University of CINCINNATI

AMITY UNIVERSITY MUMBAI

MEMORANDUM OF UNDERSTANDING ON ACADEMIC AND RESEARCH COLLABORATION

Between

University of Cincinnati

And

Amity University, Maharashtra

This Memorandum of Agreement is entered into by and between **University of Cincinnati (UC)**,2900 Reading Rd., Suite 460, Cincinnati, OH 45206-0829 and **Amity University, Maharashtra (AUM),** Mumbai - Pune Expressway, Bhatan Post-Somathne, Panvel, Mumbai, Maharashtra 410206.

Recitals:

The **University of Cincinnati** is a state institution of higher education organized under Section 3361 of the Ohio Revised Code. The University of Cincinnati serves the people of Ohio, the nation, and the world as a premier, public, urban research university dedicated to undergraduate, graduate, and professional education, experience-based learning, and research. It is committed to excellence, diversity and an inclusive environment for students, faculty, staff, and all activities. Through scholarship, service, partnerships, and leadership, UC creates opportunity, develops educated and engaged citizens, enhances the economy and enriches the University, city, state and global community. The University of Cincinnati Cancer Center delivers the most advanced cancer care available for adults in Greater Cincinnati through expert teams, pioneering research and a spirit of collaboration.

AUM has been established under Maharashtra Govt. Act of 2014 of Government of Maharashtra and is recognized as per Section 2(f) of the UGC Act with the rights to confer degrees. AUM has expertise in various areas of science, engineering, architecture, design, humanities, law and management. **Amity Institute of Biotechnology (AIB)** is a constituent unit of Amity University Mumbai established in the year 2014, with the aim to promote research and development in the broader areas of biosciences and biotechnology. AIB has facilities that support innovative research in areas of plant biotechnology, environmental biotechnology, industrial biotechnology, microbiology & food Biotechnology, Structural & Computational Biology and Stem Cells and Regenerative Medicine.

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Whereas, UC and AUM (each individually a 'Party' and collectively as 'Parties' hereinafter) are interested to take up a joint research programme / project pertaining to "Tumor cell Vaccine" as per the scope more specifically contained and detailed in Schedule – I annexed hereto.

The two institutions will encourage direct contact and co-operation between their faculty and scientists, Departments and Research Centres, within fields that are mutually acceptable and visits by and exchange of doctoral students, faculty members and scientists for research and courses.

The Parties hereto agree to the following terms and conditions for the above collaboration:

1. **Scope, Purpose of Activity**: The scope of the activity under this collaboration will be as contained and detailed in Schedule – I annexed hereto.

2. **Intellectual Property (IP):** Based on contributions from inventors of respective Party, knowledge and/or intellectual property (IP) which can be covered by patents and other IPRs will be filed by UC or AUM, on a case to case basis, based on contributions of each of the Parties and under mutually agreed to terms. Provided however, that either Party may make use of, all information and data generated during this collaborative activity hereunder for its own internal research and academic purposes. If there are any commercial benefits arising from the work, it should be shared by both the parties

3. **Publications:** Any research findings arising from this collaborative activity may be published / presented at national or international conferences as jointly authored. Acknowledgement of the contribution of the authors towards such publications will be made, as appropriate. However, the terms and conditions for such publications shall be mutually agreed upon.

4. **Confidentiality**: UC and AUM agree to hold in confidence all information/data designated as confidential, which is obtained/disclosed from either Party or created during the performance of this agreement and will not disclose the same to any third party without written consent of the other Party except as allowed under Article 3

5. **Non-Exclusive:** This relationship is on a non-exclusive basis and either AUM or UC are free to enter into other relationships or alliances with other partners.

6. **Term and Termination:** The term of this agreement shall be for a period of five (5) years from the date of execution hereof unless terminated earlier by a written notice of thirty (30) days, by a Party seeking such termination, to the other Party hereto.

7. **Changes:** Any changes / alterations to this agreement / understanding shall be made by the Parties hereto by mutual agreement, in writing, by the authorized representatives of both the Parties.

8. **Compliances**: Each Party agrees to perform its activities in compliance with all applicable statutes and regulations that are in force at that time.

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9. **Dispute Resolution:** Any and all disagreements / differences / disputes arising hereunder shall be resolved amicably by the designated senior executives / officers of the good offices of both Parties.

AGREED

REGISTRAR
AMITY UNIVERSITY MUMBAI
MUMBAI - PUNE EXPRESSWAY
PANVEL - MUMBAI - 410 206

AUM
Name: Dr. Hira Vyas

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Date: 13th April, 2021

Witness:
Name:

University of Cincinnati
Name: GEOFFREY PINSKI
Title: AVP, TECH TRANSFER
Signature:

Date: April 15, 2021

Witness:
Name:

Schedule – I: **Scope of collaboration**

1. **Title of the Project:** An Engineered Tumor Cell Vaccine that Utilizes Distinct Osteopontin Domains to Maximize Immune Stimulation
2. **Team composition of Partnering Institutions:**

   Dr. Vinoth Prasanna Gunasekaran, Assistant Professor, Amity Institute of Biotechnology, Amity University, Mumbai.

   Dr. Georg F. Weber, Professor, College of Pharmacy, University of Cincinnati, USA.
3. **Summary of the proposed research project:**

Background: Cancer vaccines that induce the immune system to eliminate cancer cell burden have emerged as a practical approach. It has become increasingly clear, however, that the outcome of cancer immunotherapy is decisively determined by the type of immune response induced. Our recent work has demonstrated the cytokine osteopontin to be a crucial regulator of type I and type II immunity. Osteopontin -/- mice fail to mount protective type I immunity to bacterial or viral challenge, which is associated with diminished production of the stimulatory cytokine IL-12 and excessive production of the antagonistic cytokine IL-10. Induction of IL-12 and inhibition of IL-10 reflect differential engagement of macrophage receptors: Phosphorylation-dependent ligation of integrin αvβ3 by the N-terminal portion of osteopontin leads to IL-12 expression, while phosphorylation independent interaction of a C-terminal domain with CD44 mediates IL-10 suppression.

Objective/Hypothesis: Since osteopontin regulates type I immunity (through IL-12) and type II immunity (through IL-10) at a more proximal level than most other cytokines, there is reason to hypothesize that it may be a more potent adjuvant for anti-cancer vaccines than most of the currently used cytokines. The identification of two functional osteopontin domains, which independently regulate IL-10 and IL-12 secretion from macrophages, provides a unique opportunity to use these fragments to modulate the immune response to cancer vaccines We hypothesize that the N-terminal domain, which induces IL-12 but does not suppress IL-10, will be more successful as a cancer vaccine adjuvant than the C-terminal domain, which selectively suppresses IL-10, or than the wild-type osteopontin.

Specific Aims:

1. Generation and testing of a tumor vaccine that secretes engineered osteopontin variants.
2. Definition of the cytokine profile induced by osteopontin transfectants in vivo.
3. Evaluation of the induction of cytotoxic T-lymphocytes by osteopontin transfectants in vivo.
4. Evaluation of the regulation of B-cell activation through osteopontin transfectants in vivo.

Study Design: The generation of cellular anti-cancer vaccines by transfection of cytokine genes into tumor cells followed by irradiation has been studied extensively in mice and has undergone some testing in humans. We will use the 4T1 murine breast cancer cells to generate

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irradiated cellular vaccines after transfection with osteopontin or genetically engineered variants of the cytokine. In particular, we will transfect a N-terminal deletion mutant that will engage integrin receptors and induce IL-12 but will not ligate CD44, so that IL-10 will remain high. The broad cytokine profile, comprising a combined Th1 and Th2 patterns, is expected to enhance the induced anti-tumor immune response more strongly than Th1 or Th2 cytokines alone. This hypothesis will be tested in our experiments.

Relevance: The proposed structure-activity analyses will allow a rational vaccine design that not only presents relevant antigens but also directs the immune system toward the most efficient mode of response. From these studies we will also learn more about the molecular regulation of cell-mediated versus antibody-mediated immunity which has implications for vaccines in general, autoimmune diseases, and organ transplantation.

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