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Summary of the Paul Ehrlich Euro-PhD Network & OneHealthdrugs COST Action MEETING dedicated to OneHealth*drugs* colleagues and young researcher innovators (YRI),

The **Paul Ehrlich Euro-PhD Network & OneHealthdrugs COST Action MEETING** took place in Rome (June 17-19,2024) and has been a great opportunity for all young investigators to share and discuss their research and to network with all attendees. The Paul Ehrlich Euro-PhD Network is the largest EU PhD network with 65 Universities from 23 Countries whose final aim is to provide an in-depth research training and mobility of PhD students in the area of Medicinal Chemistry at European level. Thus, the dedicated OneHealth*drugs* Workshop "One Health approach to tackle neglected infectious diseases challenges " has provided the ideal international platform for YRI to present their research work in the field of neglected infectious diseases: Trypanosomiasis, Leishmaniosis, Schistosomiasis, Malaria and others in the field of medicinal chemistry/green chemistry and ecotoxicology.
The meeting brought together 130 participants from 20 countries. The program included 3 plenary lectures and 1 invited lecture by leading scientists from academia as well as 31 oral communications by young and senior investigators. Moreover, 34 posters were presented in highly interactive poster sessions and flash presentations.

The OneHealth*drugs* Workshop on DAY 2 (June 18th) has been chaired by Prof.s Daniela Secci and Maria Paola Costi and opened by the inspiring and amazing lecture by Prof. Rohini Roopnarine. Rohini Roopnarine is Professor at the School of Veterinary Medicine, and adjunct professor Dept. of Public Health & Preventive Medicine, School of Medicine, at St. George's University and CA21111 member. Her research focuses in Interprofessional Education and One Health Education. Her presentation has highlighted on the importance of the One Health principles/education/awareness in the field of VBPD, with particular emphasis on the medicinal chemistry aspects. Below the abstract related to the presentation is reported. Then, Dr Elisa Uliassi presented the Young Researcher Innovators (YRI < 40 years) Horizontal Group (HG) 4 within COST Action CA21111 – OneHealth*drugs*. Her presentation introduced the HG4 aims, activities and events with the objective to stimulate YRI research, training and networking activities across all areas of VBPD, by creating new knowledge and technologies according to the *One Health goals*. HG4 is also committed to raise awareness and to make VPBD research more environment conscious. Following, 13 flash presentations delivered by YRI working in the field of VBPD have brilliantly showed the different med chem approaches pursued against VBPD. The workshop has been closed by Prof Stefano Alcaro with an excellent presentation on The Chemotheca – a computational facility containing virtual compounds developed within MuTaLig COST ACTION CA15135 -, as a promising networking tool for collecting also hits and leads developed within the OneHealth*drugs* Cost Action.

We have emphasized the critical need of broadening the range of drugs to combat VPBDs and the imperative to significantly alter the existing approaches to drug discovery and development. Medicinal chemistry/green chemistry can be integrated with ecotoxicology perspective thus allowing the design of more environmentally friendly hits and leads for VBPD. This approach increases the chances to reduce their broad toxicity to the living organisms and environment.

In this sense, we hope to have contributed to strengthening YRI's foundation in OHD topics and to make their involvement into our OHD Action even higher. By joining the HG4, YRI will have the opportunity to meet and network with other young researchers as well as with more senior researchers. The best way to do this is to become CA21111 member, join our events and activities.
Looking at the future, we are focused on establishing a new avenue to innovative therapeutics for VBPD according to the One Health principles.
I would like to express my gratitude to all organizers, speakers and participants for their invaluable contributions and active participation in this enlightening meeting. A special thank goes to the Local Organizing Committee, and in particular to Prof Daniela Secci. Our sincere thanks to Prof Rohini Roopnarine who was fundamental in the inauguration of this event. We thank Professor Maria Paola Costi for her endless enthusiasm and commitment to the OneHealth*drugs* COST Action.
Once again, we thank everyone who made this event possible
Elisa Uliassi

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Interprofessional Education (IPE): Paradigm shift to tackle global health

Current & emerging threats

Climatic change:
- Vector-borne, Zoonoses & Pandemics
- Food scarcity: Life below and above land
- Extreme heat, air pollution & Water quality
- Natural Disasters
- Loss of biodiversity

AMR

Translational research: cancer, chronic disease

Mental health-Human –pet bond, green spaces.

Stakeholders
- Universities & Interprofessional Education
- Pharmacists
- Medicinal chemists
- Educators: virologists, parasitologists
- Economists
- Public health
- Physicians
- Veterinarians
- Environmental health
- Government policy-makers
- Lawyers
- Social workers
- Mental health professionals

List of Young Researchers who were selected for reimbursement and the title of their presentation.

1. Acyclic nucleosides as potential antikinetoplastid agents
   Julie Traena, Serge Van Calenbergha, Guy Caljonb aLaboratory of Medicinal Chemistry, Ghent University, Ghent, Belgium bLaboratory of Microbiology, Parasitology and Hygiene, Antwerp University, Antwerp, Belgium, Ottergemsesteenweg 460, 9000 Gent, BelgiumUniversiteitsbaan 1, 2610 Wilrijk, Belgium

2. Design, synthesis and evaluation of reverse β-aza fosmidomycin analogues as 1-deoxy-d-xylulose-5-phosphate reductoisomerase (DXR) inhibitors as antimicrobials
   Thibaut Quennesson,a Martijn Risseeuw a, Serge Van Calenbergha

3. Deciphering host-parasite interplay in Leishmania infection through a One Health view of proteomics studies on drug-resistance
   Lorenzo Tagliazucchi a, Giulia Malpezzi a, Ana Perea Martinez b, Alexander R. Cole c, Daniele Aiello a, Ba Reum Kwon c, Bryan W. Brooksc, Eli S. J. Thoré d,Michael G. Bertram d, Francisco Gamarro b, Maria Paola Costi a

4. Preclinical investigation of H80 compared to miltefosine: imaging and proteomics for sustainable drug development.
   Giulia Malpezzia, Lorenzo Tagliazucchia, Daniele Aielloa, Alberto Venturellia, Anabela Cordeiro-da-Silvab, Nuno Santaremb, Glauco Ponterinia, Maria Paola Costia

5. Modulating the 2-position of imidazo[1,2-a]pyrazine lead CTN1122 alters its antileishmanial properties and L-CK1.2 kinase inhibition profile
   Lhana Tisseur, Marc-Antoine Bazin, Sandrine Cojean, Fabrice Pagniez, Guillaume Bernadat, Cédric Logé, Christian Cavé, Carine Picot, Olivier Leclercq, Blandine Baratte, Najma Rachidi, Stéphane Bach, Philippe Loiseau, Patrice Le Pape, Pascal Marchand

6. MolecularModellingfor medicinalchemistry: Development and application **F. Procopio**

Award to a young researcher with the best presentation on the OHD topic Additionally one special award was assigned to the below reported young scientist:

E. Van de Velde presenting a scientific work entitled Synthesis and phenotypical discovery of imidazo[2, 1-fitriazine ribosides as broad spectrum antitrypanosomal agents. See the abstract below. *The award consisted in the admission to the next COST Action meeting in presence that will take place in Athens on the 19-20 of June 2024.*

Synthesis and phenotypical discovery of imidazo[2,1-f]triazine ribosides as broad spectrum antitrypanosomal agents

Ewout Van de Velde[a*], Guy Caljon[b], Serge Van Calenbergh[a]

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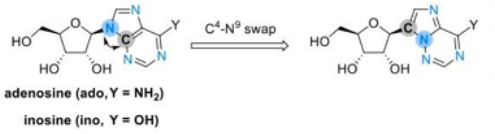
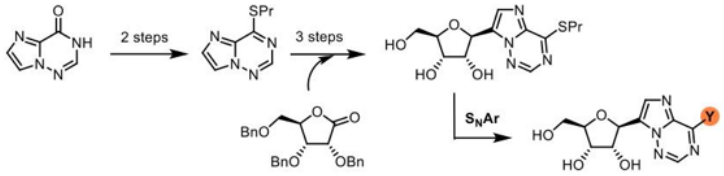
In 2019, a focused series of purine-like C-nucleosides was synthesized in our lab and evaluated phenotypically against a small panel of protozoa.[1] This study revealed that minimal changes to the nucleobase scaffold may strongly influence activity and host cell toxicity. The purine $N^9 - C^4$ atom swap in canonical nucleosides resulted in two analogues with low to sub-micromolar broad-spectrum activity against several *Trypanosoma* species at varying toxicities. This incited us to investigate the effect of substituting the canonical NH_2 and OH motifs with various amines, alcohols and thiols.

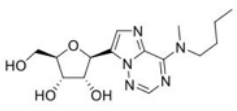


	EC_{50} (µM)	CC_{50} (µM)
Y = NH_2	0.25 - 5.15	1.41
Y = OH	0.50 - 3.17	> 64.00

Focusing on feasibility and late-stage diversification, a synthesis method was optimized for variously substituted imidazo[2,1-f]triazine ribosides. The early functionalization of the nucleobase with a thiopropyl group provided ample protection against strongly basic and acidic conditions while also allowing diversification via a direct nucleophilic aromatic substitution reaction (S_NAr) with amines, alcohols and thiols at the very last step, resulting in a very divergent synthesis route.



All analogues were assessed on a cellular level and one displayed EC_{50} values between 73 and 175 nM without any apparent toxicity at 64 µM.



EC_{50} *T. b. brucei*	**0.076 µM**
EC_{50} *T. b. rhod*	**0.073 µM**
EC_{50} *T. cruzi*	**0.120 µM**
EC_{50} *L. infantum*	**0.180 µM**
CC_{50} *MRC-5*	**> 64.00 µM**
CC_{50} *PMM*	**> 64.00 µM**

1) Bouton J. et al. Synthesis and evaluation of a collection of purine-like C-nucleosides as antikinetoplastid agents. *Eur. J. Med. Chem., 212, 113101, 2021.*