Expanding the MSU Applied Immunology Center for Education and Research (AICER)

***Strategic Plan Theme*: Sustainable Health**

***Funding Level*: More than $5 million**

***Facility Needs*: No new facilities will be needed**

***Submitting Unit*: College of Osteopathic Medicine**

Collaborating colleges/departments/units involved with this proposal.

Colleges: COM, CVM, CHM, CNS, COE, CANR Departments: Microbiology and Molecular Genetics, Pharmacology and Toxicology, Physiology, Biochemistry and Molecular Biology, Chemistry, Osteopathic Medical Specialties, Neurology, Radiology, Food Science and Human Nutrition, Pathobiology and Diagnostic Investigation, Biomedical Engineering, Medical Education, Psychiatry, Large Animal Clinical Sciences

What is the proposal's big theme or idea?

Immunotherapies that target the immune response to prevent or treat existing disease are at the forefront of biomedical research. The potential of immunotherapies to improve global health is vast but requires organized research infrastructure spanning fundamental research to clinical capabilities. COM identified a key area of need in the absence of a stand-alone immunology department at MSU and established AICER. The long-term goal of AICER is to leverage existing immunological expertise at MSU and recruit diverse immunology-related investigators to significantly and rapidly increase extramural/NIH funding while creating a nationally recognized center of excellence in Applied Immunology. AICER, an established MSU Research center (https://research.msu.edu/research-centers), is focused on discovering new immunotherapies for use against autoimmune diseases, cancers, and infectious diseases. While initiated by COM, participation in AICER spans multiple departments and colleges at MSU while synergizing with the goals of community partners such as the McLaren and Henry Ford Health systems. Over 50 signatories across 15 departments and 6 colleges, including the COM College advisory committee, and several Deans/Chairpersons across MSU, support the goals of AICER and are co-authors on this proposal. We ALL strongly believe that expanding AICER presents a growth opportunity for MSU to not only increase extramural research and educational funding, but to expand the intellectual property portfolio of the university and to rapidly translate fundamental discoveries into novel immunotherapies that improve health for all. AICER expansion will also dramatically increase the capacity of MSU to educate the next generation of diverse scholars and researchers needed to address global diseases that disproportionately harm underserved communities, all goals in line with the MSU Strategic Plan.

Budgetary commitments from MSU to maximally expand AICER to achieve the goals listed below will exceed the $5 Million range, as this level of funds would primarily support seed funding to support multi-PI grant proposals, hire a dedicated curriculum fellow, and expand hiring of research faculty (including typical start-up costs) across multiple colleges. Identification of laboratory spaces is ongoing with the AICER cluster hire initiative, but it is likely expansion of capacities at existing MSU core facilities will be needed to support the increased immunology research activities occurring at MSU because of expanded AICER efforts.

What is the proposal's goal?

The long-term goal of AICER expansion is to create a nationally recognized center of excellence in applied immunology. We will leverage existing strengths at MSU and recruit new diverse talent to improve sustainable

health globally. The expansion of AICER will achieve this goal by broadly synergizing sustainable health research across five key areas of research in alignment with MSU strategic goals. The broad goals of AICER research is described in detail below:

Autoimmunity: The number of individuals with autoimmunity is rapidly increasing worldwide. Faculty interests within AICER range from tissue specific immune dysfunction, environmental factor induced autoimmunity, and inflammatory mediators that can suppress autoimmune responses. Unified autoimmune research groups in AICER will be positioned to lead the development of new therapies that provide sustained health.

Infectious Disease: Developing new antimicrobials and vaccines against current and emerging pathogens is of the upmost importance given the impacts witnessed by the SARS CoV-2 pandemic. AICER encompasses internationally recognized infectious disease researchers studying a variety of diseases that drive severe mortality worldwide including HIV, Tuberculosis, SARS-Cov2, and Cholerae. Expanding the University's footprint in infectious disease through AICER is an important strategic investment to drive sustainable health worldwide.

Neuroinflammation: Interactions between the nervous system and the immune response is at the forefront of immunological research. A core group of scientists and physicians in AICER are driving research and therapeutic interventions in patients with diseases such as Alzheimer's, Parkinson's, autism, depression/anxiety, and multiple sclerosis. Expansion of this expertise, coupled with ongoing investments in neuroimaging at MSU will position AICER to be an international leader in neuroinflammation.

Microbiota-Immunity axis: While the microbiome is important in many diseases, there are untapped therapeutic possibilities that could drive sustained human health. AICER's expertise in microbiome-immune interactions will be leveraged to understand the fundamental role of nutrition and the microbiome on long-term health.

Cancer Immunology: Cancer immunotherapy success has driven a worldwide interest in leveraging the host response to control tumor progression. An emerging research area in AICER is cancer immunology. While cancer biology is a strength at MSU many AICER-associated investigators are now studying immune tumor surveillance and immune-based cancer therapies in partnership with MSU's strong medicinal chemistry and drug discovery infrastructure. We envision this, and all areas of AICER research focus to be further strengthened by established clinical research partnerships with McLaren/Karmanos/Henry Ford/Spectrum Health.

Expanding and unifying research efforts at AICER will help achieve our key long-term goal of a national center for excellence.

Define the significance, or impact of your big idea.

The next wave of breakthrough therapeutic advances will be in immunotherapeutics. Immunotherapies are most easily recognized by successes in cancer, but there is unlimited potential to stretch well beyond cancer to treat a variety of diseases with disparate etiologies. Tremendous opportunities exist for MSU to both excel and be nationally recognized in this sphere while impacting the lives of patients who suffer from untreated diseases. The scope of AICER is particularly focused on autoimmunity, cancer and infectious diseases that cumulatively impact hundreds of millions worldwide. While immunotherapy of cancer remains an important target area, purposeful expansion into alternative areas of translational immunology is highly significant. By doing so we will create a competitive niche where MSU can be rapidly recognized as a national leader, thereby enabling MSU and AICER to develop a novel brand. Taking this approach, MSU-AICER is already in an outstanding position to gain RAPID national recognition for its unique capacities and successes in applied immunology and expansion of these efforts will solidify these outcomes.

The AICER initiative has already brought together COM faculty alongside research faculty in CNS, CVM, CANR, COE, and CHM together investigating various aspects of immunology and immunotherapeutics. AICER has steadily grown over two years with ~50 MSU AICER PI's that transcend multiple MSU departments and colleges (see subset listed here). These faculty meet regularly in focus groups, shared symposium, and in support of new faculty hires driving new interdepartmental collaborations to lay the

groundwork for future program grants. All AICER investigators are motivated to innovate new technologies that are readily deployable into the clinics. By simultaneously fostering collaborations with McLaren Hospital, Karmanos NCI-Cancer Institute system, and the Henry Ford Health System AICER is uniquely positioned to link fundamental research with translational clinical research. One goal of AICER is to be recognized as a national center of excellence which will further amplify applied immunology research at MSU. To help achieve this goal MSU-COM is already pursuing a cluster hiring of research faculty that will directly support the goals of AICER (See the COM-AICER cluster hire job postings). From almost 50 applicants, 8 talented researchers were identified for further recruitment, all of whom fit squarely within AICER across multiple departments. If successfully recruited each faculty will augment existing strengths at MSU and accelerate AICER achievements. With further investment from MSU the number of AICER hires in this search can be expanded, helping to rapidly increase funding and achieve recognition as a center for excellence.

Who will be impacted?

AICER will impact students, faculty/staff, and our clinical partners by providing education, resources and collaborations to diverse individuals across Michigan.

Student Success: Expanding the AICER framework will include investment in important research experiences for undergraduate and graduate students, but also the development of an innovative immunology-based curriculum including formal seminar series and didactic classes in addition to less formal journal clubs, works in progress series, and professional development. AICER will be positioned to train the next generation of scientists and leaders in the field of immunology.

Staff and Faculty Success: Expanding AICER will increase the success of a broad range of staff and faculty. To date, COM has shown a commitment to improve resources for AICER-associated faculty. Directly supporting research and bringing together synergistic research programs AICER-associated faculty will position AICER to rapidly obtain more extramural funding which is essential for our faculty and staff to be successful. The success of our faculty and staff will further the success of our trainees highlighted above.

Innovation for Global Impact: Given the human, societal and economic tolls from the ongoing pandemic, there is a strong need to align research to prevent future catastrophes. While MSU has many immunological research strengths, there is a lack of unification of these interests across MSU, limiting program grants and innovative therapy development. Expanding AICER will propel discoveries that can be rapidly moved into the clinics using strategic partnerships already in place. AICER will be a cornerstone for innovation and driving interdisciplinary research that will result in new discoveries and therapies with global impact.

Stewardship and Sustainability: AICER will bring internationally recognized immunology researchers at MSU together to foster the development of new immunotherapies that improve global public health. By directly providing researchers with resources and trainee support, new collaborations can be sparked to drive new funding ventures. The long-term vision is to use initial investments in AICER to bring in a tidal wave of sustainable long-term grant and educational support.

Diversity, Equity, and Inclusion: New innovations are driven by diverse teams working towards a common goal. ALL AICER efforts will continue to be maximally inclusive including the recruitment of diverse investigators, and a focus on diseases that affect vulnerable and/or under-represented populations. AICER growth will recruit diverse immunology expertise and retain these internationally recognized researchers as we develop a new community of immunological excellence. Pursuing both recruitment and retention will promote diversity, equity, and inclusion goals at MSU.

What does sustainability for your proposal look like?

Creating a successful pipeline from research to the clinic takes upfront investment to enhance existing strengths and provide low-barrier opportunities for collaboration. With sufficient investment, AICER will become a sustainable nationally recognized center for immunology excellence. COM already committed significant resources to drive AICER growth and further investment from MSU would synergize to accelerate sustainability. For example, COM created the Dell Fellowship program for AICER PIs to support innovative post-doctoral fellows while initiating new collaborations across MSU departments. COM also instituted the

SpartanDO Research Accelerator Program, providing funds to AICER PIs accepting students into their labs to cultivate interactions between future Michigan clinicians and AICER. COM also initiated the COM-Dean's Research Facilitation Awards, which returns 50% of the College's portion of IDC returns to the PI to further drive research. Thus, COM is driving the sustainability of AICER which would be radically accelerated by further investment from MSU. A key step towards sustainability is for AICER faculty to apply for collaborative R01 project grants and program grants/training grants from the NIH. Since these awards can be in tens of millions, they will return initial AICER investment while solidifying collaborations that progress towards new therapies. AICER is already successful, as one of the COM Dell Fellowship members Dr. Watts was recently awarded MSU's only program project from NIH. Several NIH RFAs are available to recapitulate this success and foster growth, expansion, and recognition of AICER related to our core strengths such as transplantation and maternal immunity (RFA-AI-19-042 and RFA-AI-18-023) and genetics/computational studies of immune-mediated diseases (RFA-AI-19-041 and RFA-AI-19-011). Potential collaborations with clinical partners represent an opportunity to compete for prestigious NIH center and educational grants, including NIH-Clinical and Translational Science Awards (CTSA-designation), and Medical Scientist Training Program (NIH-MSTP) and additional T32 training grants. AICER sustainability will be fostered by existing investments by the MSU Foundation investments in translational incubator capacities such as the VanCamp Incubator alongside existing capacities at the McLaren/NCI Karmanos Cancer Institute to foster novel immunotherapies from the bench to the bedside. These efforts will be enhanced by existing MSU programs, such as the TSGTD, MTRAC, ADVANCE programs, start-up efforts of Spartan Innovations, Red Cedar Ventures, Michigan Rise Pre-Seed III Fund and the current capacities present at MSU supported biotechnology incubators. Finally, expanded MSU commitments to develop immunotherapeutics will resonate with many philanthropic individuals and institutions (Gates Foundation, Burroughs Wellcome Trust) who have similar aspirations to improve the greater health, and reduce global disease burden.