

Terms of reference

Final evaluation of project 6063: Antibiotic Discovery

1. Introduction

Background on funding partner

Fondation Botnar is a Swiss-based foundation established in 2003 whose purpose is to improve the health and wellbeing of children and young people in growing secondary cities around the world. We do this by investing in sustainable solutions, and by connecting and catalysing the work of diverse partners. At Fondation Botnar, we are committed to cultivating and nurturing learning both within and outside of the organization so as to effectively contribute to the change we want to see.

Background on implementing partner (“grantee”)

The project team built on established research networks within the University of Cambridge to focus on developing novel therapies for *M. abscessus* and *P. aeruginosa* through an innovative multi-disciplinary strategy delivered by an enlarged network of internationally-renowned scientists with a successful record of collaborative working:

Professor Andres Floto (Department of Medicine) and Professor Julian Parkhill (Wellcome Sanger Institute & Department of Veterinary Medicine) experts in molecular microbiology and bacterial genomics; Professor Sir Tom Blundell (Department of Biochemistry) and Professor Chris Abell (Department of Chemistry; now sadly deceased) pioneers in fragment-based drug discovery and founders of Astex.

Project description

Bacterial infections collectively cause over 40% of deaths in children under 5 years old around the world. Worryingly, the increasing failure of existing antibiotics will result in an estimated additional 10 million deaths in children and adults through drug-resistant infections by 2050. There is therefore an urgent unmet clinical need to develop new antibiotics for bacterial infections; a challenge that industry has been slow or unwilling to address.

The project team’s aim was to overcome the three major barriers to developing effective new antibiotics by:

- Rationalising target selection through forward and reverse genetic screening;
- Optimising chemical inhibition of targets through structure-guided fragment-based drug discovery (FBDD); and
- Preventing the emergence of drug resistance through defining mechanisms of antibiotic resistance and tolerance by combining computational proteomics with functional genomic analysis.

The team has chosen to focus on developing new antibiotics for children with Cystic Fibrosis (CF) although these will clearly also benefit other children with multi-drug resistant infections.

CF affects over 10,000 children and adults in the UK and results in defective ion and water handling by epithelial cells caused by deleterious mutations in the CF Transmembrane Regulator (CFTR) gene. Most importantly, dysfunctional CFTR impairs muco-ciliary clearance in the lungs and leads to chronic respiratory bacterial infections, which drive progressive inflammatory lung damage and, ultimately, lead to death. The principal therapeutic challenge in managing children with CF is to minimise lung function decline over time through effective antibiotic treatment of acute infective exacerbations and through preventing chronic bacterial infections. Conversely, respiratory morbidity and mortality in CF can be viewed as direct consequences of antibiotic failure resulting from progressive development or person-to-person acquisition of drug-resistant bacteria. The two most devastating infections for CF children are *Pseudomonas aeruginosa*, which eventually chronically infects 40% of individuals, and *Mycobacterium abscessus* (currently infecting 5-20% of CF cohorts globally, predominantly children⁴). These bacteria result in accelerated inflammatory lung damage and death.

The project's aim was to develop new antibiotics for *M. abscessus* and *P. aeruginosa* through:

- Applying forward and reverse genetic screening to discover optimal drug targets;
- Using existing and novel applications of Fragment-based Drug Discovery (FBDD) to develop and then chemically elaborate new drug-like molecules with antibacterial properties;
- Defining mechanisms of antibiotic resistance and tolerance, by combining computational proteomics with functional bacterial genomics, to inform drug development.

Project duration and funding

Fondation Botnar supported the project from 4 September 2017 to 31 March 2021 with a grant of GBP 1,829,853. The initial grant duration was up to September 2020; due to the implications of the COVID-19 pandemic, a budget-neutral half-year extension was granted by the foundation.

2. Evaluation objectives and questions

Final evaluations of Fondation Botnar grants serve to document the project and its outcomes in a form that is accessible to readers beyond its scientific community, as as to...

- meet Fondation Botnar’s accountability and knowledge management requirements, and
- support the grantee in preparing for and taking subsequent steps to further develop their research and its ultimate impact on the lives of children and young persons in low- and middle-income countries. For instance, the evaluation report or other products of the evaluation may be used in project communication and fundraising activities.

The scientific quality of the research undertaken by grantees has been reviewed by external experts in the specific field of each project. Therefore, the evaluation is not expected to assess the scientific merit of the project, or to replicate research undertaken by the project.

Evaluation questions

1. What is the place and relevance of the project in the field of antibiotic discovery?
2. What have been the outcomes of the project?
 - Which successes or promising results have been attained so far? What are the most important insights the project has generated?
 - To what extent can these research results be generalised?
 - What difference has the grant by Fondation Botnar made?
3. Which challenges were met in the course of the project – including challenges linked to the COVID-19 pandemic – and how did the grantee manage the challenges, to what effects?
4. How can its research **inform policies and practice** to improve young people’s well-being in low income countries? What steps have been undertaken, what else can be done (including questions on other actors to be involved)?

During the inception phase, the evaluation team can review and develop additional evaluation questions as necessary, in consultation with Fondation Botnar and the implementing partner.

3. Methodology

Fondation Botnar is open to a wide range of evaluation approaches and methods. Regardless of the approach chosen by the evaluation team, the evaluators are expected to foster participation at key moments of the evaluation, seeking the grantee’s advice and support (i) during the inception phase, when crafting the evaluation instruments, (ii) during the data analysis phase, and (iii) in developing recommendations.

More specifically, the external evaluator or evaluation team is expected to work in partnership with the grantee and the project lead at Fondation Botnar so as to maximise the transparency and utility of the evaluation process and products. The contracting evaluator is expected to collaborate closely with the grantee to:

- In the inception phase, reach a shared understanding of the evaluation objectives and questions with Fondation Botnar and project leadership, and develop the evaluation methodology accordingly
- unpack or develop the theory of change that is expected to lead from the project to future ('downstream') impact
- consult with the project team to boost both the validity of findings and the relevance of results and recommendations, taking into account the grantee's communication needs
- facilitate a validation workshop or consultation (online) so as to discuss initial findings and recommendations with the project team and Fondation Botnar.

As a rule, methods and perspectives should be triangulated in all evaluations. The evaluator or evaluation team is required to document the evaluation process and – if applicable – provide lessons learnt and recommendations for final evaluations of Fondation Botnar projects.

4. Evaluation logistics

Scope and field visits

The evaluation is expected to take place between September and October 2021. A budget of up to CHF 50.000 is foreseen.

Ideally, face-to-face contact with the project team should be part of the evaluation process. However, if restrictions and risks linked to the COVID-19 pandemic preclude travelling, the evaluation team can work via the phone and online platforms, such as videoconference and visual collaboration tools.

Ethical considerations

The evaluator is expected to comply with evaluation standards, including ethics, throughout the evaluation process, as set out in the OECD/DAC Quality Standards for Development Evaluation (<http://www.oecd.org/dac/evaluation/qualitystandards.pdf>).

Proposed timeline

Evaluation activities will start upon execution of the consultancy contract and conclude no later than 6 December 2021. The Final Report including the respective slide deck should be submitted no later than 30 November 2021.

Work packages/action	Responsible	Time/deadline
Interview with shortlisted candidate/s	Fondation Botnar/Grantee	28 June 2021
Selection of evaluator	Fondation Botnar/Grantee	By early July 2021
Kick-off/inception meeting	Evaluator	Early September 2021
Submission of inception report	Evaluator	Mid-September 2021
Evaluation research and analysis, including validation workshop	Evaluator/Grantee	Mid-September to mid-October 2021
Submission of draft evaluation report	Evaluator	1 November 2021
Feedback on draft evaluation report	Fondation Botnar/Grantee	15 November 2021
Submission of Final Report	Evaluator	30 November 2021

Deliverables

The deliverables expected from the evaluation are as follows:

- Inception meeting or workshop (on-line or hybrid format) with representatives of Fondation Botnar and of the project team
- Inception report of 5-15 pages (plus annexes) including (i) understanding of the evaluation purpose and scope (ii) any proposed adjustments to evaluation objectives and questions, (iii) data collection and analysis plan(s) including draft instruments, (iv) tentative work-plan and schedule for the overall evaluation process, specifying involved stakeholders' roles and moments for communication between the specific stakeholders, (iv) preliminary proposal for the dissemination of findings
- Draft evaluation report of up to 30 pages including a 3-page executive summary and methods documentation package (data collection and analysis instruments as used in the evaluation, and discussion of the evaluation process)
- Presentation and discussion of findings and recommendations in a debriefing workshop
- Final evaluation report accompanied by a brief slide deck summarising the conclusions and recommendations

5. Evaluator requirements

The evaluation or evaluation team is expected to meet the following requirements:

- At least five years of experience in evaluation
- Demonstrated experience in theory-based evaluation or theory of change development
- Excellent written and spoken English
- Experience in conducting interviews, group discussions and workshops via online platforms

Desirable:

- Experience in translating scientific research into texts that are accessible to persons beyond scientific communities
- Knowledge in the field of antibiotics development

References

Applicants are requested to include at least three evaluations or other publications that are broadly representative of the evaluator's or the evaluation team's capability vis-à-vis this call.

6. Expression of interest and deadline

Expression of Interest

The expression of interest should be no longer than **2 pages** consisting of:

- Introduction of the evaluator or evaluation team including relevant experience and skills
- Short proposal of the methodological approach
- Rough day-rate and anticipated overall evaluation budget

An annex can include further documentation such as CVs, reports and publications or other relevant documentation. The 2-pager, however, will be the main basis for decision-making.

Deadline

Interested evaluators are requested to send an expression of interest with the reference "6063 evaluation" in its title by 7 June 2021 at 11 am CET, in pdf format to m.raab@posteo.de cc. dsuhr@fondationbotnar.org, grants@fondationbotnar.org