Growing ideas through networks

COST Action CA21111 - OneHealth*drugs*

One Health drugs against parasitic vector borne diseases in Europe and beyond

General Assemblu

29 May 2024





Funded by the Horizon 2020 Framework Programme of the European Union Maria Paola Costi Action Chair





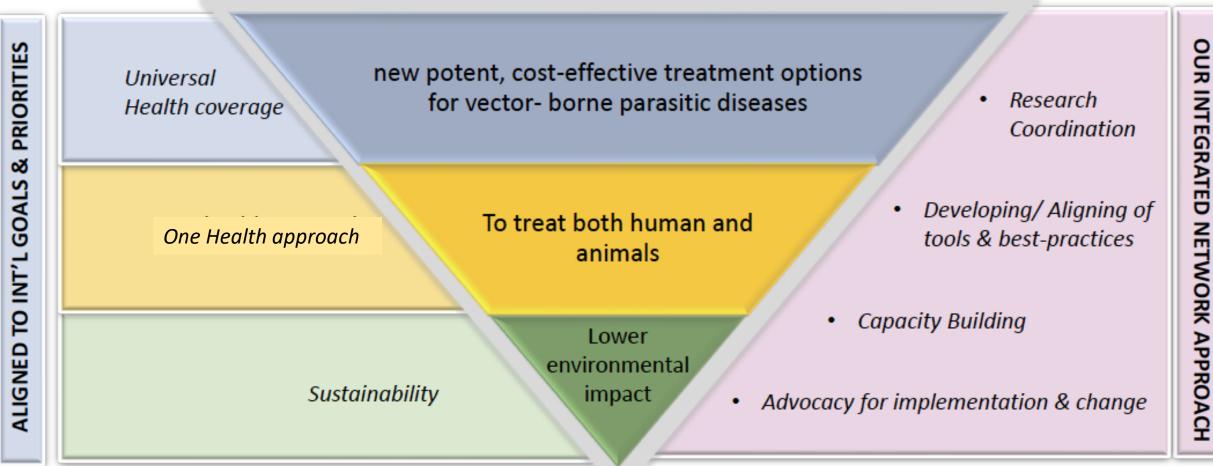
OHD PROJECTS TOWARDS OneHealthdrugs objectives

Looking for low environmental impact drugs



ONEHEALTHDRUGS

CA21111: OBJECTIVES



FOR GLOBAL IMPACT ON DISEASE AND SAFEGUARDING THE ENVIRONMENT

ACHIEVEMENTS

- 1. SURVEY 1 on Raising Awareness STEP 1 time 0. Paper is under submission.
- ACS infectious diseases Issue + publications number 10-12 + 2 editorials.
- 3. Conferences Grants given to YRI (2 in 2023 2 in 2024)
- 4. STSM leading to papers (some ongoing, others achieved)
- 5. Training schools for training achievements?
- 6. 58 meetings . 4 in presence about 200 scientists can participate (COST supported) leading to papers, some already others ongoing
- 7. OHD 1-4 projects

OneHealth*drugs* OHD 1-4 projects

OHD1-TARGET DATABASE PROJECT

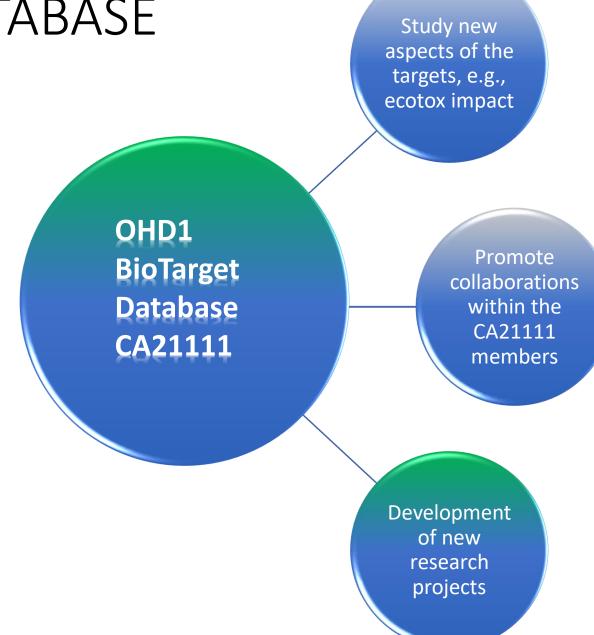
OHD2 - DATABASE COMPOUNDS PROJECT

OHD3 - ENVIRONMENTAL IMPACT OF VETERINARY DRUGS AGAINST VBPD

OHD4 – ANIMAL MODELS AND REPLACEMENT TO ENVIRONMENTALLY FRIENDLY APPROACHES

OHD1- BioTarget DATABASE

Collect info on the biological targets under study by the CA21111 members, related to OneHeathDrugs and *translate to environmentally friendly targets for drug design and discovery.*



BioTarget Database

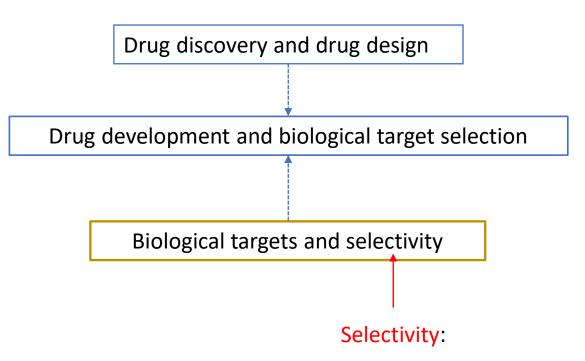
Collect info on the biological target under study by the CA21111 members, related to OneHeathDrugs

Promote collaborations within the CA21111 members

Study new aspects of the targets, e.g., ecotox impact

Development of new research projects





- versus non target species for <u>safety</u> concerns in the humans and animal bodies
- versus target species for environment safety
 - All environmentally known species
 - Selected species for evaluating the compounds toxicities

Evaluation of the eco-tox impact for designing drugs safe for humans and animals, and for the environment

Development of the BioTarget Database

— Jan/Feb 2024: Sub-group for the development of the BioTarget Database CA21111 template

March 2024: BioTarget Database CA21111 template

June 2024: Sending the template to CA21111 members for input of target under study

July 2024: Collection of info on the target available within the CA21111

Jul/Aug 2024: Generation of the BioTarget Database, available for all CA21111 members

Sep/Oct 2024: Publication

BioTarget Database

Development of the BioTarget Database

— Jan/Feb 2024: Sub-group for the development of the BioTarget Database CA21111 template

March 2024: BioTarget Database CA21111 template

Section 1 – general info

General info on the target (e.g., protein/enzyme name, synonyms, acronym, source organism, sequence, UniprotKB ID)

General info on the production for study purposes (e.g., protein production by, recombinant protein production organism)

Section 2 - protein/enzyme function

Including a brief description of the target function and other info as substrate(s), cofactor(s), post-translational modifications (PTMs).

Section 3 - Biochemical information

Including the main biochemical parameters and information (e.g., substrate's K_{M} , k_{cat} , biochemical assay protocols) and references

Section 4 - Biophysical information

Including the main biophysical information (e.g., oligomeric state, isoelectric point, molecular weight, posttranslational modifications, assay protocols) and references

Section 5/6 – HTS and activators

Including info on HTS and activators (e.g., known inhibitors, active site inhibitors, allosteric inhibitors, known activators, HTS available by, assay protocols) and references

Section 13 - Meaningful references on the target					
Section 12 – Intellectual Property					
Section 11 – Added value					
Section 10 – Selectivity/specificity					
Including the available info on selectivity and specificity of the target (e.g., homology with human, homology with other organisms)					
Section 9 – Ecotox impact					
Including the available info on the ecotox impact (e.g., predicated environmental impact)					
Section 8 - Structural information					
Including the main structural information on the targets (e.g., crystal structure available by, PDBs, predicted model) and references					
Section 7 – OMICS					

Final template for the BioTarget Database

Including the main proteomics info

BioTarget Database

CA21111 OHD1 - Target database project: the BioTarget DataBase (BioT-DB)

Ulrike Wittig^a, Andrea Ilari^b, Javier Santamaría^c, Alfonso T. Garcia-Sosa^d, Michael Bertram^e, Eli

Thoré^e, Guy Caljon[†], Annette Ives⁵, Emilio Parisini^h, Theodora Calogeropoulouⁱ, Marco Mazzorana^j, Marko Jukić^k, Anabela Cordeiro da Silva^I, Maria Paola Costi^m, Cecilia Pozziⁿ

* Heidelberg Institute for Theoretical Studies, Germany; ^b Italian National Research Council, Italy; ^c Universidad de Cantabria, Spain; ^d University of Tartu, Estonia; ^e Swedish University of Agricultural Sciences, Sweden; ^f University of Antwerp, Belgium; ⁶ AC Bioscience, Switzerland; ^h Latvian Institute of Organic Synthesis, Latvia; ⁱ National Hellenic Research Foundation, Greece; ^j Diamond Light Source Ltd., United Kingdom; k University of Maribor, Slovenia; ^I University of Porto and Institute for Molecular and Cell Biology, Portugal; ^m University of Modena and Reggio Emilia, Italy; ⁿ University of Siena, Italy

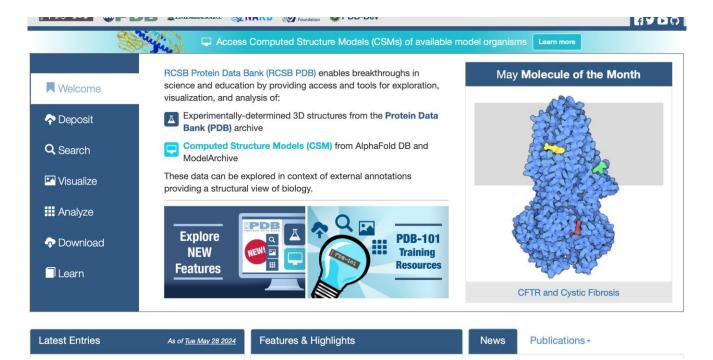
cecilia.pozzi@unisi.it

The OHD1 - Target database project aims at developing the BioTarget DataBase (BioT-DB), collecting valuable information on the biological targets currently under investigation by the CA21111 members. The BioT-DB is structured in ten main sections, each focused on different macromolecular properties related to the OneHeathDrugs theme. Following the first section, reporting general information (e.g., name and acronym, sequence, IDs for UniprotKB [1] and BRENDA [2] databases), seven sections are dedicated to report useful information on the target function, production, biochemical, and biophysical characterization, omics, medium and high throughput screening, and the selectivity/specificity profile. A specific section is dedicated to collect available structural information on the targets, investigated by different techniques (e.g., X-ray crystallography, CryoEM, BioSAXS, and NMR). Useful links to the main structural databases, PDB [3], EMDB [4], SASBDB [5], and BMRB [6], are reported together with available, yet unpublished, structural characterizations. The last section is focused on the ecotoxicological impact of target molecules, evaluated by SeqAPASS [7] or other tools.

The BioT-DB is specifically designed to promote collaborations within the CA21111 members, reporting direct contact details in each section. Furthermore, the database aims to highlight key properties of the investigated biological macromolecules combined with their selectivity and specificity profiles and the evaluation of their ecotoxicological impact. The integration of all this information allows a widen perspective for biological target selection and investigation. At a later stage, the target data, collected within the BioT-DB, will be also crossed with the molecule data, included in compound databases, also under development within the CA21111.

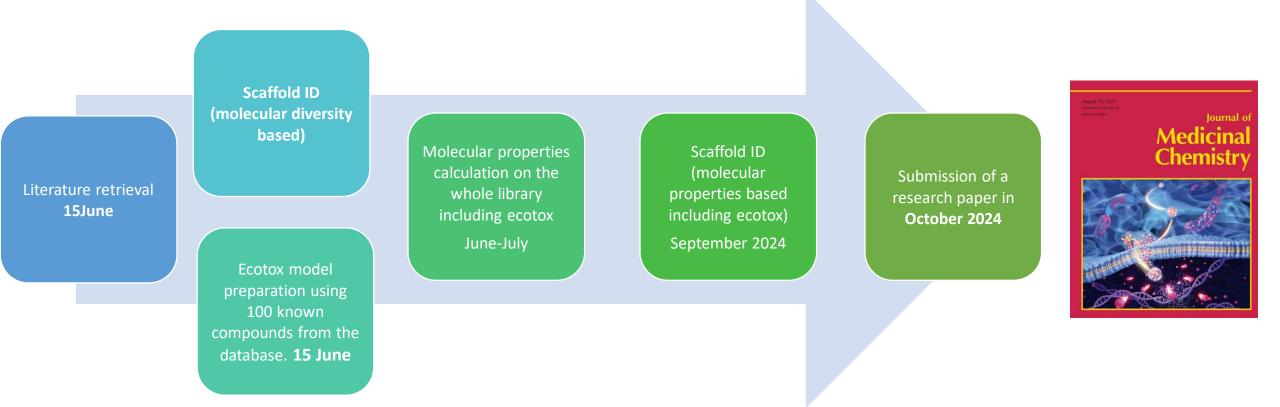
References

 https://www.uniprot.org/, [2] https://www.brenda-enzymes.org/, [3] Velankar S, et al. Methods Mol Biol. (2021), 2305:3-21, [4] wwPDB Consortium Nucleic Acids Res. (2024), 52(D1):D456-D465, [5] Kikhney AG, et al. Protein Sci. (2020), 29(1):66-75, [6] Hoch JC, et al. Nucleic Acids Res. (2023) 51:D1, [7] Doering JA, at al. Toxicol Sci. (2018), 166(1):131-145.

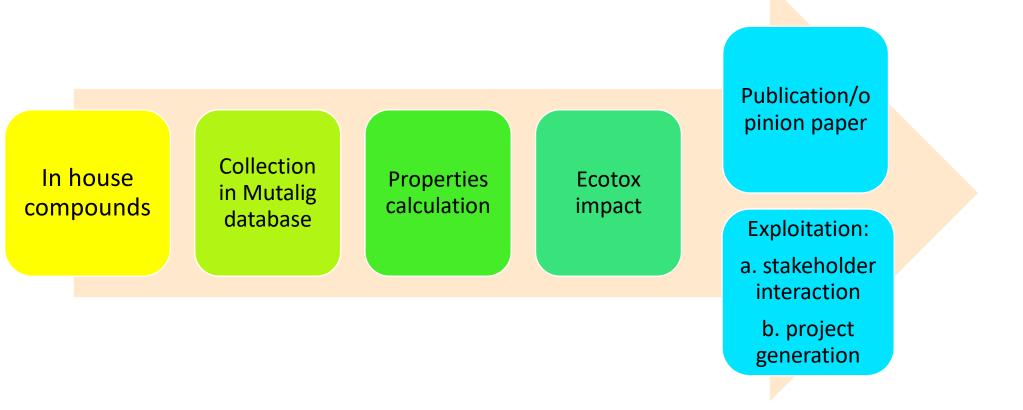


OHD2-DATABASE COMPOUNDS PROJECT

Step 1 metadata analysis and chemoinformatics



<u>Step 2</u>- Database VBPD and environmental impact



https://www.youtube.com/watch?v=pzmUXmTx9qI

http://chemotheca.unicz.it

Ortuso Fet al. The Mu.Ta.Lig. Chemotheca: A Community-Populated Molecular Database for Multi-Target Ligands Identification and Compound-Repurposing. Front Chem. 2018 Apr 19;6:130.

EUROPEAN COOPERATION



Virtual Chemotheca



Home	Welcome to the Mu.Ta.Lig Virtual Chemotheca!
Login	For each lead compound developed in medicinal chemistry research several other inactive or less active molecules are synthetized/isolated and tested.
Registration	These chemical entities are useful for deriving structure activity relationships with respect to the original target, but their development and application stops, in the best cases, in a scientific manuscript and they are forgotten in some storage area.
Search DB	Inactive or poorly active compounds could live a second life by testing them with respect to other targets.
<u>News</u>	The Mu.Ta.Lig COST Action project aims to address this by developing a virtual chemotheca. Such a computational facility contains virtual compounds kindly provided by Mu.Ta.Lig participants whose are the intellectual
Contact us	owners.
Credits	For each entry, physico-chemical and ADME properties have been theoretically computed. Experimental activity data have been stored, if available.
Tutorials	Selected molecules can be acquired directly from their owners who are absolutely free to take accord as they like, without intermediation by Mu.Ta.Lig Virtual Chemotheca management.
	Registered users have full access to Chemotheca data whereas Guest access will provide a simplified search interface to retrieve basic information (compound IDs and related 2D or 3D chemical structures, only) and some compounds could be hidden according to their owner decision.
	Registration is free of charge and allows users to upload new compounds and/or to update experimental/theoretical activity data (i.e. new target tested) related to already stored compounds. Both tasks will be very appreciated!
	This authentication procedure requires the exchange of session cookies. No other information will be kept from your browser!

Antiparasitic drug discovery and emerging scaffolds with predictive low environmental impact

Sandra Gemma¹, Elisa Uliassi², Chiara Borsari³, Michele Tonelli⁴, Federica Pellati⁵, Stephanie Blandin⁶, Elisabeth Davioud-Charvet⁷, George E. Magoulas⁸, Ioannis P. Papanastasiou⁹, Lucia Tamborini³, Laura Bertarini⁵, Valeria Francesconi⁴, Daniele Aiello⁴, Richard Becket²⁶, Gülşah Bayraktar¹⁰, Cécile Exertier¹¹, Jovana J. Ajdukovic¹², Pascal Marchand¹³, Christophe Dardonville¹⁴, Huseyin Istanbullu¹⁰, Constantina Pyrkotis¹⁵, Joana Tavares¹⁶, David C. Magri¹⁷, Andrea Ilari¹⁸, Corinne R. Ngnameko^{19, 20}, Anabela Cordeiro da Silva^{16, 21}, Michael G. Bertram²², Eli S.J. Thoré²³, Ulrike Wittig²⁴, Sheraz Gul²⁵, Maria Paola Costi⁵ and Theodora Calogeropoulou⁸.

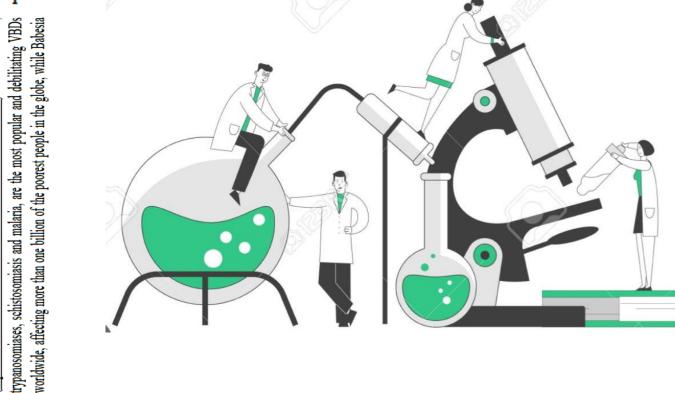
Leishmaniasis,

(https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases).

more than 17% of all infectious diseases,

causing more than 700000 deaths annually

Vector-borne diseases (VBDs) are caused by parasites, bacteria, or viruses and account for



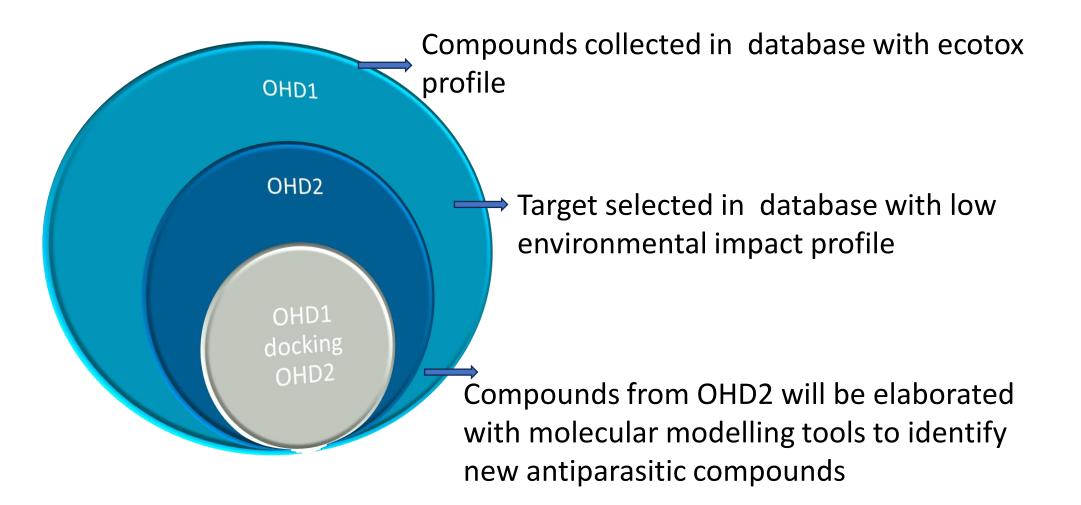
infections are exponentially increasing. These infectious diseases can be transmitted via vectors among humans, among animals, or from animals to humans or may have animals as reservoir. The existing medications for these parasitic VBDs suffer from a variety of problems including serious side effects, the requirement of long-term and expensive treatment, few therapeutic options and the development of parasite resistance other than reduction of the therapeutic efficacy due to environmental factors.

The COST Action CA21111 "OneHealthdrugs" (https://onehealthdrugs.com/) aims at coordinating the discovery of drugs halting human and animal VBDs keeping with the principles of optimal profile for both organisms. In particular, the project OHD2: Antiparasitic drug discovery and emerging scaffold with predictive low environmental impact aims to foster the collection of antiparasitic compounds from different sources and associate the chemotypes with in silico prediction of their molecular properties and ecotoxicological profile. To achieve this the following strategy 2 steps are proposed. Regarding step 1, the following is proposed. A) Collection of published compounds during the period 2019-2024 with activity against Leishmaniasis, Human African Trypanosomiasis, Chagas Disease, Malaria, Babesia and Schistosomiasis. The selection was based on Target Product Profiles (TPP) set for hit compounds for each of the mentioned diseases, ensuring a diversity of chemotypes; B) Selection of the most diverse scaffolds based on computational analysis combining structural features, biological results (on target/phenotypic) and pre-clinical data and C) Evaluation of in silico molecular and ecotoxicological properties for the identified scaffolds of interest (COMPoI).

A second step of the OHD2 compounds database project is the collection of in-house compounds from the COST Action participants and external interested collaborators in a structured Database OHD tool. The OHD database will include chemical-specific information for antiparasitic drugs enriched with target specific and off-target effects including ecotox properties (https://doi.org/10.1093/bioadv/vbad045).

This approach will enable to identify at an early stage the most appropriate scaffolds for further medicinal chemistry development in the VBPD field showing a low environmental impact in the early phase of the drug discovery process. The project OHD2 is aligned with the objectives of Working Group 1 (WG1) (Compound libraries coordination and integration of compound design) and Working Group 2 (WG2) (Integration of early phase studies and low environmental impact actions). OHD2 aims at increasing the number of compounds available for the drug screening campaigns adopting virtual or phenotypic approaches thus, fostering innovation in antiparasitic drug discovery, promoting safer and more environmentally friendly drugs not only for VBPDs but for other diseases as well broadening the scope of this coordinated activity within "OneHealthdrugs".

OHD1&OHD2 A COMMON PLATFORM



WG3 – Objective and Deliverables

Objective: Promoting and strengthening of innovative technologies required in the translation of leads and candidates from animal to humans and vice versa to ensure the progression of qualified leads and candidates to the end of the pre-clinical phase and de-risk studies in clinical phase

- D2_Report on imaging and target engagement studies. M18 (WG3)
- D 6_Report on omics and validation technologies. M24 (WG1-WG4)
- D10_Report on One Health nanotechnology system for animal models studies. M36 (WG1,WG2,WG3)
- D12_Report on HTS assays and structural biology. M42 (WG1,WG2,WG3)
- D14_Report on SOP coordination on standardization of animal experiments. M42 (WG3)
- D21_Report on internal coordination of the transfer of knowledge and exploitation plan. M48 (WG1-WG6)
- D22. Report on external coordination of the transfer of knowledge and exploitation plan. M48 (WG1-WG6)

OHD3 – ANIMAL MODELS AND REPLACEMENT TO ENVIRONMENTALLY FRIENDLY APPROACHES

1. SOP about animal models standardization in VBPD

2. Cell-based studies for drug efficacy and ecotoxicology profile

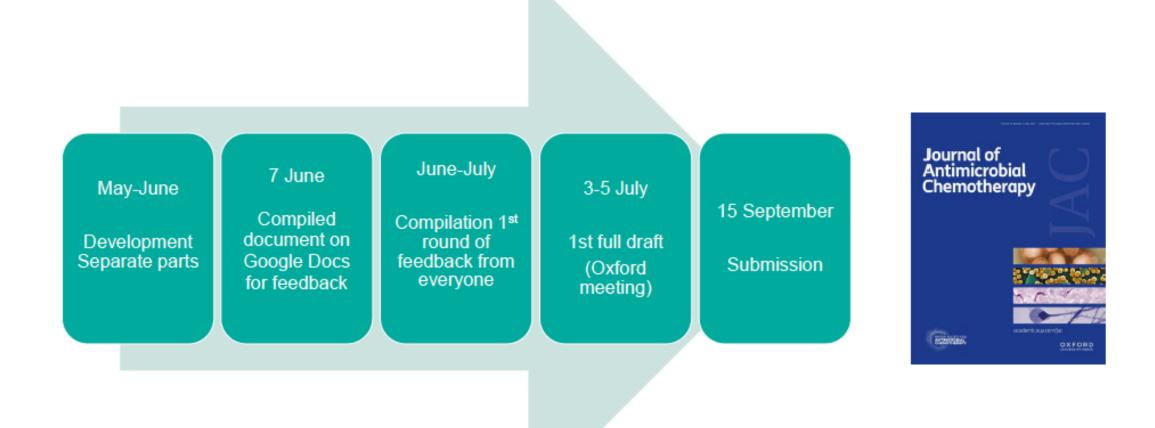
Anabela Cordeiro da Silva: Ana Tomas: Sener Cintesun: Eli Thoré: Estefania Calvo Alvarez: Fatgzim Latifi: Frédéric Frezard Guy Caljon: Jerome Estaquier: Joana Tavares: Jose Maria Alunda: Katrien Van Bocxlaer: Katarazyna Gozdzik: Kayhan Ilbeigi: Louis Maes: Michael Bertram: Maria Paola Costi Sarah Hendrickx:

Leishmania, canL, HAT, T. cruzi, immunology, Leishmania Animal experiments, toxicity, oxidative stress Ecotoxicology, chemical pollution Trypanosoma brucei Leishmania, canL Formulation, nanoformulations, repurposing, VL/CL Leishmania, HAT/AAT NHP, Leishmania Leishmania, Trypanosoma, T. cruzi, BLI, preclinical Leishmania, preclinical, VL & canL, formulation CL, skin permeation, formulation, PK/PD, preclinical

AAT, preclinical, veterinarian Leishmania, drug evaluation in vitro/in vivo Ecotoxicology, chemical pollution, new drugs, regulation Medicinal chemistry, anti-cancer, VBD Leishmania (VL, CL), preclinical, model development, insect



3



Transition from *in vitro* to *in vivo* evaluation: recommendations for obtaining high-quality leads against kinetoplastids

<u>Authors</u>:; Anabela Cordeiro da Silva, Ana Isabel Olías, Ana Tomas, Bryan W. Brooks, Şener <u>Cintesun</u>, Eli S.J. Thoré, <u>Estefania</u> Calvo-Alvarez, <u>Fatgzim Latifi</u>, Frédéric Frezard, Jerome Estaquier, Joana Tavares, José María <u>Alunda</u>, Katrien Van Bocxlaer, María J. Corral, Marta Mateo Barrientos, Michael G. Bertram, Maria Paola Costi, Kayhan Ilbeigi, Sarah Hendrickx, Louis Maes, <u>Guy Caljon*</u>

Onehealthdrugs WG3 group on SOP coordination of animal experiments *Guy.Caljon@uantwerpen.be

Given the impact of kinetoplastid diseases, the limited therapeutic options and the risk of treatment failure, a high medical need remains for the discovery of novel chemical entities and innovative drug targets. From the 3R guiding principle for the humane use of animals in research, stringent decision criteria need to be implemented during the translation from in vitro identification of hit compounds to an in vivo evaluation in infection models. Besides potency and selectivity, several experimental and in silico data, e.g. physicochemical properties, metabolic stability, (eco)toxicity, formulation and snapshot pharmacokinetics, can serve as tools in the decision-making process. Also the respective target product profiles and proper design and reporting of the experiments are key in an animal-friendly approach. A range of standard and more refined animal models exist that represent human infection and disease and have proven essential for electing clinical candidates and eventually bringing novel drugs to the patient. Nevertheless, the limitations and complementarities of the various models need to be well understood, while emerging challenges and opportunities based on clinical

Animal Models for Infectious isease

VUS

GRANT APPLICATION: ONGOING ACTIVITIES are planned in the field of mobility and research grant (MSCA)

OneHealth*drugs* ONGOING ACTIVITIES

ProfileQSAR applied D Malaria and Chagas Disease

Drug Discovery for parasiti diseases: powered by technology, enabled by oharmacology, informed by clinical sciences.

als are incased as

Joana Tavares, i3S,

How does EthoCRED work?

hould generally be blinded to the experimental treatments when conducting and s in order to avoid potential bias

operimenters blind to experimental treatment when conducting and analysing beh

Examples of reliability criteria

ara

ima,

FFUP and i3S

OHD

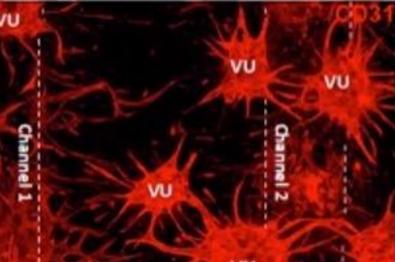
ONE HEALTH DRUGS

ils are increasingly video-recorded and analysed with automated software, reduc

OHD TOWA OneHa objecta

Looking for low env impact drugs

> Ana Tomás, ICBAS and i3S, Anabela Cordeiro da Silva.



Events planned for 2nd Working Period

IN SCIENCE & TECHNOLDGY

			hold	to be held
	2	MC Meeting	1	1
	4	Core Group meeting	2	2
	34	WG/HG -organizative Meeting	24	10
	13	Workshop (4 in presence)	6 (1)	7(3)
	2	Training School (in presence)	0	2
	5	Communication-collaborative meeting	5	0
	60	+ Several «minor» organizative events	38	22
EURO				

Planned events IN PRESENCE for 2nd Working Period

WG3,WG4, WG6, HG4, HG5 Thematic Workshop "Animal friendly and environmentally relevant systems to replace or refine animal tests during drug developmental procesess for VBD" I3S, Porto, Portugal, 14-15 May 2024 DONE – about 50 participants, 15 in person attendants supported by the ACTION

1st Training School "Natural products in parasitic diseases".

17-19/6/2023 -3days school. University of Naples, Naples (Italy)

Workshop "Medicinal chemistry process within the OneHealth perspective for YRI 18th June 2024 9:00-13:00 Rome (Italy)

WG1 WG2 Conference "One health and structural biology approaches for vector-borne diseases". Oxford (UK) 3-5 July 2024

WG1 WG2 HG7 Thematic Workshop: "Novel leads and drugs for vector borne diseases: Targets and off targets (toxicity and ecotoxicity) and mechansim of action" September 19-20 2024, National Hellenic Research Foundation, Athens, Greece

2nd Training School "Cell culture as in vitro models for newly developed drugs against vector borne parasitic diseases within the One Health perspective".

25-27 September 2024 - 3 days school. University of Warsaw, Faculty of Biology, I. Miecznikowa 1, 02-096, Warsaw,

Poland

Workshops Participants

WG2 HG7 Workshop "Green chemistry approaches and innovative drug delivery	
systems towards reducing environmental impact in antiparasitic drug discovery" 1 5th	
March 2024 14:00-17:00pm (VIRTUAL)	29
WG6-WG5 Workshop "Minimising the risk of rapid-onset (cross) resistance in PVBD drug	
development [strategies to assess the risk of rapid resistance developing]" 18th March	
2024 14:00-16:00 pm CET (VIRTUAL)	22
WG1 Workshop " Structural and functional aspects of targets involved in vector borne	
diseases" 17th April 2024 (VIRTUAL)	39
WG3,WG4, WG6, HG4, HG5 Thematic Workshop "Animal friendly and environmentally	
relevant systems to replace or refine animal tests during drug	
developmental procesess for VBD"	
I3S, Porto, Portugal, 14-15 May 2024	51



Pre-Final list Training School Napel Approved

Received	Surname	First name	Email	e-COST invited
5/15/24	Aiello	Daniele	daaiello@unimore.it	28052024
4/30/24	Gattringer	Jasmin	jasmin.gattringer@meduniwien.ac.at	28052024
5/10/24	Surucic	Relja	relja.surucic@med.unibl.org	28052024
5/15/24	Ahmed	Shahira	shahira_ahmed@med.suez.edu.eg	28052024
5/14/24	Francesconi	Valeria	valeria.francesconi@edu.unige.it	28052024
5/15/24	MARIMUTHU	PARTHIBAN	parthiban.marimuthu@abo.fi	not eligible for reimboursement
5/15/24	Lesanavičius	Mindaugas	mindaugas.lesanavicius@gmc.vu.lt	28052024
5/15/24	Sergeeva	Alisa	alisa.sergeeva@fu-berlin.de	Requested e-COST registration on 28052024
5/15/24	Ouni	Samiha	ouni samiha@yahoo.fr	Requested e-COST registration on 28052024
5/15/24	Granith	Philip	philip.granith@abo.fi	Requested e-COST registration on 28052024
4/29/24	Doko	lori	dokolori6@gmail.com	Requested e-COST registration on 28052024



STSM

Ivan Bassanini	DCG	Submitted	TARGETING MOLECULAR CHAPERONES FOR THE DEVELOPMENT OF NOVEL ANTIPROTOZOAL AGENTS: QU'EST-CE QUE C'EST?	1000.00	2 Dissemination
Eli Thoré	DCG	🖂 Grant letter sent	Meds and motions: Understanding fish behavior in medicated habitats	1000.00	= 2.000 €
Lorenzo Tagliazucchi	STSM	Grant letter sent	Revealing the MoA of the innovative antileishmanial agent H80, leveraging MS omics tools combined with ADME/Tox Chemoinformatic	2900.00	
Theano Fotopoulou	STSM	🖂 Grant letter sent	Development of NMT-A004-loaded biodegradable nanocarriers	2400.00	7
Daniele Aiello	STSM	aid Paid	Computational approach for calpain inhibitors discovery with potential antiparasitic activity against Leishmania Infantum.	2400.00	9 STSM = 18.263 €
Narimantas Cenas	STSM	🖂 Grant letter sent	Redox reactions of plasmodione with oxyhemoglobin or heme (Fe2+)	1200.00	- 10.203 €
Dafni Graikioti	STSM	Grant letter sent	Libraries of analogues of Eucalyptus G-endoperoxides, antiparasite activities, mechanisms of action	2400.00	
Elisabeth Davioud- Charvet	STSM	Grant letter sent	Fluorometric detection of heme(Fe2+) produced through PfNDH2-catalyzed cascade of redox reactions from plasmodione	1200.00	
Aleksandar Cvetkovski	STSM	Grant letter sent	Modelling of binding affinity of siderophores with redox Fe3+/Fe2+ system as a potential new class of anti-parasitic drugs	1163.00	
Rodrigue Keumoe	STSM	🛛 Grant letter sent	Imaging of Fe2+ gradients as a ferroptosis marker in malaria parasites	1200.00	
Şener Çintesun	STSM	Grant letter sent	Investigation of the bifunctional enzyme dihydrofolate reductase-thymidylate synthase (DHFR-TS) from Leishmania major	3400.00	



OXFORD meeting participants

- 43 overall
- 7 speakers





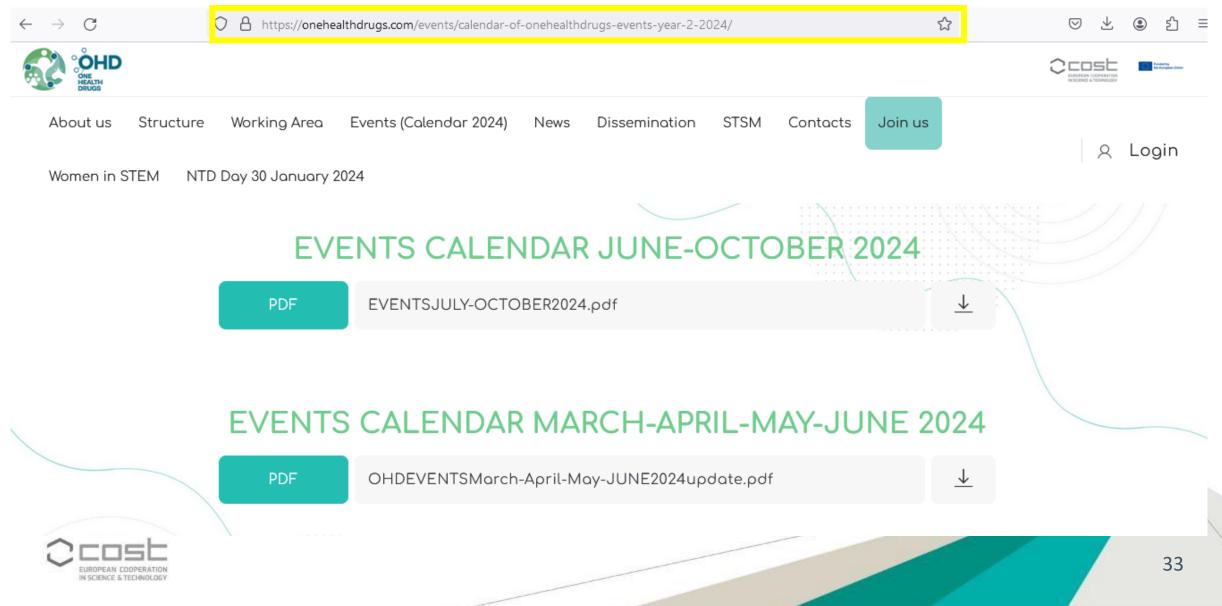
Porto meeting 15-16 May

16 participants supported





CALENDAR of the planned events for 2nd Working Period



What next?

- Survey technologies
- Survey medicinal chemistry programs

Important: how to integrate One Health aspects in my medicinal chemistry/drug development project?



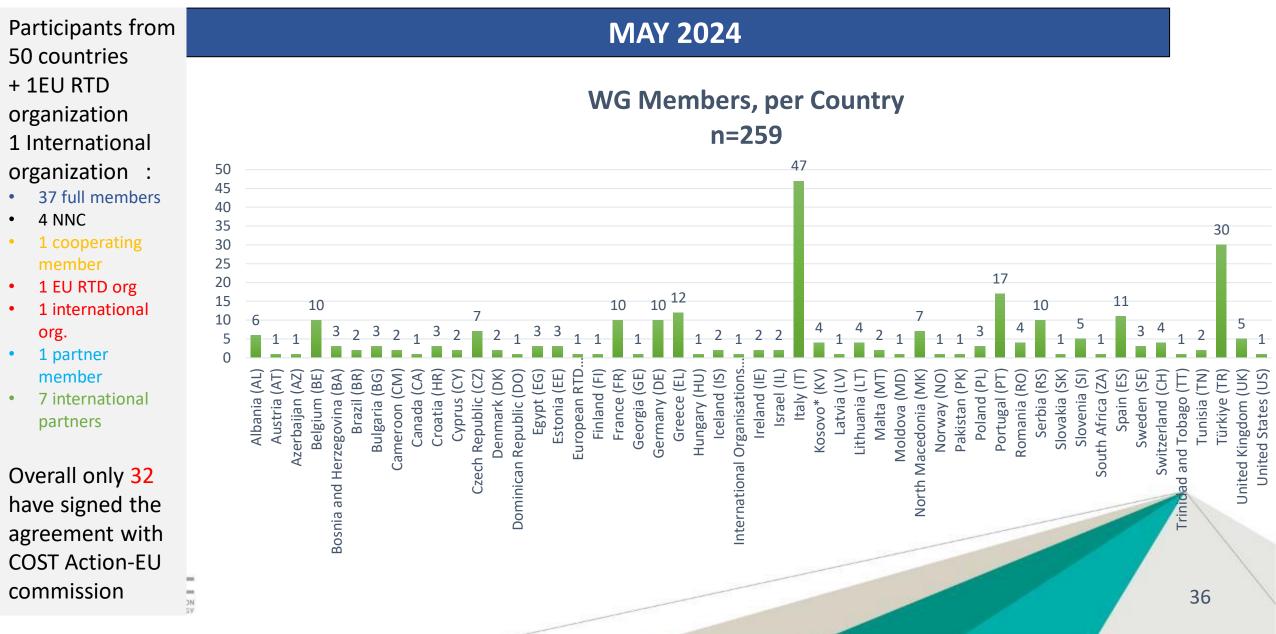


Stakeholder interaction





Action WG Members



Participating COST countries

NNC/IPC institutions and

Specific Organisations

May 2024 (signed MoU)				
Albania	• Israel			
Bosnia-Herzegovina	• Italy			
• Belgium	• Latvia			
• Bulgaria	Lithuania			
Croatia	North Macedonia			
Cyprus	Norway Malta			
Czech Republic	Poland			
Denmark	Portugal			
Estonia	Romania			
Finland	Serbia			
France	Slovenia			
Georgia	Slovakia			
Germany	• Spain			
Greece	Sweden			
• Iceland	Switzerland			
	• Turkey			
	United Kingdom			

Country	at Proposal	Signed MoU May2024
Member Countries	23	33
NNC	2	1
Cooperating Country	1	1
International Countries	5	
EU RTD Organization	1	
Total (ITC)	32 (17)	32 (20)

- COST Member Countries
- Inclusiveness Target Countries
- Cooperating Member Country
- Near Neighboring Countries

