

Research Sub-Award Agreement

This Research Sub-Award Funding Agreement (the “Agreement”) is made effective as of DATE (“Effective Date”)

Between:

Unity Health Toronto, at
its St. Michael’s Site
with offices at 30 Bond Street
Toronto, ON, M5B 1W8
Canada (“UHT”)

AND

Oswaldo Cruz Foundation (FIOCRUZ) a public entity created and maintained by the Brazilian Federal Union in the form of Law No. 5,019, of 07/06/1966, modified by Decree No. 66,624, of 05/22/1970; with statute approved by Decree No. 4,725 of 06/09/2003, member of the Indirect Federal Public Administration and linked to the Ministry of Health, by determination of Law No. 7,596 of 04/10,1987, and Decree No. 2,477, of 01/28/1998, registered under CNPJ No. 33,781,055/0001-35, with headquarters located at Avenida Brasil 4365, Manguinhos, Rio de Janeiro, RJ, Zip Code 21045-900, Brazil, CNPJ 33.781.055/0001-35, through its unit INSTITUTO OSWALDO CRUZ, in this act represented by its Director, TANIA CREMONINI DE ARAUJO JORGE, found at the address indicated above, appointed by the Ordinance of the Executive Secretariat of the Ministry of Health No. 3.426, published in the DOU, Issue No. 232, Section No. 02, on December 10, 2021
 (“FIOCRUZ”)

AND

FUNDAÇÃO PARA O DESENVOLVIMENTO CIENTÍFICO E TECNOLÓGICO EM SAÚDE (FIOTEC), a non-profit private foundation created to provide administrative support to the functions of teaching, research, institutional, scientific and technological development, production of inputs and services, information and management implemented by FIOCRUZ, as described in its Statute drawn up according to the determinations of Law no. 8.958/1994, regulated by Decree no. 7.423/2010.

(“FIOTEC”)

Known collectively as the parties and individually as a party

WHEREAS the details of this Agreement are as follows:

UHT #23-0279-SUB

UHT Principal Investigator: Dr. Claudia dos Santos

University Investigator: Dr. Tatiana Maron-Gutierrez

Project Title: The role of therapeutic nanoparticles containing microRNAs in mitigating cecum ligation and puncture (CLP)-induced Sepsis (the “Study”)

Funder: Pitts Chair

Funder Award Number: 2021-2026 (Activity 21383-27001)

Period of Collaboration: 8 months from last signature (“Effective Date”) (together the “Term”)

Budget: As per Appendix A

WHEREAS UHT Principal Investigator located at UHT has received an award/grant by the Funder and is prepared to transfer the funds to the University for work on the Study as described in Appendix A (“Funds”).

WHEREAS FIOCRUZ is a governmental foundation under Brazilian law which mission is to produce, disseminate and share knowledge and technologies aimed at the strengthening and consolidation of the Unified Health System (SUS – Brazilian Health System) and contribute to the promotion of health and quality of life of the population.

WHEREAS FIOTEC is a private nonprofit foundation that provides financial and administrative management for projects conducted by the Oswaldo Cruz Foundation (FIOCRUZ). While FIOCRUZ is responsible for the technical and scientific aspects of the projects, FIOTEC is the receiver and administrator of the funds awarded under the agreement in support of the project and thereby responsible for administrative and financial management.

NOW THEREFORE, the parties agree as follows:

1. Funds

Payment Schedule:

University shall submit invoices to UHT according to the Payment Schedule in Appendix A. Invoices will be paid by UHT within forty five (45) days of receipt, providing that the Funds for the Study have been made available to UHT from the Funder.

University is **restricted** from transferring the Funds to a tertiary **institution**.

Invoices should be sent to the attention of the UHT Principal Investigator as per the address in the Notice Section. Each invoice shall clearly state the Study name, UHT contract ID located in the footer on first page this Agreement, description of the work, invoice number, and dated.

The payment shall be used by the University in accordance with the budget (as outlined in Appendix A). Payments will also be subject to UHT and the UHT Principal Investigator's approval and satisfactory progress. All payments will be conditional upon continued support from Funder. If funding is reduced or terminated from Funder, UHT may reduce or terminate its financial obligations under this Agreement accordingly.

UHT accepts no responsibility or obligations for Funds expended in excess of the amounts quoted in the budget or for Funds expended before or after the stated period of collaboration. University shall ensure that prior approval from UHT is obtained before exceeding line item amounts. In no case shall the allowed budget adjustment result in an increase to the total UHT transfer of Funds to the University.

Upon completion of the Study, end of the Period of Collaboration or early termination of this Agreement, any and all unused Funds are to be promptly returned to UHT.

2. Reporting Requirements:

The University will complete and send a Statement of Account (i.e. Tri-Council Form 300) by April 30 of each year to cover the year ending March 31 as well as copies of all supporting documentation and receipts detailing expenditures in the Tri Council Form 300 to the attention of Manager, Research and Trust Accounting, St. Michael's Hospital, Office of Research Administration, 30 Bond Street, Toronto, ON M5B 1W8; research.finance@unityhealth.to. Future payments may be withheld if financial reports are not provided.

The University will ensure that proper and accurate accounts and records, including but not limited to, contracts, invoices, statements, receipts and vouchers, in respect of the Study, and in accordance with requirements under the Tri-Agency Financial Administration Guide if applicable, are kept for at least seven (7) years (https://www.nserccrsng.gc.ca/InterAgency-Interorganismes/TAFA-AFTO/guide-guide_eng.asp).

3. Intellectual Property and Publication

Except as expressly provided herein, nothing in this Agreement shall affect the ownership and rights of intellectual property and/or CONFIDENTIAL INFORMATION owned by each of the PARTIES prior to the effective date of this Agreement, or that arise after the execution of this Agreement independently by either PARTY, and that are not related to the subject matter of this Agreement.

Rights in intellectual property, including data created in performance of the work, if any, will vest in and be held by UHT. UHT shall grant to the University a non-exclusive right to use the intellectual property rights from the Study, free of royalties, whether or not they are patentable, for internal research and teaching purposes.

Each party shall have the right to disseminate the results generated from the Study provided that such dissemination (i) shall not misrepresent the data, results, analyses or conclusions, and (ii) is consistent with academic practice, the rights of any third party publisher, and applicable laws. Any dissemination of the results from the Study shall properly acknowledge the Parties and Funders support; and (iii) UHT makes the first multisite publication to such dissemination of the Study data and results.

4. General Terms and Conditions

A separate account will be set up for the University Investigator, who will direct and supervise the work under this Agreement on behalf of the University.

The University agrees to abide by these terms and conditions and further agrees not to distribute any Funds on behalf of the grantee until all required certifications (i.e. ethics, animal care, biohazards) are on file in its office.

University will allow, upon reasonable written notice and during normal business hours, a representative from UHT and/or Funder access to its premises and records to review, monitor, and/or audit the administration and use of the Funds. The University and University Investigator shall respond fully and accurately to any inquiries the Funder and/or UHT may make for the purpose of verifying adherence to their requirements.

5. Compliance with Legal Requirements

All parties shall conduct the Study and perform their obligations set out in this Agreement in accordance with all applicable laws, government regulations and guidelines, including those pertaining to confidentiality, use and disclosure of patient health information and animal ethics. Without limiting the foregoing, this obligation includes all requirements in each party's respective provincial health information legislation (as applicable) and regulations pursuant thereto.

6. Confidential Information

Confidential Information as used herein is defined as all proprietary, commercial and technical information related to the Study disclosed by the UHT or UHT Principal Investigator to the University or University Investigator in writing and plainly marked "CONFIDENTIAL". If communicated orally, such Confidential Information shall be reduced to writing, marked "confidential" and submitted to the University and/or University Investigator within thirty (30) days of first disclosure.

All obligations of confidence and nonuse created under this Agreement shall terminate five (5) years from the completion or termination of this Agreement.

The obligations of Paragraph 6 herein shall not apply to Confidential Information which:

- a) can be shown by the University or University Investigator to have been in their possession before disclosure by UHT and/or UHT Investigator;

- b) at time of disclosure is, or thereafter becomes, through no fault of the University or University Investigator, part of the public domain by publication or otherwise;
- c) is furnished to the University or University Investigator by a third party;
- d) is developed by the University or University Investigator independently of the disclosure by the UHT or UHT Investigator;
- e) is required by statute or judicial process to be disclosed.
- f) must reasonably be disclosed to regulatory authorities, the REB and/or REBs of participating centers reviewing the Study; or,
- h) is published in accordance with the Agreement; or

The obligations of confidentiality and non-use provided for herein shall continue in full force and effect for a period of 5 years from the later of completion of the Study.

7. Liability

Except as otherwise provided in this Agreement:

- (i) Each party assumes its/his/her own liability for any costs, suits or claims on account of injuries (including death) to persons participating in the Study or damage to property to the extent that such injuries or damage arise out of its/his/her activities in the course of the Study or the activities of those for whom in law it/he/she is responsible; and
- (ii) No party or its trustees, directors, officers, employees and agents (the "first Party") shall be liable to any other party (the "second Party") for any costs, suits or claims made by the second Party or made against the second Party except to the extent caused by the negligence or wilful misconduct of the first Party;
- (iii) No party shall be responsible for any lost profits, lost opportunities, or other indirect or consequential damages suffered by another party.

8. Insurance

UHT agrees to maintain appropriate policies of liability insurance with appropriate limits against any and all foreseeable risks of loss arising out of this Agreement.

FIOCRUZ recognizes that it is liable, within the limits of its obligations for all its acts (action and/or omission) which, by proven intent or fault of its partners, statutory members, agents, employees, servants, providers, etc., may, directly or indirectly or indirectly, cause or cause loss and damage to the other Party, to the research participant and/or third party, due to the non-compliance with the provisions of this Agreement, provided that such non-compliance is not due to acts or omissions of the other Party.

The Parties acknowledge that according to Article 37 Paragraph 6 of the Brazilian Federal Constitution, the FIOCRUZ's Collaborators are exempt from the obligation to have insurance cover because any liability and damage caused will be subject to indemnification by the Brazilian Government.

9. Termination

Notwithstanding the Term of this Agreement, either party may cancel this Agreement (i) without cause by giving the other party not less than thirty (30) days prior written notice;

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or (ii) if the other party materially breaches this Agreement and fails to cure such breach within fifteen (15) days after receipt of written notice thereof from the non-breaching party or Parties.

Upon termination of the Study, UHT's sole obligation shall be to pay a prorated amount for actual work performed in accordance with Appendix A pursuant to the Study. In the event that UHT has overpaid for work actually performed up to the date of the termination of the Study, the University shall refund to UHT, as soon as reasonably practicable but in no event later than thirty (30) days after termination, any amounts already paid by UHT that are in excess of amounts due under this Agreement.

Nothing in this Agreement shall be construed to limit the freedom of individuals participating in this Study, whether paid under this Agreement or not, to engage in similar research independently under other grants, contracts, or agreements with parties other than the above mentioned institutions.

10. Notices

Unless otherwise specified herein, all notices, reports and requests for approvals under this Agreement shall be sent as follows:

For UHT:

Director, Office of Research Administration Unity
Health Toronto, St. Michael's Hospital
Office of Research Administration
30 Bond Street
Toronto, ON M5B 1W8
Email: researchcontracts@unityhealth.to

For UHT Principal Investigator:

Dr. Claudia C dos Santos
St Michael's Hospital
30 Bond Street, Bond Wing room 4-008
Toronto, ON, M5G1W8
Tel: 416-860 6060 ext 3198
Email: Claudia.dossantos@unityhealth.to

For University:

NIT
Aline Morais – Coordinator NIT/IOC
Rua Sizenando Nabuco, 100
Pavilhão Herman Lent - 2° andar - sala 1A
Manguinhos - Rio de Janeiro/RJ
Brasil
CEP.: 21041-250
E-mail: nit@ioc.fiocruz.br

For University Investigator:

Tatiana Maron-Gutierrez, PhD
Pesquisadora Associada em Saúde Pública
Laboratório de Imunofarmacologia
Instituto Oswaldo Cruz, Fiocruz
Av. Brasil, 4365, Pavilhão 108, sala 45
Tel: (21) 2562-1311 | 2562-1332

For FIOTEC:

Fundação para o Desenvolvimento Científico e
Tecnológico em Saúde (FIOTEC)
Avenida Brasil, Manguinhos, 4036
Rio de Janeiro, Brazil 25085-262
Tel/Fax: +1 636 283 0288
internationalprojects@fiotec.fiocruz.br

10. Use of Name

Except as otherwise required by law and for formal routine research activity reports required by governments and funding foundations, or in an investigator's curriculum vitae, neither party shall use the name of the other party or the name(s) of its employee(s) or the investigators in publicity, promotions, news releases, advertising or similar public statements that endorse any products, services or organizations without the prior written consent of the party whose name is proposed to be used.

11. Dispute Resolution

The parties shall attempt in good faith to resolve any dispute arising out of or relating to this Agreement promptly by negotiation between officials or representatives who have authority to settle the controversy and who are at a higher level of management or responsibility than the persons with direct responsibility for administration of this contract. Should this attempt fail to be amicably settled within three (3) months from the notification of the dispute by a Party to the other Party, such dispute shall be submitted to the court of the defendant's domicile having jurisdiction over the subject matter at stake.

12. Assignment

No part of this Agreement may be assigned, delegated or subcontracted by any party to any other person or third party without the prior written approval of the other parties.

13. Independent Contractors

The parties hereto are independent contractors. Nothing contained herein shall be deemed or construed to create between the Parties hereto a partnership or joint venture or employment relationship. No party shall have the authority to act on behalf of any other party, or to commit any other party in any manner or cause whatsoever or to use any other party's name in any way not specifically authorized by this Agreement.

14. Force Majeure

Neither party to this Agreement shall be liable to the other for any failure or delay in performance caused by circumstances beyond its reasonable control, including but not limited to, acts of God, fire, flood, medical emergencies, epidemics, pandemics, quarantine and/or disease, inability to procure necessary supplies or labour, or governmental action the effect of which impact research facilities, research, or research-related activities. Upon the occurrence of a Force Majeure circumstance the affected party shall notify the other party as soon as practicable of becoming aware of such event(s) upon which the parties shall mutually agree on any possible remedial courses of action during the disruption. If after the passage of six (6) months the work is unable to be continued in a manner acceptable to one or the other party acting reasonably, either party may terminate this Agreement in accordance with Article 8.

15. Survival

The terms and provisions contained in this Agreement which require their performance by the parties after the completion or termination of this Agreement shall remain in force notwithstanding such completion or other termination of this Agreement.

16. Severance

In the event that any part, article, clause, paragraph or sub-paragraph of this Agreement shall be held to be indefinite, invalid, illegal or otherwise voidable or unenforceable, the entire agreement shall not fail on account thereof, and the balance of the Agreement shall continue in full force and effect.

17. Amendment

This Agreement may only be amended in writing by all parties.

18. Choice of Law:

This Agreement shall be governed by and construed in accordance with the laws of the Province of Ontario, the laws of Canada and the laws of Brazil applicable therein.

19. Counterparts

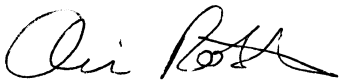
This Agreement may be executed in one (1) or more counterparts, each of which when executed and delivered, shall be deemed to be an original but all of which when taken together shall constitute one (1) and the same Agreement.

[signature page follows]

IN WITNESS WHEREOF the duly authorized officers of the Parties have executed this Agreement effective as of the date of the last signature below.

UNITY HEALTH TORONTO

**Read and acknowledged:
PRINCIPAL INVESTIGATOR**



Signature

Name: Ori Rotstein

Title: VP Research & Innovation

Dec 8, 2023

Date:

DocuSigned by:



B718F97478FE4BC

Signature

Name: Claudia C dos Santos

Date: 08/12/2023

UNIVERSITY

**Read and acknowledged:
UNIVERSITY INVESTIGATOR**

DocuSigned by:



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Signature

Name: Tania Cremonini de Araujo Jorge

Title: IOC Director

Date: 28/11/2023

DocuSigned by:



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Signature

Name: Tatiana Maron-Gutierrez, PhD

Date: 29/11/2023

FIOTEC

DocuSigned by:



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Signature

Name: Cristiane Sendim

Title: Executive Director

Date: 01/12/2023

Appendix A

Project Description: The role of therapeutic nanoparticles containing microRNAs in mitigating cecum ligation and puncture (CLP)-induced Sepsis
Deliverables and Due dates: Deliverables Due March 30th 2024

Payment Schedule:
Two payments of \$12,500 CDN
1st Payment - Immediately after signing the contract;
2nd Payment - December 2023

Detailed budget

University	Amount in Canadian Dollars
PDF salary support	\$ 18,000.00
10-day survival experiment – (mice and reagents)	\$ 2,363.63
Behavioural assessment experiments (14 days)	\$ 2,363.64
Overhead	\$ 2,272.73
TOTAL	\$ 25,000.00

WORK PLAN

1. Project Title

The role of therapeutic nanoparticles containing microRNAs in mitigating cecum-ligation and puncture (CLP)-induced Sepsis

2. Project's goal

The aim of this study is to evaluate the therapeutic potential of lipid nanoparticles (LNP) as a vehicle for the *in vivo* delivery of miRNA-based mimics, on a mouse model of Sepsis-Associated Encephalopathy (SAE). We hypothesize that these treatments will reduce neuroinflammation, improve behavioral alterations, and increase survivability in model mice.

3. Object of the Work Plan

The goal is to evaluate the effects of LNPs containing two miRNA-based mimics, miR-193b-5p and miR187, on behavioural and cognitive damage from SAE. The cecal-ligation and puncture sepsis model will be used. Six hours after CLP surgery animals will receive the treatments intravenously. Then 15 and 30 days after the surgery behavioural and cognitive tests will be performed in order to measure the long-term neurological consequences of SAE. Cognitive tests will include Morris Water Maze, Novel Object Recognition, Y-maze and fear conditioning test. Behavioural tests will include Elevated plus maze, Tail suspension, open field and forced swimming.

4. Background

Sepsis is an exacerbated inflammatory host response against an infection resulting in dysfunction in multiple organs. It is the leading cause of deaths in ICUs in the United States and 20% of all deaths worldwide are linked to sepsis (1). As a multiorgan dysfunction, it does not spare the brain. Sepsis-associated encephalopathies (SAE) are neurological complications which occur during or after sepsis events. They may occur even without direct infection of the central nervous system. The prevalence of SAE varies from 30 to 70% in sepsis-diagnosed patients. SAE is considered a risk factor for mortality and may lead to long-term consequences (2). Among these long-term consequences we can highlight cognitive damage, delirium and mood disorders, such as depression and anxiety (3). Currently, there is no treatment available for SAE-induced neurological damage. Therefore, it is necessary to investigate new therapeutic approaches. Mesenchymal stem cells (MSCs) have a well-established therapeutic potential due to their immunomodulatory capacity and are being tested as a therapy for several conditions, including sepsis. Our group has demonstrated beneficial effects of MSC therapy in reducing neuroinflammation and cognitive damage caused by SAE. Further, conditioned media from MSCs has been shown to reduce astrogliosis in an *in vitro* model, suggesting that MSCs may act in a paracrine way, by releasing mediators (4). Extracellular vesicles (EVs) are lipid bilayer-delimited particles carrying proteins, nucleic acids and lipids. EVs from MSCs (MSC-EVs) are promising candidates for different types of therapy due to their capacity to carry and deliver mediators originated in these cells (5). For example, in a recent report using a model of neonatal ischemic-hypoxia, it was shown that MSC-EV administration reduces neuroinflammation, increases the expression of neural growth factors, and promotes neural cell proliferation (6). Further, the effects of MSC-EVs have in many cases been linked to the transfer of miRNAs to target cells (7). Indeed, results suggest that one of the possible mechanisms by which MSCs exert their protective effects may be through microRNAs (8). However, although MSCs and MSC-EVs administration have been shown to produce beneficial effects such as attenuating inflammation, the mechanism(s) involved, and the contributions of the host immune system to these potentially therapeutic effects, remain elusive.



The Dos Santos Lab, our Canadian collaborators in this project, found in 2021 that treatment with MSCs decreases expression of host-derived microRNA (miR)-193b-5p and increases expression of its target gene, the tight junction protein occludin, in the lungs of septic mice. When administered *in vivo*, MSC conditioned media recapitulated the effects of MSC administration on pulmonary miR-193b-5p and occludin expression, suggesting a paracrine mechanism of action(8). They also showed that other miRNAs are differentially regulated in septic mice after MSC administration, including miR187- which negatively regulates Tumor Necrosis Factor (TNF)- α and Interleukin (IL)-6. Further, they showed in 2020 that MSC administration decreases inflammatory and apoptotic pathways, while increasing cardiac-specific structural and functional gene expression (9), also suggesting that MSC administration regulates host-derived miRNA production to protect cardiomyocytes from sepsis-induced cardiopathy. Considering these previous results, as well as the broader literature, it is reasonable to expect both MSCs and their EVs to modulate miRNAs in the host, likely impacting its response to sepsis. Currently, the Lab has been working on using lipid nanoparticles (LNP) as a vehicle for the *in vivo* delivery of those 2 miRNAs-based mimics, miR-193b-5p and miR187, already shown to have a role to play in both lung and heart injury from sepsis. LNPs are a novel and useful tool (10) for isolating the effects of different cargo found in MSC-EVs. They also hold promise in terms of translatability, as they can be more easily standardized for clinical use.

5. Justification / Relevance of Cooperation

This collaboration is ongoing and will be strengthened by this project. Dr. Santos holds the expertise for producing MSC-EVs and LNPs, and this approach holds promise for treating SAE.

6. Expected results

We expect that LNPs will improve cognitive function and behavioral deficits in CLP model mice.

7. Term

Indicate the period of execution of the project.

Start: date of the last signature

End: 8 months from the last signature

8. Transfer of Financial Resources

Unity Health Toronto will transfer financial resources to FIOCRUZ in the amount of 25,000 CAD (twenty-five thousand Canadian dollars), as per the schedule below:

Immediately after signing the contract– 12,500 CAD

December 2023 – 12,500 CAD

The amounts specified in the above item will be received by FIOTEC in a specific account.

Any financial gains with application will be reversed to ensure the full execution of the subject matter of this Agreement.

Any increase to the budget of the Work Plan implemented by this Agreement, which makes it necessary to provide additional resources by CHAR, shall be prior and formally analyzed and approved by the Parties and shall be implemented only after conclusion of an additive term.

Of the total amount passed on, FIOTEC may use up to 10% (ten percent) to cover operating expenses.

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9. Description of the Work Plan

Metas	Goal(Target)	Responsible	Cost	Term	Ending Milestone
1	MicroRNAS selection	Claudia dos Santos – dos Santos Lab UofT	-	-	miRNA previously selected
2	LNPs Production	Claudia dos Santos – dos Santos Lab UofT		1 Month	LNPs ready to test
3	LNPs quality control	Claudia dos Santos – dos Santos Lab UofT		7 days	LPNs checked and ready to use
4	Shipment of LNPs to Brazil	Claudia dos Santos – dos Santos Lab UofT	Personnel and reagents, consumables	14 days	LNPs delivered and received by Immunopharmacology lab
5	Generate CLP mice to model SAE	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ	Personnel and laboratory mice	2 months	A sufficient number of CLP-mice for all planned experimental groups is reached.
6	Treat mice with LNPs	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ	Personnel and reagents, consumables	1 month	A sufficient number of treated mice are produced.
7	Execute behavioral experiments in model mice	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ	Personnel	3 months	All treated and control mice have been analyzed.
8	Measure cognitive function in model mice	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ	Personnel	3 months	All treated and control mice have been analyzed.
9	Analyze data	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ	Personnel	2 months	Data is ready for publication.
10	Prepare the manuscript in collaboration with both teams	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ and Claudia dos Santos – dos Santos Lab UofT	Personnel	2 months	Data is ready for publication.
11	Publish the paper	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ and Claudia dos Santos – dos Santos Lab UofT	Personnel	-	Paper published

Subtitle

ACTIVITIES - List the characteristic elements of the goal.

COSTS - Indicate the estimated cost for carrying out the activity

START - Start of the activity execution.

END - End of the activity execution.

FINISHING MARK - Indicate the rite of passage for the next phase

10. Technical Team

COLLABORATOR	ROLE IN THE PROJECT	RESPONSABILITIES AND COMPETENCES	FUNCTION IN INSTITUTION / INSTITUTION	E-MAIL	TELEPHONE	LINK CURRICULUM LATTES
Maria Carolina Barbosa da Silva	Postdoc	Run experiments, analyze data	Postdoc	m.carolinabarbosa@yahoo.com.br	21 992030999	http://lattes.cnpq.br/9666775206754325
Claudia dos Santos	PI	Manage the team, acquire funds and produce the LNPs that will be tested within the project.	Physician, Full Professor / UofT Unity Health	cdossantos@snh.ca	-	NA

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11. Risk Management

ACTIVITY	EVENT RISK	PROBABILITY OF OCCURRENCE	IMPACT	CATEGORIZATION/ PRIORITY	ANSWER	RESPONSIBLE
LNPs production	Errors during production	low	strong	high	New production	Claudia dos Santos – dos Santos Lab UofT
LNPs shipment to Brazil	Loss	low	Medium	high	New production and shipment	Claudia dos Santos – dos Santos Lab UofT
Stablsh CLP model	Problems during CLP surgery	low	strong	high	Another surgery CLP	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ
Treatment administration	Problems during treatment administration	low	strong	high	Another surgery CLP and treatment	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ
Behavioral tests	Unappropriated execution of the test	low	strong	high	Another CLP surgery, treatment, and a new round of tests	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ
Cognitive tests	Unappropriated execution of the test	Low	strong	high	Another CLP surgery, treatment, and a new round of tests	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ
Data analyze	NA	low	strong	high	New analysis	Maria Carolina Barbosa da Silva/Tatiana Maron Gutierrez – Laboratory of Immunopharmacology FIOCRUZ

Subtitle:
RISK EVENT - Brief description of the risk.
PROBABILITY OF OCCURRENCE - estimate - high, medium or low.
IMPACT - Estimate - strong, medium or weak.
CATEGORIZATION / PRIORITY - Definition of the event priority - high, medium or low.
ANSWER - Short description of the risk action plan.
RESPONSIBLE - Responsible for responding to the risk event.

12. Schedule

MONTHS												
ACTIVITIES	01	02	03	04	05	06	07	08	09	10	11	12
01	X											
02	X											
03	X											
04	X	X										
05		X										
06		X	X	X								
07				X	X	X						
08							X	X				
09								X				
10								X				
11								X				

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SIGNATURES/STAMPS (INITIALIZE ALL OTHER PAGES)

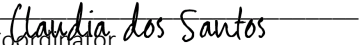
APPROVAL:

For FIOCRUZ

DocuSigned by:

Coordinator
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29/11/2023
Local/Date

For Unity Health Toronto

DocuSigned by:

Coordinator
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08/12/2023
Local/Date

AGREED/DE ACORDO:

For Unity Health Toronto


Dr. Ori Rotstein
VP Research & Innovation

Dec 8, 2023
Local/Date

For FIOCRUZ

DocuSigned by:

Dra. Tania Cremonini de Araujo Jorge
E7D2FE70C9DE4D1
Director IOC/FIOCRUZ

28/11/2023
Local/Date: