS

Number	Name	Country
	See enclosed attendance list	

2. DESCRIPTION OF THE ACTIVITIES

Diverse presentations were delivered, covering the fields of parasitology and nanomedicine. A detailed summary of each speaker's content will be provided.

The program included 6 lectures under the theme of Novel diagnosis, Ecotoxicology and One Health. All speakers were present and able to deliver their talks, as described below.

The session was co-chaired by Elisa Uliassi and Clara Lima. After each presentation, a short discussion and interaction with the audience allowed all participants interested in the topics to raise questions.

The first lecturer was Jérôme Estaquier from the *Institut National de la Santé et de la Recherche Médicale* (INSERM), Paris Descarts University, Paris, France, and the *Centre de Recherche (CHU) de Québec*, *Université Laval*, Québec, Canada. Jérôme presented research work on leishmaniasis in a lecture entitled "Single cell transcriptomics reveals altered myeloid cell profile despite the administration of an early miltefosin cure *in Leishmania infantum*-infected rhesus macaques". Jerome outlined the utilization of a monkey models (namely rhesus macaques) to assess the effectiveness of emerging drugs, citing specific compounds such as amphotericin B and miltefosine as examples. The model underwent thorough characterization in both parasitological and immunological aspects, highlighting its close parallels to human infection. This investigation successfully illustrated the immunological changes triggered by these particular molecules.

The second lecture was presented by Elisabeth Davidoud-Charvet from the *University of Strasbourg, Laboratoire d'Innovation Moléculaire et Applications (LIMA), Bio(IN)organic and Medicinal Chemistry Team (CBM)*. Elisabeth's presentation was entitled "Synthesis of chemical probes based on the early lead redox-active antiplasmodial agent, plasmodione, for metabolic and imaging studies". In her work, Elisabeth tries to identify putative plasmodione targets in the *P. falciparum* proteome through the affinity- based protein profiling (ABPP) strategy. This approach aims to photolabel *Plasmodium* protein targets by using photoreactive and 'clickable' PD-derived probes and identify them by mass spectrometry methods.

The third lecture was presented by Dijana Blazhekovikj-Dimoska from *St. Kliment Ohridske University*, Faculty of Biotechnical Sciences, Bitola, North Macedonia. Dijana´s presentation was entitled "Fish-borne zoonotic diseases with special emphasis on parasites and risks for public health". During her presentation, Dijana reflected on aspects associated to the importance of fish for healthy nutrion and the impact of fish parasitosis in public health and their relevance in aquaculture settings. Dijana also reviewed some of the major fish-associated parasitic diseases.

The fourth lecture was given by Asghar Talbalaghi, a medical entomologist working at the Italian Mosquito Control Association and a Freelance Entomologist consultant for vector control of public administrations. Asghar´s lecture was entitled "Prevention of Leishmaniasis through Personal Protection by Use of Repellent Textile" and approached novel and environmental friendly solutions for the control of vector-borne diseases of medical and veterinary impact, focusing on personal/ individual protection as a prevention approach. For the purpose, Asghar proposed the use of fabric with repellent properties as a measure to prevent exposure to vectors.

The fifth lecture was presented by Clara Lima, a Veterinarian and PhD candidate at the Faculty of Pharmacy and i3S, University of Porto. Clara´s lecture was entitled "Changing paradigm to confront zoonotic Leishmaniasis: One Health perspective from Portugal" and reflected some of the research strategies applied during her PhD work to update the epidemiology of leishmania in Portugal, under One Health framework. Clara focused on the importance of multifactorial and multidisciplinary collaborations to unveil the different intervenient in leishmaniasis transmission in Portugal, and how this is being materialized at i3S.

The sixth and last presentation was lectured by Rolf-Alexander from Justus Liebig University, Germany. Rolf´s presentation explored aspects of avermectin´s toxicity to the environment and some of the ecotox laboratory models employed be address this issue. During his presentation, Rolf reflected the importance of considering ecotoxicological assessment to address the environmental impact of endectocides applied in animals and humans for parasitic vector-borne diseases. For the purpose he presented a case study from Burkina Faso´s livestock treated with these drugs and where his team assessed impact of ivermectin and a ivermectin-reformulation on the organisms (including insects) and plants that depend on the soil and the dung to thrive.

After Rolf´s presentation, Clara Lima and Elisa Uliassi made a summary of the YRI sessions held on the OHD Marathon day 3 and presented the YRI awarded with an ITC conference grant and a Dissemination grant. The awards were distributed by a committee formed by Elisa Uliassi, Clara Lima, Anabela Cordeiro da Silva and Elisabeth Davidoud-Charvet. Selection of the best work was determined based on the scientific quality of the presented work and following the COST rules and criteria. All the YRI who received a COST grant during the 1st grant period were excluded.
The two YRI awarded with a ITC Conference Grant and a Dissemination Grant were Marko Jukič and Ivan Bassanini.

Marko Jukič is an Associate Professor in the fields of pharmacy, pharmaceutical chemistry, and bioinformatics at the Faculty of Mathematics, Science, and Information Technologies of the University of Primorska (UPR FAMNIT) and the Faculty of Chemistry and Chemical Technology, University of Maribor (UM FKKT). He´s working on the development of new pharmaceuticals using molecular modeling and computational tools for drug design, with special emphasis on biosynthesis of bacterial cell walls and development of new antibiotics. Additionally, he studies human and viral proteases, their involvement in the pathology of cancer diseases, and their potential use in the development of new antiviral drugs. Besides, Marko is the developer of widely used software (CmDOck) and the author or co-author of more than 50 scientific works. On the OHD Marathon YRI session, Marko presented a talk on "Strategic Evolution of SiDOCK@HOME: From COVID-19 Drug Design to a Broad- Spectrum Drug Search" where he elucidated the audience on how SiDOCK@HOME can be applied to drug development, with the particular case of anti-parasitic drugs.

Ivan is an organic synthetic chemist with a master's degree and a PhD in Chemical Sciences (UniMi department of Chemistry, short missions to AVCR Prague). His research work targets the preparation of bioactive compound, exploiting different approaches from traditional synthetic protocols, to biocatalyzed transformations and peptide synthesis. During his PostDoc (UniMi department of Pharmaceutical Sciences),

Ivan focused on the design and preparation of compounds with antiprotozoal or/and antiproliferative activity. More recently, Ivan is working independently at SCITEC CNR on target-oriented development of novel antiprotozoal agents. On the YRI session, Ivan explored a talk on "A basic celastrol carboxamide derivative acts as a middle-domain, potent and selective allosteric inhibitor of *Leishmania braziliensis* 90kDa Heat Shock Protein". During his talk, Ivan described his aims to develop novel leishmanicidal agentes by targeting protozoan Hsp90 *via* an allosteric mechanism of action. Synthetic derivates of the triterpene celastrol, a cytotoxic natural compound known as Hsp90 interactor, have been designed, prepared, and screened *in vitro* against cultures of *Leishmania* promastigotes and intramacrophage amastigotes. SS2, a pyrrolidine celastrol derivative, was identified as the most potent and selective leishmanicidal agent and, thus, its molecular interaction with the *Leishmania* Hsp90 has been deeply investigated. By combining *in vitro* assays, high-resolution NMR experiments and *in silico* simulations, SS2 profile as Hsp90 modulator was elucidated.

It was the Committees decision to make a public statement and special mention to Darline Dize who, despite the scientific merit and quality of the work, is not eligible to be granted with a COST grant, following the COST rules. Darline is a PhD student at the University of Yaoundé I, Cameroon. On the YRI session, she presented a talk on "Novel antitrypanosomal diaminoquinazoline analogues from repurposing the Medicines for Malaria Venture Open Access Pathogen Box library (MMVPBox)" where she explained the audience how she is screening antitrypanosomal activity against *Trypanosoma brucei brucei* using the resazurin-based cell viability assay in a group of drugs selected from the from the MMVPBox library. Besides, Darline is also addressing cytotoxicity of the selected drugs on Vero cells. Darline is now exploring a small library of analogues of one (MMV675968) of the identified hits with antitrypanosomal cytotoxicity, by including DMPK prediction and mode of action studies (*in vitro* and *in silico* enzymatic studies, time-kill kinetic, DNA fragmentation).

The two awardees were informed they will be contacted by a OHD secretariat member with further instructions on the grant management and applications.