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Supplementary information

Tres Cantos Open Lab: celebrating a decade of innovation in collaboration to combat endemic infectious diseases

In the format provided by the authors

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Acronyms

CALIBR, California Institute for Biomedical Research; CIC BIOGUNE, acronym in Spanish for Centre for Cooperative Research in BioSciences; CONICET, acronym in Spanish for National Council for Science and Technology; CRESIB, acronym in Catalan for Barcelona Centre for International Health Research; CSIC, acronym in Spanish for National Council for Scientific Research; HTS, high-throughput screening; IBR, acronym in Spanish for Institute for Molecular and Cellular Biology, Rosario; INSERM, acronym in French for French National Institute of Health and Medical Research; LSHTM, London School of Hygiene and Tropical Medicine.

1. **List of targets explored in the Open Lab**

PROJECT ID / PARTNER	TARGET / PATHWAY	REF
TC001 CICBIOGUNE	*P. falciparum* Ubiquitylation system	1,2
TC002 Durham University	*L. donovani* inositol phosphorylceramide synthase, *Ld*IPC	3
TC004 Cornell University	HTS in replicating/non-replicating Mycobacteria	48-50
TC006 Imperial College London	*P. falciparum* calcium-dependent protein Kinase 1,4 and 5, *Pf*CDPK1, *Pf*CDPK4 and *Pf*CDPK5	51
TC007 Northeastern & CSIC	Kinase inhibitors for kinetoplastids	5,6
TC027 Seattle Biomedical Research Institute	*M. tuberculosis* dihydrofolate reductase, *Mtb*DHFR	9
TC044 University of Minnesota	*M. tuberculosis* biotin protein ligase, *Mtb*BirA	51
TC050 University of Glasgow	*T. brucei* cyclic adenosine monophosphate, *Tbc*AMP	51
TC053 University of Georgia	Development of anti-*T. cruzi* drugs targeting fatty acid utilization	51
TC054 McGill University & Edinburgh University	Targeting the trypanosome editosome for drug discovery	51
TC109 Harvard T. H. Chan School for Public Health	*P. falciparum* dihydroorotate dehydrogenase, *Pf*DHODH	15
TC112 Cornell University	*M. tuberculosis* membrane protein Large 3, *Mtb*MmpL3	16
TC125 University of Leicester	*P. falciparum* Cyclin-dependent-like protein Kinase 3, *Pf*CLK3	18
TC130 University of Birmingham	*M. tuberculosis* aspartyl-tRNA synthetase, *MtbAspRS*	51
TC131& TC189 Harvard Medical School	*M. tuberculosis* ClpC1P1P2 system	19

TC132 University of San Pablo CEU	Use of metabolomics to determine modes of action of novel anti-leishmanial compounds	20, 21
TC149 University of Washington	*P. falciparum* N-myristoyltransferase, *Pf*NMT	23
TC162 Dundee University	*M. tuberculosis* enoyl acyl carrier protein reductase, *MtbInhA*	27
TC167 LSHTM	*Plasmodium* cyclic GMP-dependent protein kinase, *PfPKG*	33
TC185 Oxford University	*P. falciparum* Elongation factor 2, *Pf*Ef2	51
TC185 Oxford University	*P. falciparum* SET1, *PfSET1*	51
TC206 University of Birmingham	*M. tuberculosis* membrane protein Large 3, *Mtb*MmpL3	51
TC236 University of Melbourne	*P. falciparum* proteasome system	42
TC261 CONICET	*T. cruzi* bromodomain 2, *Tc*BRD2	active
TC261 CONICET	*T. cruzi* bromodomain 5, *Tc*BRD5	active
TC262 University of Zaragoza	*M. tuberculosis* virulence-regulator *Mtb*PhoP	active
TC266 Sanger Institute	*P. falciparum* liver stages target ID	active
TC273 Dundee University	*S. flexneri* UDP-3-O-acyl-N-acetylglucosamine deacetylase, *Sf*LpxC	active
TC279 Durham U University	Deconvoluting the mode of action of a suite of novel anti-leishmania and anti-*T. cruzi*	active
TC292 University of California, San Diego	*P. falciparum* GCN5, *Pf*GCN5	active
TC292 University of California, San Diego	*P. falciparum* leucine tRNA-synthetase, *Pf*LRS	active
TC292 University of California, San Diego	*P. falciparum* prolyl tRNA-synthetase, *Pf*PRS	active

2. Impact from published programs to date (June 2021)

2a. Screening programs

PROJECT ID / PARTNER	TARGET/ PATHWAY	PROJECT OUTPUT	REF.
TC001 CICBIOGUNE	*P. falciparum* ubiquitylation	Analysis of the interconnection between *Plasmodium* and human red blood cells ubiquitin-regulated proteins in the context of infection. A number of human and *Plasmodium* proteins whose ubiquitylation pattern changes during the asexual infective stage were identified.	1,2
TC002 Durham University	*L. donovani* inositol phosphorylceramide (IPC) synthase	Yeast-based HTS to identify selective inhibitors of *L*dIPC synthase. Identification of the benzazepanes as a new class of antileishmanial compounds with a new mode of action.	3
TC004 Cornell University	HTS in replicating/non-replicating Mycobacteria	Identification of novel, nontoxic scaffolds that target metabolically diverse subpopulations of Mycobacterium tuberculosis (Mtb)	48-50
TC007 Northeastern University & CSIC	*T. brucei* phenotypic screening	Phenotypic screening of a collection kinase inhibitors to identify novel inhibitors of *T. brucei* growth. 797 sub-micromolar inhibitors with at least 100-fold selectivity over HepG2 cells were identified. 242 of these hit compounds acted rapidly in inhibiting cellular growth, 137 showed rapid cidality. Further triage allowed the identification of the most promising chemical series.	5,6
TC008 New York University	*T. cruzi* Phenotypic screening	HTS (1.8 m compounds) to identify inhibitors of *T. cruzi*. 'Chagas box' has been shared with more than 70 groups in the field	7
TC027 Center for Infectious Disease Research	*M. tuberculosis* Dihydrofolate reductase (DHFR)	Identification and characterization of novel *Mtb*DHFR inhibitors though an *in vivo* screening of a curated focused library of 2508 potential antifolates	9
TC109 Harvard T. H. Chan School of Public Health	*P. falciparum* di-hydroorotate dehydrogenase (DHODH)	HTS to identify specific inhibitors of *Pf*DHODH resistant mutants. Extensive cross-resistance profiling was performed allowing to identify compound pairs demonstrating the potential for mutually incompatible resistance. These combinations represent promising starting points for exploiting collateral sensitivity (existence to one compound confers hypersensitivity to another) to extend the useful lifespan of new antimalarial therapeutics	15
TC112 Cornell University	*M. tuberculosis* MmpL3	Development of a cell-based assay that utilizes a two-way regulation of *Mtb*MmpL3 expression to identify *Mtb*MmpL3-specific inhibitors. The assay was validated with the identification of a novel guanidine-based MmpL3 inhibitor from a library of 220 compounds that inhibit growth of *Mtb* by largely unknown mechanisms	16
TC125 University of Leicester	*P. falciparum* cyclin-dependent–like (CLK) protein kinase 3	The screening of a focused library identified a probe molecule that selectively inhibited *Pf*CLK3 and killed *Pf* blood-stages. This tool compound was the basis of the validation of the *Pf*CLK3 as a multistage cross-species malarial drug target	18

TC131 & TC189 Harvard Medical School	*M. tuberculosis* ClpC1P1P2 system	Development of an assay based on the ATP-dependent degradation of a fluorescent protein substrate to identify new inhibitors of the *Mtb* ClpC1P1P2 system. The hits obtained were further characterized with a set of secondary assays. A large library of compounds was screened and led to the identification of a ClpC1 ATPase inhibitor demonstrating that this approach can be used in future searches for anti-TB agents	19
TC144 University of British Columbia	Combinations for Mtb treatment	Synergetic antibiotics partners for Ripamicin. Cephalosporins were identified as the most promising group of drugs	22
TC149 University of Washington	*Plasmodium* N-myristoyl-transferase (NMT)	Screening of 1.8m compounds against *Plasmodium vivax* NMT. Hits were triaged based on potency, physicochemical properties, activity in *P. falciparum* NMTs and selectivity over human NMT1 and NMT2. Data obtained revealed insights into the activity of a collection of selective inhibitors of *Plasmodium* NMT which serve as a starting points for subsequent medicinal chemistry efforts.	23
TC162 University of Dundee	*M. tuberculosis* InhA	Identification of novel InhA fragment hits using STD-NMR screening, as well as orthogonal InhA biochemical and SPR assays. Results published provide support for the rational design, synthesis and screening of novel diverse fragments with built in functional groups. The described InhA Fragment based-leads showed good InhA enzymatic activity as well as ligand efficiency metrics	27
TC167 LSHTM	*Plasmodium* cyclic GMP-dependent protein kinase (PKG)	HTS using recombinant *P. falciparum* PKG. Promising compounds were then tested for activity against *P. falciparum* asexual blood stage growth, selectivity and cytotoxicity. By using a scoring system, the 66 most promising PKG inhibitors (comprising nine clusters and seven singletons) were selected	33
TC181 CALIBR	*T. cruzi* and *L. donovani* phenotypic screening	Whole-cell phenotypic assays to screen a set of 150,000 compounds against *L. donovani* and *T. cruzi*, with the objective of finding new starting points to develop novel drugs to effectively treat and control these diseases. The screening campaign, conducted with the purpose of global open access, identified 12 novel chemotypes with low to sub-micromolar activity	36
TC236 University of Melbourne	*Plasmodium falciparum* proteasome system	500,000 compounds were tested for the inhibition of the chymotrypsin-like activity of the P. *falciparum* proteasome using a Proteasome-GLO luminescence assay. Hits were confirmed in an orthogonal enzyme assay using Rho110-labeled peptides, and selectivity was assessed against the human proteasome. Four nonpeptidomimetic chemical families with some selectivity for the *P. falciparum* proteasome were identified and characterized in assays of proteasome trypsin and caspase activities and in parasite growth inhibition assays. Target engagement studies were performed, validating the approach.	42

2b. Medicinal chemistry programs

PROJECT ID / PARTNER	DISEASE	PROJECT OUTPUT	REF.
TC028 Sapienza University	TB	*In vivo* efficacious anti-tubercular 1,3,5-trisubstituted pyrazole that potentially works by inhibiting *Mtb*MmpL3 (SAR analysis published)	10
TC042 University of Liverpool	Malaria	*In vivo* efficacious antimalarial chemical class that potentially works by inhibition of a novel serine protease target (SAR analysis published). Remaining challenge: Improve ADME profile (blood stability)	11
TC045 University of Helsinki	Malaria	*In vivo* efficacious new antimalarial chemotype, N-[3-[(benzimidazol-2-yl)amino]propyl]amides, with promising *in vivo* pharmacokinetics and efficacy, a fast-acting mode of action (comparable to artemisinins), and amenability for optimization from a medicinal chemistry perspective (SAR analysis published). Remaining challenge: Improve safety profile (Cardiotoxicity)	12
TC113 University of Sydney	TB	*In vivo* efficacious antitubercular chemical class (spirocyclic core) with good pharmacokinetic properties (SAR published). Remaining challenge: Improve safety profile (several risks identified)	17
TC149 University of Washington	Malaria	Understanding of molecular selectivity of *Plasmodium* NMT inhibitors versus the human ortholog, enabling rational design of new inhibitors	23
TC150 Monash University	Trypan-osome-mediated diseases	Identification of a broad-spectrum novel chemical class [N-(2-(2-phenylthiazol-4-yl)ethyl)amides] of trypanocides with *in vivo* activity. Remaining challenge: Improve ADME profile (avoid CYP51 inhibition)	24
TC152 University of Halle	TB	Identification of a promising Wollamide B analog as antitubercular agents (SAR analysis published). Remaining challenge: Improve ADME profile (metabolic stability)	25, 26
TC164 Northeastern University	Human African trypano-somiasis	Lead repositioning approach identified benzoxazepinoindazoles as potential therapeutic opportunity for human African trypanosomiasis. The lead compound showed efficacy in a systemic *T. brucei* infection model but not in a CNS model. Remaining challenge: Ability to clear parasitaemia in a CNS model of the disease	28, 29, 30, 31
TC188 University of British Columbia	TB	SAR analysis of 2-(thioalkyl)benzoxazoles as antitubercular agents (SAR analysis published). Remaining challenge: Identification of an *in vivo* active analogue with an optimal developability profile	37
TC217 LSHTM	Malaria	Optimization of a *Plasmodium* GMP-dependent protein kinase (PKG) inhibitor scaffold, leading to the identification of novel (PKG/SRPK2 inhibitor) chemical entities with very potent, similar to artemisinins, fast-killing potency against asexual and sexual stages of the parasite (SAR analysis published). Remaining challenge: Identification of an *in vivo* active analogue with an optimal developability profile	40
TC232 Utrecht University	Gut Health	Identification of potent inhibitors of the Shiga toxin.	41
TC247 University of Georgia and BIOASTER	Trypanoso me mediated diseases	*In vivo* efficacious acylaminobenzothiazole analog with antitrypanosomal replication activity (SAR published) independent to CYP51. Remaining challenge: Improve *in vivo* efficacy	47

2c. Platform development programs

PROJECT ID / TARGET	DISEASE	PROJECT OUTPUT	REF.
TC001 CICBIOGUNE	Malaria	Procedure that combines Percoll and sorbitol treatments, the use of magnetic columns, and the optimization of the *in vitro* culture conditions to reach high parasitaemia levels (up to 40% at any intra-erythrocytic stage) for synchronized Plasmodium falciparum cultures. High parasitaemia levels are obtained only one day after magnetic column purification without compromising the parasite viability and synchrony.	1,2
TC003 CRESIB	Malaria	Demonstration that CD34+hHSCs from peripheral blood and bone narrow CD34+ human haematopoietic stem cells are permissive *to P. vivax* and *P. falciparum* infection	4
TC055 University of British Columbia	TB	Development and validation of an intracellular HTS assay for finding new antituberculosis compounds active in human macrophages. The assay consists of a luciferase-based primary identification assay, followed by a green fluorescent protein-based secondary profiling assay. Standard tuberculosis drugs and 158 previously recognized active antimycobacterial compounds were used to evaluate assay robustness.	14
TC132 University of San Pablo CEU	Leishmaniasis	Validation of Metabolomics as a tool to rationally select hits for Drug Optimization programs considering the effects of drugs in real biological or clinical settings. It has been shown that compounds with different chemical structure and physicochemical properties can disturb the same metabolic pathways, while others with more similar structures can have different downstream effects. Validated with the screening of 28 compounds.	20, 21
TC178 University Autónoma Madrid/University of Leon	Leishmaniasis	Development of a red-shifted luminescent *Leishmania infantum* strain that enables long-term monitoring of parasite burden in individual animals with an *in vivo* limit of detection of 106 intracellular amastigotes 48 h post-infection. The emission of light from the target organs demonstrated the sequential parasite colonization of liver, spleen and bone marrow. When miltefosine was used as proof-of-concept, spleen weight parasite burden and bioluminescence values decreased significantly.	34
TC180 INSERM	Malaria	Development of an HTS platform to determine splenic retention of parasitized erythorcytes. The team developed a 384-well microsphiltration microplates coupled to dual, morpho-metabolic imaging readouts, enabling the screening of large chemical collections for the discovery of compounds that stiffen *Plasmodium falciparum* gametocytes, with the aim of interrupting malaria transmission.	35

TC216 University of Birmingham	TB	Using *M. tuberculosis* H37Rv augmented with anhydrotetracycline-inducible expression of mCherry, a phenotypic screen was developed for the identification of protein synthesis inhibitors in a medium throughput screening format. The assay was validated using known inhibitors of protein synthesis to show a dose-dependent reduction in mCherry fluorescence.	39
TC241 Oxford University	TB	Cysteine-selective fluorogenic probes enable the fluorescence-based screening of inhibitors of LdtMt2, a transpeptidase antibiotic target in *M. tuberculosis*. The assay, which is amenable to HTS, demonstrates the efficacy of the penem and carbapenem classes of β-lactam antibiotics	43
TC246 University of Washington	Shigellosis	Development of robust *in vitro* and *in vivo* tools to study antibiotic efficacy against *Shigella flexneri*. A novel bioluminescent *S. flexneri* strain (S. flexneri lux1) was generated, which can be used in a mammalian epithelial cell co-culture assay to evaluate antibiotic intracellular and extracellular efficacy. In addition, the *S. flexneri* lux1 strain was used with an intraperitoneal murine model of shigellosis to test the efficacy of ciprofloxacin and ampicillin. Both antibiotics significantly reduced the observed radiance from the gastrointestinal tissue of infected mice compared to vehicle control. Compared to traditional methods, these models can be utilized for efficient screening of novel antibiotics aiding in the discovery of new treatments against shigellosis.	44

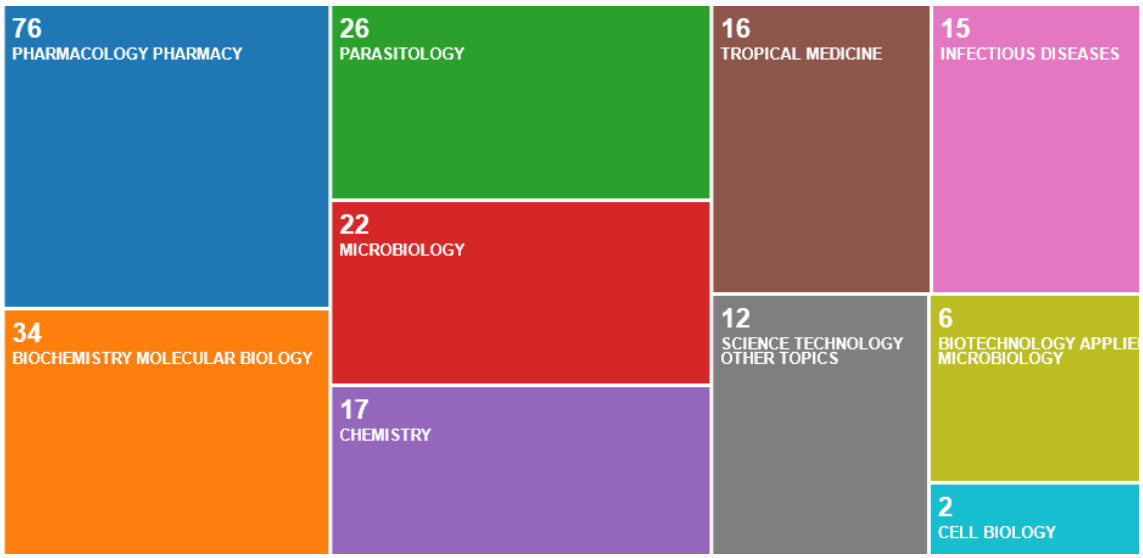
3. Impact of kinetoboxes on Trypanosome research

Reference 7: Peña, Imanol et al. "New compound sets identified from high throughput phenotypic screening against three kinetoplastid parasites: an open resource." *Scientific reports* vol. 5 8771. 5 Mar. 2015, doi:10.1038/srep08771

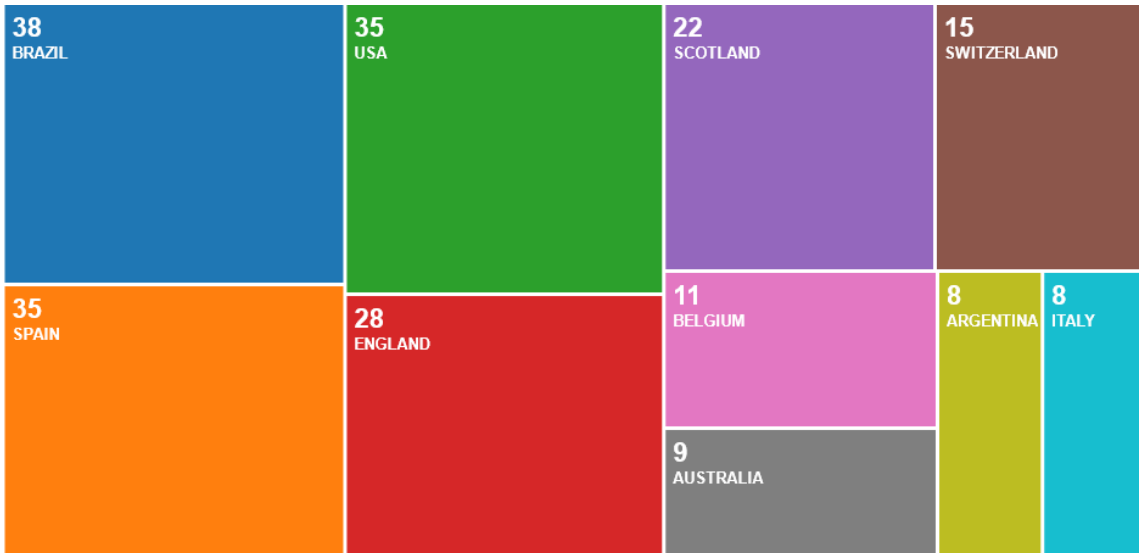
Analysis of papers citing this phenotypic screening campaign against *T. brucei, T. cruzi* and *L. infantum* reveals that the publication had the following impacts:

- Stimulated further improvements in phenotypic screening methodologies and stimulated screening of additional compound collections from other sources
- Facilitated the use of kinetoboxes in novel target-based screens
- Provided novel start points for medicinal chemistry hit-to-lead efforts in academia
- Identified potential targets (kinases, proteases, etc) for further discovery efforts
- Resulted in certain compound series and targets being de-prioritised

In agreement with the above comments, Web of Science (5th July 2021) identified 143 citations associated with the following discipline areas:



A breakdown of citations by country shows the global impact of this publication. The UK is the top citer (50 if Scotland and England are combined), closely followed by Brazil, Spain and the USA.



4. What our partners say about their Open Lab experience

4a. Quotes from Principal Investigators

"We learned a lot about hepatocyte quality and how that impacts assay performance, but most importantly we performed the first larger scale screens in our lab. This suggested to us that the assay is actually suitable for larger scale screens, and not only for single compound testing as we did before"

Dr. Clemens H.M. Kocken, PhD
Principal Investigator for TC237 "Optimization of hepatocyte culture to support drug screening for malaria hypnozoites"

Chairman Department of Parasitology at the Biomedical Primate Research Centre (BPRC), Rijswijk, The Netherlands

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"The funding enabled the largest yeast-based, target directed screen to date. The outcomes were a suite of compounds that remain under investigation at Durham. Furthermore, the success of this work facilitated, in part, several grant funding bids. Most notably the MRC GCRF Global Network for NTDs (MR/P027989/1), which has transformed the approach developed world laboratory scientists take by engaging fully with researchers in LMICs. The legacy of this on the research community is expected to be significant."

Professor Paul Denny, PhD
Principal Investigator for TC002 "IPCS-kinetoplastid target"

Professor in the Department of Biosciences, Durham University, UK

"Cross interaction with the GSK team helped my research focus and better integrate with current TB drug discovery campaigns. Without the Open Lab support my research would be much slower. I will probably miss some of the opportunities provided by the open lab team"

Professor Yossef Av-Gay, PhD
Principal Investigator for TC005 "HTS for new small molecules enabling eradication of M tuberculosis inside infected macrophages"

University of British Columbia, Infectious Diseases, Life Sciences Institute, Canada

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"The work builds our reputation in studies of the plasmodium proteasome as a drug target"

Professor Leann Tilley, PhD
Principal Investigator for TC236 "High throughput screening to identify selective proteasome inhibitors as new antimalarials with a novel mode of action"

Department of Biochemistry and Molecular Biology, Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne, Victoria, Australia

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"TCOLF provided critical support to initiate research in a new area for our lab (shigellosis). Without this support, it would have been very difficult for our lab to make this transition"

Professor Wesley C. Van Voorhis, MD, PhD
Principal Investigator for TC246, "PK/PD modelling for anti-Shigella drug candidates"

Professor, Allergy and Infectious Diseases, Director, Center for Emerging and Re-emerging Infectious Diseases (CERID), University of Washington, USA

"The biggest impact has been the securing of nearly a decade of NIH funding to support the follow-on work, and the subsequent papers that we have published. Many dozens of people have worked on this follow-up work, at multiple institutions"

Professor Michael Pollastri
Principal Investigator for TC007 "mTOR/PI3K inhibitors for kinetoplastids"

Senior Vice Provost for Portland and Academic Lead for the Roux Institute at Northeastern University, Boston, Massachusetts, USA

"Very positive impact, it helped us markedly upgrade the red blood cell filtering method as well as our expertise in the culture of malaria parasites (sexual stages) and our understanding of drug development in general"

Professor Pierre Buffet, MD, PhD
Principal Investigator of TC180 "BlockBackMalaria- Block rings and gametocytes in the spleen to block Malaria"

INSERM, U945, Paris, France, Université Pierre et Marie Curie-Paris6, UMR S945, Paris, France, AP-HP, Groupe hospitalier Pitié-Salpêtrière, Service Parasitologie-Mycologie, Paris, France

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"We probably would not have entered into the field of antimalarial drug discovery, instead we would have continued our research focused to antibacterial drug discovery"

Professor Jari Yli-Kauhaluoma, PhD
Principal Investigator of TC045, "Identifying benzimidazole-derived leads against P falciparum"

Professor, Vice Dean for Research, Faculty of Pharmacy, Biocenter Viikki, Drug Research Program, Division of Pharmaceutical Chemistry and Technology, University of Helsinki, Finland

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"*Networking with lasting substantial effects, accessibility of data, mutual stimulation of Open Lab researchers and guests"*

Professor Peter Imming, PhD
Principal Investigator of TC152 "Turning small potent antimycobacterial cyclo(depsi)peptides into drug-like scaffolds"

Head of the Department of Pharmaceutical/Medicinal Chemistry and Clinical Pharmacy, Martin-Luther-Universität Halle-Wittenberg, Halle (Saale), Germany

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"It has accelerated this area into a new era. The identification of new antimicrobials is often overlooked, and we have made it in trend again". "None of this work would have happened and we would have not been able to generate new interest in new generation antimicrobials. This is an excellent scheme allowing researchers from all over the world access to great people and facilities to conduct new research"

Professor Stephen Baker, PhD
Principal Investigator of TC239 "Hit discovery for new antimicrobials against Shigella spp".

The Department of Medicine, CITIID, The University of Cambridge, Box 157, Hills Road, Cambridge, UK

"We would not have been able to undertake this project"

Professor Roland J. Pieters, PhD
Principal Investigator of TC232 "Attacking Shigella by blocking its disease-causing Toxin"

Department of Chemical Biology & Drug Discovery, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, The Netherlands

"The development of a new method for rapid and robust HTS for anti TB drugs can certainly improve drug discovery in the field", "It would have been impossible to carry out several of the experiments proposed in the project at the home institution"

Professor Mariana Piuri, PhD
Principal Investigator of TC194 "Reporter mycobacteriophages for full-scale activity testing of antitubercular compounds"

Assistant Professor, University of Buenos Aires, Adjunct Investigator CONICET, Argentina

"It provided means to test a hypothesis and evaluate a potential drug target", "We would not have been able to screen for inhibitors. While a potent inhibitor was not identified, we learned a lot in the process"

Professor Sabine Ehrt, PhD
Principal Investigator of TC156 Studies towards the identification of orally available I-lactams with efficacy against *Mycobacterium tuberculosis.*

Professor of Microbiology and Immunology, Microbiology and Immunology , Weill Cornell Medical College, USA

"Our TCOLF project was instrumental for establishing target/pathway-directed screens in my lab"

Professor Dirk Schnappinger, PhD
Principal Investigator of TC112 "Whole-cell assays for the identification and classification of Mtb growth inhibitors"

Professor of Microbiology and Immunology, Microbiology and Immunology , Weill Cornell Medical College, USA

"This project allowed to perform the first High Throughput Screening for the parasite Trypanosoma cruzi that causes Chagas disease. Selected compounds were included in the 'Chagas box' that was shared with investigators in the field"

Professor Ana Rodriguez, PhD
Principal Investigator of TC008 "Identification of hits for T cruzi"

Professor at New York University School of Medicine, Dept. of Microbiology, USA

"The TCOLF project was a wonderful experience, we learned a lot and it provided outstanding training to the visiting scientist from my lab"

Professor Courtney Aldrich, PhD
Principal Investigator of TC044 "Antitubercular BirA inhibitors"

Professor, Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, USA

"We never could have made a such compound screening without the TCOLF support"

Esteban Serra, PhD
Principal Investigator of TC261 "Trypanosoma cruzi bromodomains: druggable readers to look out!"

Instituto de Biología Molecular y Celular de Rosario (IBR), Consejo Nacional de Investigaciones Científicas y Técnicas, Rosario, Argentina

'OL funding may have increased my success with subsequent funding applications to e.g. the Wellcome Trust as having the OL funding increases our credibility somewhat both in translational research and seeking fundamental research support. This is because the funder can see that you have a translational goal to your more basic research projects.'

Professor David Baker, PhD
Principal Investigator of TC217 "Optimization of imidazopyridine and thiazole scaffolds targeting plasmodial kinases to generate a fast killing compound to treat malaria infection and block transmission"

Professor of Malaria Parasite Biology, Faculty of Infectious and Tropical Diseases, Department of Infection Biology, LSHTM

4b. Quotes Open Lab fellows

"TCOLF projects are unique as it's one of the major programs that bring vastly different interest groups together. This opportunity was fundamental to developing my understanding of the process from both an industrial and academic perspective and an exercise in knowledge and tech transfer. When on-site, we were exposed to experts from several fields of science including chemistry, biochemistry, pharmacology, animal care in addition to biology fostering a highly collaborative environment critical for an early career researcher"

Shipra Grover
Open Lab Fellow of TC112 "Whole-cell assays for the identification and classification of Mtb growth inhibitors"

Current position: Research Associate in Microbiology and Immunology, Cornell University

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"Working with the team from Tres Cantos help me tremendously to understand better the early stage of drug discovery."

Jürgen Brem
Open Lab Fellow of TC241 "Structural biology and assays enabling β-lactams that target Mycobacteria tuberculosis"

Current position: Project leader – Oxford University

"I've had chance to work with a professional research group and approached many new technologies. It helped me know the difference of research between industrial and academic field. There are a lot of things that I can apply in my workplace that improve efficacy at work"

Voong Vinh Phat
Open Lab Fellow of TC239 "Hit discovery for new antimicrobials against Shigella spp."

Current position: Senior Research Assistant at Wellcome Trust Major Overseas Programme, Oxford University Clinical Research Unit, The Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam

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"I have found my long-term contract thanks to the TCOLF experience. I have learned a lot during my contract at GSK"
"Indeed, after my thesis and my studies I was consider as an organic chemist but after this work I was consider as a medicinal chemist. So, its help me a lot for my career in pharmaceutical company."

Charlotte Tabey-Fleau
Open Lab Fellow of TC247 "Chagas AABLO (Chagas AcylAminoBenzothiazol Lead Optimization)"

Current position: Researcher in Medicinal Chemistry at Inventiva Pharma

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"It has given me new skills, especially related to project planning, knowledge of the functions of different drug discovery departments, research strategy and alliances"

Bjorn Sunde
Open Lab Fellow of TC193 "Self-poisoning of Mycobacterium tuberculosis by inhibiting siderophore secretion"

"It has been a huge impact since it gave me the opportunity to relate with a big company environment and work in a more structured way. I really enjoyed the facilities and the cross-functional team work to enhance the research and I started loving to work in a company"

Martina Cocozza
Open Lab Fellow of TC028 "Hit to Lead development for a new class of antimycobacterial agents"

Current position: Medical Affairs Manager in AbbVie

"It has allowed me to progress in my career. I would not have had my current job if I had not got the OL Fellow funding"

Open Lab Fellow, anonymous

"The experience obtained from the TCOLF project provided me an insight into the workings of scientific research in the pharmaceutical industry. The working environment I experienced during this project has allowed me to transition smoothly to my current position". "The knowledge and experience gained during my TCOLF experience, in particular pertaining to drug discovery, has helped me to contribute effectively to my new position"

Andrew Lim
Open Lab Fellow of TC239 "Hit discovery for new antimicrobials against Shigella spp."

Current position: Research Associate, The ALBORADA Drug Discovery Institute, University of Cambridge

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"As a researcher, my experience as a TCOLF Fellow showed me the drug development process from a holistic point of view; being able to interact with all the stakeholders involved without leaving the building".
"It also taught me how research is done in industry (as opposed to academia) as well as the importance of networking; being able to relate with researchers from very different places (relationships that I currently still hold)"

Mariano Tilve
Open Lab Fellow of TC053 Development of anti-T cruzi drugs targeting fatty acid utilization

Current position: Project Manager at an R&D focused Pharmaceutical Company

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"The impact was very positive and definitely opened some new opportunities after that experience. I learnt a lot from the experienced team and the research that was being carried out was very inspiring"

Jessica Baiget Gonçalves
Open Lab Fellow of TC113 "An Open Source Hit-to-Lead campaign in Tuberculosis drug discovery"

Current position: Medicinal chemist in a Pharmaceutical Company

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"The TCOLF project increased experience in private pharma industry", "Excellent and successful professional experience. Really grateful"

Julien Duez
Open Lab Fellow of TC180 "BlockBackMalaria" – Block rings and gametocytes in the spleen to block Malaria

Current position: Project manager tebu-bio

"The TCOLF project has had a great impact on my professional career. Thanks to this experience I had the opportunity to network with peers, create scientific relationships and learn the job from experts in multidisciplinary fields. Ultimately, this experience also enriched my CV and made it more attractive to recruiters"

Federica Patri
Open Lab Fellow of TC162 "Tuberculosis focused fragment-based drug discovery"
Current position: Senior Medicinal Chemistry Scientist at Angelini Pharma

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"Our research approach and strategies are heavily influenced by the norms and standards employed at GSK and this has helped us in conducting quality research, leading to the training of post-graduate students and publication of articles at journals with good impact factor"
"A number of research collaborations have been established with a number of groups, and the experience from TCOLF has helped us identify relevant and good partners"

Winston Nxumalo
Open Lab Fellow of TC005 "Pool for Open Innovation against Neglected Tropical Diseases"

Current position: Associate Professor at the University of Limpopo, South Africa

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"The TCOLF was instrumental in helping me to shape my career focus in Medicinal Chemistry. Basically, TCOLF was the basis for me to start my independent academic career"

David Khanye
Open Lab Fellow of TC005 "Pool for Open Innovation against Neglected Tropical Diseases"

Current position: Associate Professor at Faculty of Pharmacy, Rhodes University, South Africa

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"The project allowed me to work at the interface of academia and industry for the first time and to expand my understanding on the industry way-of-thinking".
"It was an educational experience regarding collaboration between different organizations and sharing the project-relevant expertise has been useful in both directions".
"The position allowed me to start working at EMBL Heidelberg, where I am now continuing in another postdoctoral project."

Milka Hammarén
Open Lab Fellow of TC255 "Unravelling new combinatorial therapies against Shigellosis"

Current position: Postdoctoral research fellow at EMBL, Heidelberg

4. Full list of references to date

1. Mata-Cantero, Lydia et al. “Magnetic isolation of Plasmodium falciparum schizonts iRBCs to generate a high parasitaemia and synchronized *in vitro* culture.” *Malaria journal* vol. 13 112. 21 Mar. 2014, doi:10.1186/1475-2875-13-112
2. Mata-Cantero, Lydia et al. “New insights into host-parasite ubiquitin proteome dynamics in P. falciparum infected red blood cells using a TUBEs-MS approach.” *Journal of proteomics* vol. 139 (2016): 45-59. doi:10.1016/j.jprot.2016.03.004
3. Norcliffe, Jennifer L et al. “Identifying inhibitors of the Leishmania inositol phosphorylceramide synthase with antiprotozoal activity using a yeast-based assay and ultra-high throughput screening platform.” *Scientific reports* vol. 8,1 3938. 2 Mar. 2018, doi:10.1038/s41598-018-22063-9
4. Fernandez-Becerra, Carmen et al. “Red blood cells derived from peripheral blood and bone marrow CD34$^+$ human haematopoietic stem cells are permissive to Plasmodium parasites infection.” *Memorias do Instituto Oswaldo Cruz* vol. 108,6 (2013): 801-3. doi:10.1590/0074-0276108062013019
5. Diaz, Rosario et al. “Identification and characterization of hundreds of potent and selective inhibitors of Trypanosoma brucei growth from a kinase-targeted library screening campaign.” *PLoS neglected tropical diseases* vol. 8,10 e3253. 23 Oct. 2014, doi:10.1371/journal.pntd.0003253
6. Amata, Emanuele et al. “Identification of "Preferred" Human Kinase Inhibitors for Sleeping Sickness Lead Discovery. Are Some Kinases Better than Others for Inhibitor Repurposing?.” *ACS infectious diseases* vol. 2,3 (2016): 180-186. doi:10.1021/acsinfecdis.5b00136
7. Peña, Imanol et al. “New compound sets identified from high throughput phenotypic screening against three kinetoplastid parasites: an open resource.” *Scientific reports* vol. 5 8771. 5 Mar. 2015, doi:10.1038/srep08771
8. Alonso-Padilla, Julio et al. “Automated high-content assay for compounds selectively toxic to Trypanosoma cruzi in a myoblastic cell line.” *PLoS neglected tropical diseases* vol. 9,1 e0003493. 23 Jan. 2015, doi:10.1371/journal.pntd.0003493
9. Kumar, Anuradha et al. “A Focused Screen Identifies Antifolates with Activity on Mycobacterium tuberculosis.” *ACS infectious diseases* vol. 1,12 (2015): 604-14. doi:10.1021/acsinfecdis.5b00063
10. Poce, Giovanna et al. “Novel Pyrazole-Containing Compounds Active against *Mycobacterium tuberculosis*.” *ACS medicinal chemistry letters* vol. 10,10 1423-1429. 18 Sep. 2019, doi:10.1021/acsmedchemlett.9b00204
11. McConville, Matthew et al. “Carbamoyl Triazoles, Known Serine Protease Inhibitors, Are a Potent New Class of Antimalarials.” *Journal of medicinal chemistry* vol. 58,16 (2015): 6448-55. doi:10.1021/acs.jmedchem.5b00434
12. Keurulainen, Leena et al. “A Developability-Focused Optimization Approach Allows Identification of *in vivo* Fast-Acting Antimalarials: N-[3-[(Benzimidazol-2-yl)amino]propyl]amides.” *Journal of medicinal chemistry* vol. 58,11 (2015): 4573-80. doi:10.1021/acs.jmedchem.5b00114
13. Tegazzini, Diana et al. “A Replicative *In vitro* Assay for Drug Discovery against Leishmania donovani.” *Antimicrobial agents and chemotherapy* vol. 60,6 3524-32. 23 May. 2016, doi:10.1128/AAC.01781-15
14. Sorrentino, Flavia et al. “Development of an Intracellular Screen for New Compounds Able To Inhibit Mycobacterium tuberculosis Growth in Human Macrophages.” *Antimicrobial agents and chemotherapy* vol. 60,1 640-5. 26 Oct. 2015, doi:10.1128/AAC.01920-15
15. Ross, Leila Saxby et al. “Identification of Collateral Sensitivity to Dihydroorotate Dehydrogenase Inhibitors in Plasmodium falciparum.” *ACS infectious diseases* vol. 4,4 (2018): 508-515. doi:10.1021/acsinfecdis.7b00217

16. Grover, Shipra et al. “Two-Way Regulation of MmpL3 Expression Identifies and Validates Inhibitors of MmpL3 Function in *Mycobacterium tuberculosis*.” *ACS infectious diseases* vol. 7,1 (2021): 141-152. doi:10.1021/acsinfecdis.0c00675
17. Guardia, Ana et al. “Easy-To-Synthesize Spirocyclic Compounds Possess Remarkable *in vivo* Activity against Mycobacterium tuberculosis.” *Journal of medicinal chemistry* vol. 61,24 (2018): 11327-11340. doi:10.1021/acs.jmedchem.8b01533
18. Alam, Mahmood M et al. “Validation of the protein kinase *Pf*CLK3 as a multistage cross-species malarial drug target.” *Science* vol. 365, 6456 (2019): eaau1682. doi:10.1126/science.aau1682
19. Fraga, Hugo et al. “Development of high throughput screening methods for inhibitors of ClpC1P1P2 from Mycobacteria tuberculosis.” *Analytical biochemistry* vol. 567 (2019): 30-37. doi:10.1016/j.ab.2018.12.004
20. Armitage, Emily G et al. “Metabolic Clustering Analysis as a Strategy for Compound Selection in the Drug Discovery Pipeline for Leishmaniasis.” *ACS chemical biology* vol. 13,5 (2018): 1361-1369. doi:10.1021/acschembio.8b00204
21. Armitage, Emily G et al. “Complex Interplay between Sphingolipid and Sterol Metabolism Revealed by Perturbations to the Leishmania Metabolome Caused by Miltefosine.” *Antimicrobial agents and chemotherapy* vol. 62,5 e02095-17. 26 Apr. 2018, doi:10.1128/AAC.02095-17
22. Ramón-García, Santiago et al. “Repurposing clinically approved cephalosporins for tuberculosis therapy.” *Scientific reports* vol. 6 34293. 28 Sep. 2016, doi:10.1038/srep34293
23. Harupa, Anke et al. “Identification of Selective Inhibitors of *Plasmodium* N-Myristoyltransferase by High-Throughput Screening.” *Journal of medicinal chemistry* vol. 63,2 (2020): 591-600. doi:10.1021/acs.jmedchem.9b01343
24. Russell, Stephanie et al. “Hit-to-Lead Optimization of a Novel Class of Potent, Broad-Spectrum Trypanosomacides.” *Journal of medicinal chemistry* vol. 59,21 (2016): 9686-9720. doi:10.1021/acs.jmedchem.6b00442
25. Asfaw, Henok et al. “Design, synthesis and structure-activity relationship study of wollamide B; a new potential anti TB agent.” *PloS one* vol. 12,4 e0176088. 19 Apr. 2017, doi:10.1371/journal.pone.0176088
26. Asfaw, Henok et al. “An efficient synthetic route for preparation of antimycobacterial wollamides and evaluation of their *in vitro* and *in vivo* efficacy.” *Bioorganic & medicinal chemistry letters* vol. 28,17 (2018): 2899-2905. doi:10.1016/j.bmcl.2018.07.021
27. Prati, Federica et al. “Screening of a Novel Fragment Library with Functional Complexity against Mycobacterium tuberculosis InhA.” *ChemMedChem* vol. 13,7 (2018): 672-677. doi:10.1002/cmdc.201700774
28. Klug, Dana M et al. “Hit-to-Lead Optimization of Benzoxazepinoindazoles As Human African Trypanosomiasis Therapeutics.” *Journal of medicinal chemistry* vol. 63,5 (2020): 2527-2546. doi:10.1021/acs.jmedchem.9b01506
29. Tear, Westley F et al. “Selectivity and Physicochemical Optimization of Repurposed Pyrazolo[1,5-*b*]pyridazines for the Treatment of Human African Trypanosomiasis.” *Journal of medicinal chemistry* vol. 63,2 (2020): 756-783. doi:10.1021/acs.jmedchem.9b01741
30. Singh, Baljinder et al. “Medicinal Chemistry Optimization of a Diaminopurine Chemotype: Toward a Lead for *Trypanosoma brucei* Inhibitors.” *Journal of medicinal chemistry* vol. 63,17 (2020): 9912-9927. doi:10.1021/acs.jmedchem.0c01017
31. Klug, Dana M et al. “Structure-property studies of an imidazoquinoline chemotype with antitrypanosomal activity.” *RSC medicinal chemistry* vol. 11,8 950-959. 10 Jul. 2020, doi:10.1039/d0md00103a
32. Singh, Baljinder et al. “Medicinal Chemistry Optimization of a Diaminopurine Chemotype: Toward a Lead for *Trypanosoma brucei* Inhibitors.” *Journal of medicinal chemistry* vol. 63,17 (2020): 9912-9927. doi:10.1021/acs.jmedchem.0c01017
33. Penzo, Maria et al. “High-throughput screening of the Plasmodium falciparum cGMP-dependent protein kinase identified a thiazole scaffold which kills erythrocytic and sexual stage parasites.” *Scientific reports* vol. 9,1 7005. 7 May. 2019, doi:10.1038/s41598-019-42801-x

34. Álvarez-Velilla, Raquel et al. “A chronic bioluminescent model of experimental visceral leishmaniasis for accelerating drug discovery.” *PLoS neglected tropical diseases* vol. 13,2 e0007133. 14 Feb. 2019, doi:10.1371/journal.pntd.0007133
35. Duez, Julien et al. “High-throughput microsphiltration to assess red blood cell deformability and screen for malaria transmission-blocking drugs.” *Nature protocols* vol. 13,6 (2018): 1362-1376. doi:10.1038/nprot.2018.035
36. Roquero, Irene et al. “Novel chemical starting points for drug discovery in leishmaniasis and Chagas disease.” *International journal for parasitology. Drugs and drug resistance* vol. 10 (2019): 58-68. doi:10.1016/j.ijpddr.2019.05.002
37. Moure, Abraham L et al. “MymA Bioactivated Thioalkylbenzoxazole Prodrug Family Active against *Mycobacterium tuberculosis*.” *Journal of medicinal chemistry* vol. 63,9 (2020): 4732-4748. doi:10.1021/acs.jmedchem.0c00003
38. Fraga, Hugo et al. “Development of high throughput screening methods for inhibitors of ClpC1P1P2 from Mycobacteria tuberculosis.” *Analytical biochemistry* vol. 567 (2019): 30-37. doi:10.1016/j.ab.2018.12.004
39. Burke, Christopher et al. “Development of a novel secondary phenotypic screen to identify hits within the mycobacterial protein synthesis pipeline.” *FASEB bioAdvances* vol. 2,10 600-612. 20 Aug. 2020, doi:10.1096/fba.2020-00022
40. Matralis, Alexios N et al. “Development of Chemical Entities Endowed with Potent Fast-Killing Properties against *Plasmodium falciparum* Malaria Parasites.” *Journal of medicinal chemistry* vol. 62,20 (2019): 9217-9235. doi:10.1021/acs.jmedchem.9b01099
41. Haksar, Diksha et al. “Fighting *Shigella* by Blocking Its Disease-Causing Toxin.” *Journal of medicinal chemistry* vol. 64,9 (2021): 6059-6069. oi:10.1021/acs.jmedchem.1c00152
42. Mata-Cantero, Lydia et al. “High Throughput Screening to Identify Selective and Nonpeptidomimetic Proteasome Inhibitors As Antimalarials.” *ACS infectious diseases* vol. 7,6 (2021): 1818-1832. doi:10.1021/acsinfecdis.1c00110
43. de Munnik, Mariska et al. “A Fluorescence-Based Assay for Screening β-Lactams Targeting the Mycobacterium tuberculosis Transpeptidase Ldt_{Mt2}.” *Chembiochem : a European journal of chemical biology* vol. 21,3 (2020): 368-372. doi:10.1002/cbic.201900379
44. McCloskey, Molly C et al. “Evaluation of *in vitro* and *in vivo* antibiotic efficacy against a novel bioluminescent Shigella flexneri.” *Scientific reports* vol. 9,1 13567. 19 Sep. 2019, doi:10.1038/s41598-019-49729-2
45. Arnold, Samuel L M. “Target Product Profile and Development Path for Shigellosis Treatment with Antibacterials.” *ACS infectious diseases* vol. 7,5 (2021): 948-958. doi:10.1021/acsinfecdis.0c00889
46. Hulverson, Matthew A et al. “Repurposing Infectious Disease Hits as Anti-*Cryptosporidium* Leads.” *ACS infectious diseases* vol. 7,5 (2021): 1275-1282. doi:10.1021/acsinfecdis.1c00076
47. Fleau, Charlotte et al. “Chagas Disease Drug Discovery: Multiparametric Lead Optimization against *Trypanosoma cruzi* in Acylaminobenzothiazole Series.” *Journal of medicinal chemistry* vol. 62,22 (2019): 10362-10375. doi:10.1021/acs.jmedchem.9b01429
48. Warrier, Thulasi et al. “Identification of Novel Anti-mycobacterial Compounds by Screening a Pharmaceutical Small-Molecule Library against Nonreplicating *Mycobacterium tuberculosis”* *ACS Infect. Dis.* Vol. 1, 12 (2015): 580–585
49. Warrier, Thulasi et al.” *N*-methylation of a bactericidal compound as a resistance mechanism in *Mycobacterium tuberculosis”* Proc Natl Acad Sci U S A. 2016 Aug 2;113(31):E4523-30. doi: 10.1073/pnas.1606590113
50. Lopez Quezada, Landys et al. “Dual-Pharmacophore Pyrithione-Containing Cephalosporins Kill Both Replicating and Nonreplicating *Mycobacterium tuberculosis”*. ACS Infect Dis. 2019 Aug 9;5(8):1433-1445. doi: 10.1021/acsinfecdis.9b00112.
51. Unpublished data, contact info@openlabfoundation.org for details

5. Full list of projects (completed and active) – June 2021

PROJECT ID	Project Title	PARTNER	Disease
Completed			
TC001	Ubiquitylation profile of Pf and Mtb infected cells	CICBioGUNE	Malaria
TC002	IPCS-kinetoplastid target	Durham univ	Leishmaniasis
TC003	*In vitro* culture for P vivax	CRESIB	Malaria
TC004	HTS in replicating/non-replicating Mycobacteria	Weill Medical College of Cornell University	TB
TC005	Scientists to Drug Discov Chem	iThemba	TB
TC006	CDPKs (screening of TCAMS)	ICL - Imperial College London	Malaria
TC007	mTOR/PI3K inhibitors for kinetoplastids	NEU/CSIC	Sleeping sickness
TC008	Identification of hits for T cruzi	NYU	Chagas
TC027	Identification of potent and specific inhibitors of Mtb DHFR	CIDR - formerly Seattle Biomedical Research Institute	TB
TC028	Hit to Lead development for a new class of antimycobacterial agents	Sapienza, Univ of Roma	TB
TC029	A metabolomic approach to decipher Mtb permeability	Weill Medical College of Cornell University	TB
TC030	Identification of Mtb Leucyl-tRNA synthetase inhibitors	Omnia Molecular	TB
TC042	TCAMS triazole series as potential serine protease inhibitors	University of Liverpool	Malaria

TC044	Antitubercular BirA inhibitors	University of Minnesota	TB
TC045	Identifying benzimidazole-derived leads against P falciparum	University of Helsinki	Malaria
TC046	Assay development of *in vivo* rate of killing of intracellular Leishmania and T. cruzi spp by standard and novel chemical entities	LSHTM	Leishmaniasis
TC048	Identification of inhibitors of M tuberculosis topoisomerase I for novel anti-TB therapy	Florida International Univ	TB
TC049	Optimization of a class of oxadiazole compounds target	Institute Pasteur Korea	TB
TC050	Modulation of trypanosomal cAMP signalling for sleeping sickness therapeutic discovery	University of Glasgow/Marine Biological Lab/ NEU	Sleeping sickness
TC053	Development of anti-T cruzi drugs targeting fatty acid utilization	University of Georgia	Chagas
TC054	Targeting the trypanosome editosome for drug discovery	McGill Univ/Edinburgh Univ	Sleeping sickness
TC055	HTS for new small molecules enabling eradication of M tuberculosis inside infected macrophages	University of British Columbia	TB
TC096	New Medicines for TB through Rifamycin semisynthesis	TeagueMedChem	TB
TC109	Identifying and developing partner drugs for pyrimidine biosynthesis inhibitors that supress the development of resistance in Pf	Harvard School for Public Health	Malaria
TC111	Development of a liver stage mouse model for Plasmodium falciparum	SUNY Upstate Medical University	Malaria
TC112	Whole-cell assays for the identification and classification of Mtb growth inhibitors	Weill Medical College of Cornell University	TB

TC113	An Open Source Hit-to-Lead campaign in Tuberculosis drug discovery	University of Sydney	TB
TC125	Screening of PfCLK	University of Leicester / MRC	Malaria
TC130	Hit-to-lead optimisation of a small-molecule inhibitor targeting the M. tuberculosis aspartyl-tRNAAsp synthetases	University of Birmingham	TB
TC131	Screen for small molecule inhibitors and activators of Clp degradation system from Mtb	Harvard Medical School	TB
TC132	Use of metabolomics to determine modes of action of novel anti-leishmanial compounds	University San Pablo CEU / University of Glasgow	Leishmaniasis
TC134	Reversal of Artemisinin Resistance by means of Chemical Genetics	Mahidol University	Malaria
TC135	Development of a platform dedicated to translate the transmission blocking (TB) efficacy of anti-P. falciparum drugs to P. vivax	Caucaseco Scientific Research Center (CSRC)	Malaria
TC144	The development of synergistic combinations of rifampicin and cephalosporins against Mycobacterium tuberculosis	University of British Columbia	TB
TC149	Identification of small-molecule inhibitors of Plasmodium N-myristoyltransferase	Seattle BioMed	Malaria
TC150	Hit to Lead Optimization for kinetoplastid diseases: single agents for Chagas and HAT	Monash University	Chagas
TC152	Turning small potent antimycobacterial cyclo(depsi)peptides into drug-like scaffolds	U. of Halle	TB
TC156	Studies towards the identification of orally available I-lactams with efficacy against Mycobacterium tuberculosis	Weill Medical College of Cornell University	TB
TC162	Tuberculosis focused fragment-based drug discovery	Dundee	TB
TC164	T. brucei drug discovery: ADMET and PK support for hit-to-lead optimization	NEU/CSIC	Sleeping sickness
TC167	Screening and identification of inhibitors of the Plasmodium falciparum cGMP-dependent	LSHTM	Malaria

	protein kinase (PfPKG) as novel antimalarial drugs		
TC178	Small-molecule screening against Visceral Leishmaniasis using ex-vivo splenic explant cultures	UAM/UL	Leishmaniasis
TC180	“BlockBackMalaria” - Block rings and gametocytes in the spleen to block Malaria	INSERM	Malaria
TC181	Phenotypic screening to identify small molecule inhibitors of Visceral Leishmaniasis and Chagas disease	Calibr	Leishmaniasis
TC185	Identification of small molecule inhibitors targeting plasmodium methyltransferase SET1 and elongation factor 2	University of Oxford - Structural Genomics Consortium	Malaria
TC188	Intra-macrophage driven optimization of confirmed hit GSK421197A	University of British Columbia	TB
TC189	Biochemical and Structural Characterization of Mtb ClpC1P1P2 and ClpXP1P2 inhibitors - first step towards new TB therapeutics (CPPI)	Harvard Medical School & Institut de Biologie Structurale - IBS	TB
TC192	Optimisation of Fidaxomicin analogs	Birmingham University (initially Swiss Federal Institute of Technology in Zürich - ETHZ)	TB
TC193	Self-poisoning of Mycobacterium tuberculosis by inhibiting siderophore secretion	University of Alabama at Birmingham	TB
TC194	Reporter mycobacteriophages for full-scale activity testing of antitubercular compounds	IQUIBICEN, Univ. of Buenos Aires	TB
TC197	Mode of action and target identification of anti-Chagasic compounds	LSHTM	Chagas
TC206	ChemPro_Target_ID - A Chemical Proteomics Approach to Confirm – or Otherwise – the Results of Whole-Genome Sequencing of Spontaneous Resistant Mutants Generated Against Hits from a Phenotypic Screening Campaign: Is MmpL3 Really the Target for Such a Diverse Range of Structures?	University of Birmingham	TB
TC214	Exploring TB Space: Optimization of novel, high quality phenotypic hits (EXPTBS)	University of Birmingham	TB

TC215	Rapid selection of *in vivo* active anti-Trypanosoma cruzi compounds	University of Georgia	Chagas
TC216	Whole cell protein synthesis inhibition assay for high-throughput drug discovery	University of Birmingham + Texas A&M University	TB
TC217	Optimization of imidazopyridine and thiazole scaffolds targeting plasmodial kinases to generate a fast killing compound to treat malaria infection and block transmission	LSHTM	Malaria
TC232	Attacking Shigella by blocking its disease causing Toxin	Utrecht University	Gut Health
TC236	High throughput screening to identify selective proteasome inhibitors as new antimalarials with a novel mode of action.	University of Melbourne	Malaria
TC237	Optimization of hepatocyte culture to support drug screening for malaria hypnozoites	Biomedical Primate Research Centre	Malaria
TC239	Hit discovery for new antimicrobials against Shigella spp.	Oxford University Clinical Research Unit	Gut Health
TC241	Structural biology and assays enabling β-lactams that target Mycobacteria tuberculosis	Oxford University	TB
TC246	PK/PD modeling for anti-Shigella drug candidates	University of Washington	Gut Health
TC247	Chagas AABLO (Chagas AcylAminoBenzothiazol Lead Optimization)	University of Georgia + Bioaster	Chagas
TC249	Targeting Virulence Regulators as a Novel Approach to Antibiotics for Shigellosis	University of Michigan	Gut Health
TC255	Unravelling new combinatorial therapies against Shigellosis	EMBL	Gut Health
TC256	Predicting optimal dosing schedules and clinical outcomes of beta-lactams for TB therapy using PKPD and mechanistic models Carbapenem vs. cephem: the beta-lactam paradigm	Research and Development Agency of Aragon (ARAID) Foundation, Spain	TB
Active			
TC257	High throughput small molecule screen for drugs that alter the shape of Campylobacter jejuni	University of Cambridge	Gut Health
TC261	*T. cruzi* bromodomains: druggable readers to look out!	IBR-CONICET_UNR Instituto de Biología Molecular y Celular de Rosario	Chagas

TC262	TB antivirulence therapeutics: small molecule inhibitors against M. tuberculosis replication and persistence pathways as novel alternatives to classic antibiotics.	University of Zaragoza	TB
TC263	Synthesis of Kalihinol Analogues with Improved Pharmacokinetic and Pharmacodynamic Profiles	University of California, Irvine	Malaria
TC264	High Throughput Screening for Inhibitors of Shigella Virulence Determinants	University of Washington	Gut Health
TC266	A chemogenomic overexpression screen to identify malaria liver stage targets	Sanger Institute	Malaria
TC267	Antimalarial drug discovery targeting pre-erythrocytic stages of Plasmodium falciparum	University of South Florida (USF), WRAIR and NIH	Malaria
TC269	Generation, characterization and *in vivo* evaluation of a novel live malaria vaccine	IMM Lisboa	Malaria
TC273	Design of novel inhibitors of Shigella LpxC	University Dundee	Gut Health
TC275	Microbiome modulators for the treatment of environmental enteric dysfunction (EED) and associated stunted childhood growth	University Tubingen	Gut Health
TC277	recapitulation of ATQ infection results using TCOL mosquitoes/parasites/facilities	Harvard T.H. Chan School of Public Health	Malaria
TC279	Deconvoluting the mode of action of a suite of novel antimanials-GCFR	Global Network for Neglected Tropical Diseases	Chagas
TC281	Shortening and improving compliance to Buruli ulcer therapy- Four weeks daily triple betalactam	Research and Development Agency of Aragon (ARAID) Foundation, Spain	Mycobacterial infection
TC283	Tebipenem-pivoxil as an alternative to ceftriaxone for clinically non-responding children with shigellosis	International Centre for Diarrhoeal Disease Research	Gut Health

TC285	Optimisation of a screen for antimicrobials that enhance pyrazinamide activity against Mycobacterium tuberculosis	Public Health England	TB
TC287	Evaluation of P450 humanized mouse model (8HUM) as a tool to assess the impact of drug combinations on pharmacology	University of Dundee	TB
TC288	Designing optimal regimes for tuberculosis therapy using one-step high content dynamic *in vitro* kill kinetic assay linked to hollow fiber studies	Research and Development Agency of Aragon (ARAID) Foundation, Spain	TB
TC290	DnaJ-DnaK-GrpE complex as a selective drug target in Mycobacterium tuberculosis	Rhodes University	TB
TC292	Malaria Lead Discovery Engine : A Fast track approach to identify novel antimalarial chemical classes with multi-stage activity	University of California, San Diego	Malaria
TC295	Addressing drug resistance in chemo prophylaxis	Harvard T.H. Chan School of Public Health	Malaria
TC297	Studies on Nucleophilic Cysteine Enzymes Involved in Bacterial Cell Wall Biosynthesis- iCASE	Oxford University	TB
TC298	Development of a Drug Discovery Platform Targeting Salmonella Typhimurium Persister Cells	University of Dundee	Gut Health