

COLLABORATIVE RESEARCH AGREEMENT

BETWEEN:

THE UNIVERSITY OF BRITISH COLUMBIA, a corporation continued under the *University Act* of British Columbia with offices at 103 – 6190 Agronomy Road, Vancouver, British Columbia, V6T 1Z3

(**"UBC"**)

AND:

MYND LIFE SCIENCES INC., a corporation incorporated under the laws of British Columbia, with a head office at 719 Finns Road Kelowna, BC V1X 5B7 and with a registered mailing address at PO Box 20002, Towne Centre PO, Kelowna, British Columbia, V1Y 9H2.

PO Box 20002, Towne Centre PO, Kelowna, British Columbia, V1Y 9H2

(the **"Sponsor"**)

(collectively referred to as the **"Parties"**)

WHEREAS:

It is UBC's objective to generate research in a manner consistent with UBC's status as a non-profit, tax exempt educational institution; and

The research program contemplated by this Agreement is of mutual interest and benefit to UBC and to the Sponsor, will further the instructional and research objectives of UBC in a manner consistent with its status as a non-profit, tax-exempt, educational institution, and may derive benefits for both the Sponsor and UBC through inventions, improvements and discoveries.

THE PARTIES AGREE AS FOLLOWS:

1.0 DEFINITIONS

1.1 In this Agreement:

- (a) **"Confidential Information"** means all information, regardless of its form:
 - (i) disclosed by UBC to the Sponsor and which is clearly identified in writing as "Confidential" either at the time of disclosure or within 30 calendar days thereafter,

or

- (ii) disclosed by the Sponsor to UBC and which is clearly identified in writing as "Confidential" either at the time of disclosure or within 30 calendar days thereafter,

except that "Confidential Information" does not include information:

- (iii) possessed by the recipient (the "**Recipient**") prior to receipt from the disclosing Party (the "**Discloser**"), other than through prior confidential disclosure by the Discloser, as evidenced by the Recipient's business records;
- (iv) published or available to the general public otherwise than through a breach of this Agreement;
- (v) obtained by the Recipient from a third party with a valid right to disclose it, provided that the third party is not under a confidentiality obligation to the Discloser in respect of the same; or
- (vi) independently developed by employees, agents or consultants of the Recipient who had no knowledge of or access to the Discloser's information as evidenced by the Recipient's business records;

(b) "**Contract Period**" means the period commencing on the Effective Date and ending 12 months after the Start Date as set out in Article 2.1 of this Agreement.

(c) "**Effective Date**" means the date on which the last of the Parties executes this Agreement.

(d) "**Invention**" means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter.

(e) "**Investigator**" means Dr. Wilfred A. Jefferies of the Faculty of Science at UBC.

(f) "**Joint Intellectual Property**" means any and all Inventions made jointly by UBC and the Sponsor during the Contract Period in the performance of the Project.

(g) "**Project**" means the research project as described in Schedule "A".

(h) "**Sponsor Intellectual Property**" means any and all Inventions made solely by the Sponsor during the Contract Period in the performance of the Project.

(i) "**UBC Intellectual Property**" means any and all Inventions made solely by UBC during the Contract Period in the performance of the Project.

2.0 RESEARCH WORK

2.1 UBC will commence the performance of the Project after UBC's receipt of the first payment set out in Article 4.1 (the "**Start Date**") and will use reasonable efforts to perform the Project substantially in accordance with the terms and conditions of this Agreement. The Sponsor and UBC may at any time amend the Project by mutual written agreement.

2.2 If the Investigator becomes unable or unwilling to continue the Project, and a mutually acceptable substitute is not available, UBC and the Sponsor will each have the option to terminate the Project and this Agreement by providing the other Party with written notice of same.

3.0 REPORTS & CONFERENCES

3.1 During the Contract Period, UBC will keep the Sponsor informed, orally or in writing, as to the progress of the Project. UBC will submit a final report to the Sponsor within 60 calendar days after the conclusion of the Contract Period or early termination of this Agreement, whichever is sooner.

3.2 During the term of this Agreement, representatives of UBC will meet with representatives of the Sponsor at times and places mutually agreed upon to discuss the progress and results, as well as ongoing plans, or changes to the Project.

4.0 COSTS, INVOICES & OTHER SUPPORT

4.1 The Parties understand and agree that, subject to Article 4.3, and excluding any intellectual property related costs under Section 7, the total costs to the Sponsor hereunder will be \$199,990 (Canadian funds). The Parties acknowledge that any budget categories that may be described in the Project are estimates only and that changes from category to category may be made at UBC's discretion. The Sponsor will pay to UBC the total amount of CAD \$199,990 upon receipt of an invoice to be sent upon the Effective Date of this Agreement.

The Sponsor may make payments by wire transfer or direct deposit to:

Beneficiary Bank: HSBC Bank Canada
Vancouver Main Branch
885 West Georgia Street Vancouver, B.C. V6C 3G1
Institution: 016
Transit: 10115
SWIFT CODE: HKBCCATT

Beneficiary: 115000399 045
The University of British Columbia
4th Floor, Suite 409
Vancouver, BC, Canada, V6T 1Z3

Remittance detail: Dept./contact/phone (maximum 24 characters)
Please email AR@Finance.ubc.ca – Ref FAS #F20-05975

UBC reserves the right to suspend work on the Project or to terminate the Project and this Agreement by delivering written notice of same to the Sponsor if the Sponsor fails to pay any invoiced amount within 30 calendar days from the due date.

The Sponsor will pay interest on all amounts owing to UBC not paid on the due date, at the rate of 12.68% per annum. The interest accrues on the outstanding balance from the due date.

4.2 UBC will retain title to any equipment purchased with funds provided by the Sponsor under this Agreement.

4.3 Notwithstanding anything contained in this Article 4, in the event of early termination of this Agreement, the Sponsor will pay all costs and liabilities relating to the Project which have been incurred by UBC as of the date of receipt of notice of such termination. Such costs and liabilities will include all non-cancellable obligations including payments in lieu of reasonable notice for technicians, graduate students and other staff assigned to the Project, but will not, in the aggregate, exceed the total amount payable by the Sponsor set out in Article 4.1.

4.4 Any funds that may remain after the conclusion of the Contract Period and the delivery of the final report will be retained by UBC.

5.0 CONFIDENTIALITY

5.1 The Recipient will keep and use the Discloser's Confidential Information in confidence and will not, without the Discloser's prior written consent, disclose the Discloser's Confidential Information to any person or entity, except to the Recipient's directors, officers, employees, faculty, students and professional advisors who require the Confidential Information to assist the Recipient in performing its obligations and exercising its rights under this Agreement.

5.2 A Recipient required by judicial or administrative process to disclose the Discloser's Confidential Information will, where legally permissible, promptly notify the Discloser and allow it reasonable time to oppose the process before disclosing the Confidential Information. If the Discloser is unable to successfully oppose the disclosure or if the Discloser decides not to oppose the disclosure, the obligations under Section 5.1 shall not apply, though only for the legally required disclosure and only for such Confidential Information that is required to be disclosed.

5.3 The Sponsor requires of UBC, and to the extent permitted by law UBC agrees, that this Agreement, and each part of it, is confidential and will not be disclosed to third parties. Notwithstanding anything contained in this Article 5, the Parties acknowledge and agree that either Party may identify the title of the Project, the Parties to this Agreement, the name of the Investigator, the Contract Period and the amount of funding provided by the Sponsor for the Project.

5.4 Notwithstanding any termination or expiration of this Agreement, the obligations set out in this Article 5 survive and continue to bind the Parties, their successors and assigns until 3 years after such termination or expiration.

6.0 PUBLICATION

6.1 UBC is not restricted from presenting at symposia, national or regional professional meetings, or from publishing in journals or other publications, results from the Project, provided that the Sponsor is provided with copies of the proposed disclosure at least 60 calendar days

before the presentation or publication date and does not, within 30 calendar days after delivery of the proposed disclosure, give notice to UBC indicating that it objects to the proposed disclosure.

6.2 The Sponsor may object to the proposed disclosure on the grounds that (i) it contains Confidential Information that was disclosed to UBC by the Sponsor; or (ii) that it discloses patentable subject matter which needs protection. If the Sponsor makes objection on the grounds of the inclusion of the Sponsor's Confidential Information, UBC will remove such Confidential Information immediately from the proposed disclosure, after which UBC is free to present and/or publish the proposed disclosure. If the Sponsor makes an objection on the grounds of protection of patentable subject matter:

(i) it will be deemed to be a direction to UBC to file a patent application as set out in Article 7.5; and

(ii) UBC will delay the proposed disclosure until UBC has filed one or more patent applications with one or more patent offices directed to such patentable subject matter (the "Delay"). A provisional patent application will be considered to be a patent application in the United States of America for the purposes of this Agreement. The Delay will be no longer than six (6) months from the date UBC delivered the proposed disclosure to the Sponsor, after which UBC is free to present and/or publish the proposed disclosure.

6.3 Notwithstanding anything in this Agreement, the Parties acknowledge and agree that no delay is permitted for the defense of a student's thesis.

7.0 INTELLECTUAL PROPERTY

7.1 The Sponsor acknowledges and agrees that UBC owns all right, title and interest in and to UBC Intellectual Property.

7.2 UBC acknowledges and agrees that the Sponsor owns all right, title and interest in and to Sponsor Intellectual Property.

7.3 The Parties acknowledge and agree that UBC and the Sponsor have joint right, title and interest in and to Joint Intellectual Property. Notwithstanding the applicable patent or other intellectual property laws in any jurisdiction, neither of the Parties may commercially exploit any Joint Intellectual Property, except as specifically provided for in Article 7.8 and 8.

7.4 UBC will promptly notify the Sponsor of any UBC Intellectual Property. The Parties will promptly notify one another of any Joint Intellectual Property.

7.5 The Sponsor may direct that UBC file one or more patent applications for UBC Intellectual Property and/or Joint Intellectual Property. UBC will then promptly prepare, file and prosecute patent applications in the name of UBC for UBC Intellectual Property and/or in joint names of UBC and the Sponsor for Joint Intellectual Property. UBC will be responsible for making final decisions regarding the scope and content of the patent applications and their prosecution. UBC will notify the Sponsor of any significant developments on all patent applications and will promptly supply the Sponsor with copies of papers received and filed in connection thereto in sufficient time for the Sponsor's review and input.

7.6 The Sponsor will bear all costs incurred in connection with the preparation, filing, prosecution and maintenance of the patent applications. Within 30 calendar days of UBC's written request, the Sponsor will pay to UBC a reasonable payment as an advance against expected patent expenses. The Sponsor will assist UBC in a timely manner to ensure that the patent applications cover, to the best of the Sponsor's knowledge, all items of commercial interest and importance.

7.7 If UBC wishes to obtain patent protection for UBC Intellectual Property and/or Joint Intellectual Property over and above that for which the Sponsor wishes to provide its financial support pursuant to Article 7.6, UBC will be free to file any patent applications, including new applications, at its own expense. If Sponsor discontinues its financial support for prosecution or maintenance of any patents or patent applications for UBC Intellectual Property and/or Joint Intellectual Property, UBC will be free to continue the prosecution or maintain such patents or patent applications at its own expense. In any event, UBC will not have any obligation to the Sponsor under Article 8 (Grant of Rights) relating to such patent protection.

7.8 In the event that the Sponsor wishes to discontinue the financial support for prosecution or maintenance of any patents or patent applications for Joint Intellectual Property (the "**Event**"), the Sponsor will notify UBC in writing at least 30 calendar days prior to the Event (the "**Notice to Discontinue**") and UBC will be free to continue the prosecution or maintenance of any such patents or patent applications for Joint Intellectual Property. The Sponsor will then promptly execute and deliver to UBC any assignment or documents UBC may deem necessary or desirable to vest in UBC all right, title and interest in the patents and patent applications. Sponsor will pay for all expenses incurred in connection with the patents and patent applications prior to the Event and for 30 calendar days from UBC's receipt of the Notice to Discontinue.

8.0 GRANT OF RIGHTS

8.1 UBC grants the Sponsor the option to obtain a royalty-bearing license to use and exploit UBC Intellectual Property and UBC's rights in Joint Intellectual Property subject to terms and conditions determined in accordance with Article 8.2 (the "**Option**"). The Option will subsist with respect to each item of UBC Intellectual Property and Joint Intellectual Property for a period of 6 months after UBC has disclosed said item in writing to the Sponsor (the "**Option Period**"). The Sponsor may exercise the Option within the Option Period by delivering written notice of same to UBC.

8.2 If the Sponsor exercises the Option pursuant to Article 8.1, the Parties will negotiate in good faith to determine the specific terms and conditions on which a license will be granted by UBC to the Sponsor. Such license will contain commercially reasonable financial terms and will be generally consistent with the terms and conditions of the license agreements then being entered into by UBC with its other licensees. If UBC and the Sponsor, acting reasonably, are unable to agree upon such specific terms and conditions within a period of 6 months after the date when the Sponsor exercised the Option, the Parties acknowledge and agree that the Option will expire.

8.3 If the Sponsor does not exercise the Option pursuant to Article 8.1, UBC will be entitled to license from the Sponsor the Sponsor's interest in Joint Intellectual Property and the Parties will negotiate in good faith to determine the specific terms and conditions, including royalty rates, on which the license will be granted by the Sponsor to UBC. The Sponsor will have no right to use Joint Intellectual Property for any purpose and will not license, sell, assign or otherwise transfer the Sponsor's interest in the Joint Intellectual Property to any third party.

8.4 The Sponsor acknowledges and agrees that UBC may use Joint Intellectual Property without charge in any manner at all for research, scholarly publication, educational and all other non-commercial uses.

9.0 TERM

9.1 This Agreement will be effective from the Effective Date for the full duration of the Contract Period unless terminated earlier under Article 10.

10.0 TERMINATION

10.1 Either Party may terminate this Agreement upon 30 calendar days prior written notice to the other.

10.2 If either Party commits any breach or default of any terms or conditions of this Agreement and also fails to remedy such breach or default within 30 calendar days after receipt of a written notice from the other Party, the Party giving notice may terminate this Agreement by sending a notice of termination in writing to the Party in breach. This termination will be effective as of the date of the receipt of such notice. The termination may be in addition to any other remedies available at law or in equity.

10.3 This Agreement may be terminated by UBC if the Sponsor is in breach of any other agreement between the Sponsor and UBC, which breach has not been cured within the time provided for the curing of such breach under the terms of such other agreement.

10.4 The Parties acknowledge that as a result of the current global pandemic UBC may need to suspend or cease the Project contemplated herein. In such circumstances UBC will notify the Sponsor in a timely fashion and the Parties will discuss whether to amend or terminate this Agreement

10.5 No termination of this Agreement, however effectuated, will release the Parties from their rights and obligations under Articles 4.3, 4.3, 4.4, 5.0 (Confidentiality), 7.0 (Intellectual Property), 8.0 (Grant of Rights), 10.6 (cessation of use of Confidential Information) and 12 (Indemnity).

10.6 Upon the termination of this Agreement, the Recipient will cease to use the Discloser's Confidential Information in any manner whatsoever and upon the written request of the Discloser, will deliver to the Discloser all of the Discloser's Confidential Information in the Recipient's possession or control.

10.7 The Parties may extend this Agreement in writing for additional periods under mutually agreeable terms and conditions. Said extension will be effective upon signature by both Parties.

11.0 DISCLAIMER OF WARRANTY

11.1 UBC makes no representations or warranties, either express or implied, regarding data or other results arising from the Project or regarding Confidential Information UBC may disclose to the Sponsor. UBC specifically disclaims any implied warranty of non-infringement or merchantability or fitness for a particular purpose and UBC will, in no event, be liable for any loss, whether direct, consequential, incidental or special or other similar damages arising from any defect, error or failure to perform, even if UBC has been advised of the possibility of such

damages. The Sponsor acknowledges that the Project is of an experimental and exploratory nature, that no particular results can be guaranteed, and that the Sponsor has been advised by UBC to undertake its own due diligence with respect to all matters arising from this Agreement.

12.0 INDEMNITY

12.1 The Sponsor indemnifies, holds harmless and defends UBC, its Board of Governors, directors, officers, employees, faculty, students, invitees and agents against any and all claims (including all reasonable legal fees and disbursements) arising out of the receipt, use or transfer by the Sponsor of any UBC's Confidential Information, UBC Intellectual Property, Joint Intellectual Property, or any data or other results arising from the Project including, without limitation, any damages or losses, consequential or otherwise, arising from or out of the Project, however they may arise.

13.0 INSURANCE

13.1 UBC has liability insurance applicable to its directors, officers, employees, faculty, students and agents while acting within the scope of their employment by UBC. UBC has no liability insurance policy that can extend protection to any other person. Therefore, subject to Article 12.1 (Indemnity), each Party hereby assumes any risks of personal injury and property damage attributable to the negligent acts or omissions of that Party and its directors, officers, employees and agents, and where applicable faculty and students.

14.0 GOVERNING LAW

14.1 This Agreement is governed by, and will be construed in accordance with, the laws of British Columbia and the laws of Canada in force in that province, without regard to its conflict of law rules. The Parties agree that by executing this Agreement, they have attorned to the exclusive jurisdiction of the Supreme Court of British Columbia.

15.0 ASSIGNMENT

15.1 Neither Party may assign this Agreement without the prior written consent of the other Party, which consent will not be unreasonably withheld.

16.0 NOTICES

16.1 All payments, reports and notices or other documents that a Party is required or may want to deliver to any other Party will be delivered:

- (a) in writing; and
- (b) either by personal delivery, email or by registered or certified mail (with all postage and other charges prepaid) at the address for the receiving Party as set out in Article 16.2 or as varied by any notice.

Any notice personally delivered or by email is deemed to have been received at the time of delivery. Any notice mailed in accordance with this Article 16.1 is deemed to have been received at the end of the fifth business day after it is posted.

16.2 Addresses for delivery of notices:

Sponsor

Jordan Cleland
Chief Operating Officer
PO Box 20002
Towne Centre PO
Kelowna, BC V1Y 9H2
Telephone: (403)599-6779
Email: jordanc@myndsciences.com

UBC

Industry Contracts Manager
Re. UBC File No. F20-05975
University-Industry Liaison Office
#103 – 6190 Agronomy Road
The University of British Columbia
Vancouver, British Columbia
Canada V6T 1Z3
Telephone: (604) 822-8580
Email: Lianne.Boon@uilo.ubc.ca

16.3 The Sponsor may direct questions of a scientific nature or regarding financial matters to UBC through the following contacts:

Scientific Matters

Dr. Wilfred A. Jefferies
Michael Smith Laboratories
The University of British Columbia
MSL 215
2185 East Mall
Vancouver, British Columbia
Canada V6T 1Z4
Telephone: (604) 822-2006
Email: wilf@msl.ubc.ca

Financial Matters

Manager, Research Finance Office
The University of British Columbia
4th Floor – TEF 3
409 - 6190 Agronomy Road
Vancouver, British Columbia
Canada V6T 1Z3
Telephone: (604) 822-3275
Fax: (604) 822-2417

17.0 GENERAL

17.1 Nothing contained in this Agreement is to be deemed or construed to create between the Parties a partnership or joint venture. Neither Party has the authority to act on behalf of any other Party, or to commit the other Party in any manner at all or cause the other Party's name to be used in any way not specifically authorized by this Agreement. Neither Party may use the other Party's name, trademarks or insignia for any advertising or any promotional purposes, including but not limited to media releases, without the other Party's prior written consent.

17.2 Subject to the limitations in this Agreement, this Agreement operates for the benefit of and is binding on the Parties and their respective successors and permitted assigns.

17.3 No condoning, excusing or overlooking by either Party of any default, breach or non-observance by the other Party at any time or times regarding any terms of this Agreement operates as a waiver of that Party's rights under this Agreement. A waiver of any term, or right under this Agreement will be in writing signed by the Party entitled to the benefit of that term or right, and is effective only to the extent set out in the written waiver.

17.4 No exercise of a specific right or remedy by either Party precludes it from or prejudices it in exercising another right or pursuing another remedy or maintaining an action to which it may otherwise be entitled either at law or in equity.

17.5 Headings in this Agreement are for reference only and do not form a part of this Agreement and are not to be used in the interpretation of this Agreement.

17.6 All terms in this Agreement which require performance by the Parties after the expiry or termination of this Agreement, will remain in force despite this Agreement's expiry or termination for any reason.

17.7 Part or all of any Article that is indefinite, invalid, illegal or otherwise voidable or unenforceable, may be severed from this Agreement and the balance of this Agreement will continue in full force and effect.

17.8 At the request of UBC or the Sponsor, the non-requesting Party will obtain the execution of any agreement or instrument (including from its employees, agents, contractors, consultants or representatives) that may be required to consummate the transactions contemplated in this Agreement, including assigning any rights, waiving any rights or perfecting any rights in such Party's name.

17.9 This Agreement and the Schedules set out the entire understanding between the Parties and no changes to this Agreement are binding unless in writing and signed by the Parties to this Agreement. The Parties will be bound by the Schedules, except to the extent that they may conflict with the terms and conditions contained in this Agreement, in which case the terms and conditions of this Agreement will govern.

17.10 In this Agreement, unless the contrary intention appears, the singular includes the plural and vice versa and words importing a gender include other genders.

17.11 Neither of the Parties shall be deemed to be in default of, or to have breached, any provision of this Agreement as a result of any delay, failure in performance or interruption of service, resulting directly or indirectly from natural disasters, acts of civil or military authorities, civil disturbances, wars, strikes or other labor disputes, fires, transportation contingencies, laws, regulations, acts or orders of any government or agency or official thereof, other catastrophes or any other similar occurrences beyond such Party's reasonable control. In every case, the delay or failure in performance or interruption of service must be without the fault or negligence of the Party claiming excusable delay, and the Party claiming excusable delay must promptly notify the other Party of such delay. Performance time under this Agreement shall be considered extended for a period of time equivalent to the time lost.

17.12 This Agreement may be executed in counterpart by the Parties, either through original copies or by facsimile or electronically each of which will be deemed an original and all of which will constitute the same instrument.

[SIGNATURE PAGE FOLLOWS]

SIGNED BY THE PARTIES AS AN AGREEMENT effective as of the date on which the last of the Parties executes this Agreement.

SIGNED FOR AND ON BEHALF of
THE UNIVERSITY OF BRITISH COLUMBIA
by its duly authorized signatories:

(signed)



Mario Kasapi
2020.12.18 13:31:05
-08'00'

Name:
Title: Associate Director, UILO
Date:

(signed)

Dr. J.P. Heale
2020.12.21
12:12:30 -08'00'

Name:
Title:
Date:

SIGNED FOR AND ON BEHALF of
MYND LIFE SCIENCES INC.
by its duly authorized officer:

(s) "Jordan Cleland"

Name: Jordan Cleland
Title: Chief Operating Officer
Date: December 18, 2020

I have read and understood the foregoing Agreement and understand my responsibilities as the Investigator. I further confirm that I will not commence the performance of the Project until UBC receives the first payment from the Sponsor.

(s) "Dr. Wilfred A. Jefferies"

Dr. Wilfred A. Jefferies
Michael Smith Laboratories
Date: December 18, 2020

**SCHEDULE "A"
RESEARCH PROPOSAL
AND BUDGET**

Title: The Role of ATP-binding cassette protein ABCF1 in Disease

Lay Abstract:

The microbiome is the term describing the microbes that live in a defined area. The gut microbiome describes the microbes (bacteria, fungi, viruses, etc) that live in the gut, including small and large intestines, and it has previously been shown that the microbiome can influence the host immune system. Dysregulation of the immune system can contribute to the disease symptoms. We have recently discovered a protein (ABCF1) that act as a molecular switch from an inflammatory condition towards the resolution of inflammation. Therefore, we plan to explore the role of ABCF1 in disease, using mouse models, with a particular look at how ABCF1 affects the microbiome.

In the last decade, it is becoming apparent that many antidepressant drugs also have anti-inflammatory properties. The antidepressant selective serotonin receptor inhibitor (SSRI), escitalopram, has been identified as influencing anti-inflammatory pathways in patient populations, and was concluded that ABCF1 is a putative therapeutic target of escitalopram. In our *Immunity* paper published in February, 2019, we described the function of ABCF1 as a negative regulator of inflammation. Therefore, we propose to examine the role of ABCF1 and our studies will include molecular and cell-based research, as well as extensive use of mouse models for microbiome research.

Scientific Abstract:

Major depressive disorder (MDD), often referred to as "depression", affects psychosocial functioning and diminishes the quality of life¹. It affects an estimated 300 million people worldwide and is associated with ~800,000 suicide deaths annually. Some forms of depression may be viewed as a psycho-neuroimmunological disorder MDD. The gut microbiome and the brain have implications for psychiatric disorders and the microbiota-gut-brain axis is drawing more interest by those seeking to understand the association between inflammation and depression. The microbiota in patients with MDD compared to controls have been found to exhibit differences in some 50 bacterial taxa.

In addition, studies on humans and animals have documented that chronic activation of M1 microglial cells may trigger mood disorders through the release of a variety of immune-related factors thereby potentiating neuronal dysfunction. In our 2019 *Immunity* paper, we described the role of the ABCF1 gene as necessary to achieve macrophage polarization in the "anti-inflammatory" **M2b** state and the lack of **ABCF1** anchors macrophages in the pro-inflammatory **M1** state. Recently, in a truly remarkable and timely study, **ABCF1** was identified in peripheral blood mononuclear cells (PBMCs) by the **Genome-Based Therapeutic Drugs for Depression Project**, as the putative therapeutic target of **escitalopram**, a widely prescribed **SSRI** used to treat clinical depression.

Hypothesis: We hypothesize that disruption of ABCF1 function exacerbates inflammatory processes that impact the microbiota and psychosocial function of the afflicted subjects, and that ABCF1 is the target of escitalopram, which will reverse these effects.

Experimental plan: In this proposal, we plan to address whether **escitalopram** targets **ABCF1** and **ABCF1**-regulated pathways. Additionally, we have generated the first **genetic knockout** of

the **ABCF1** gene in mice and we are poised to examine the role of ABCF1 in influencing the microbiota composition and diversity. Additionally, we will examine the role of ABCF1 and the effect of escitalopram and psilocybins and the NLRP3 inflammasome inhibitor, MCC950 to reduce inflammation in models of inflammation. We also plan to determine if the gut microbiota contribute to MDD and if ABCF1 deficient mice exhibit increased MDD and finally, whether escitalopram or MCC950 or psilocybins can reverse depression in these mouse models.

Impact: These studies seek to establish a novel relationship between **ABCF1, the microbiota and inflammation-triggered forms of MDD**. Our results will support the development of treatments for MDD beyond current therapies and potentially establish a new paradigm for inflammation and the microbiota underpinning psychosocial function. Clinical translation of these results will likely be profound, resulting in state-of-the-art interventions and therapies to treat MDD, and perhaps treatment-resistant depression and inflammation. Perhaps most immediately and profoundly, this work may also help end the stigma of depression by establishing a root causal relationship with chronic inflammation.

Budget

Research Costs	
Materials	
Animals (purchase, husbandry)	15,000.00
Consumables (chemicals, antibodies, plasticware, etc)	18,775.00
Computers and Software	7,000.00
Services	
Sequencing, Mass spectrometry, Flow cytometry, Microscopy/Histology	11,000.00
Total Research Expenses	51,775.00
Research Team Salaries	
Graduate Student (1)	30,600.00
Research Postdoctoral Fellow (1)	60,500.00
Total Research Team Salaries	91,100.00
UBC Overhead - 40%	
Total UBC Overhead	57,140.00
Total Expenses	199,990.00