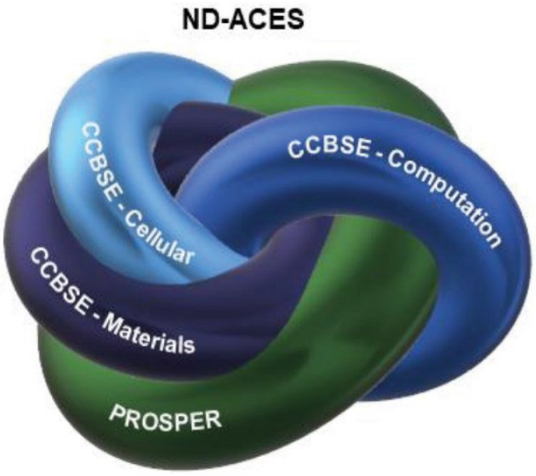
NSF EPSCoR RII Track-1 Strategic Plan 2020-2025



ND-ACES: New Discoveries in the Advanced Interface of Computation, Engineering, and Science

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ND EPSCoR

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Executive Summary

North Dakota (ND) EPSCoR's Strategic Plan details the conceptual, programmatic, and management framework for successfully accomplishing the goals of ND-ACES (New Discoveries in the Advanced Interface of Computation, Engineering, and Science), ND's National Science Foundation (NSF) Research Infrastructure Improvement (RII) Track-1 Cooperative Agreement. ND-ACES is a $24M five-year (July 1, 2020 – June 30, 2025) federal ($20M)/state ($4M) partnership of 11 institutions of higher education within the jurisdiction focused on understanding of biological and engineered materials biointerfaces.

ND-ACES capitalizes on and supports the continued growth in research capacity and capability at the two research universities (RUs; NDSU and UND), one master's college/university (MCU; Minot State University [MiSU]), three primarily undergraduate institutions (PUIs; Dickinson State University [DSU], Mayville State University [MaSU], and Valley City State University [VCSU]), and five tribal colleges/universities (TCUs; Cankdeska Cikana Community College [CCCC], Nueta Hidatsa Sahnish College [NHSC], Sitting Bull College [SBC], and Turtle Mountain Community College [TMCC] and United Tribes Technical College [UTTC]). ND-ACES will catalyze ND's research and computing capabilities by leveraging prior and new investments to create knowledge that expands ND's bioscience research, capacity, and expertise through the collaborative work of personnel at the above eleven institutions within a unified Center for Cellular Biointerfaces in Science and Engineering (CCBSE). The CCBSE has two integrated Pillars of scientific inquiry: 1) Materials Design at Biointerfaces; and 2) Cellular Systems at the Materials Interface; and a new 3) a TCU Pilot Pillar.

The impact and reach of ND-ACES' research efforts/intellectual merit are enhanced via the simultaneous and linked broader impact efforts of the Promoting Sustainable Partnerships in Education and Research (PROSPER) team. PROSPER activities span each of the eleven institutions listed above. The goals of these efforts will be achieved through the establishment of diverse and sustainable STEM education and professional development pathways and expanded bioscience partnerships and internships designed to enhance success in future federal funding and support the transformation of research into practical use via trained personnel and new products. PROSPER will also expand underserved (i.e., rural, inner city, or low income) and underrepresented (i.e., American Indians, Alaska Natives, Blacks, Hispanics, women, or persons with disabilities) participation, and inform the residents of ND.

Strategic Plan

Vision

ND-ACES will be the Northern Plain's leading scientific and educational driver in new and sustainable biosciences technologies; particularly in knowledge and translational activities in biointerfaces related to cancer progression and metastasis.

Mission

ND-ACES will contribute to cancer research in ways that have state, national, and international ramifications and underpin sustainable activities for a trained and diverse workforce and informed populace and lead to future efforts focused on new therapeutic solutions (beyond the scope of this effort).

Goal

Build capacity and innovation within the bioscience sector in sustainable fundamental, applied, and translational research broadening participation and economic engagement to diversify the state's economy.

Introduction

ND-ACES brings together 11 institutions of higher education within the jurisdiction to help drive the continued growth of the state's emerging biosciences ecosystem through a series of interdisciplinary and transdisciplinary research efforts and outreach activities. Participating institutions include:

Research Universities (RUs)
North Dakota State University (NDSU)
University of North Dakota

Primarily Undergraduate Institutions (PUIs)
Dickinson State University (DSU)
Mayville State University (MaSU)
Valley City State University (VCSU)

Master's college/university (MCU)
Minot State University (MiSU)

Tribal colleges/universities (TCUs)
Cankdeska Cikana Community College (CCCC)
Nueta Hidatsa Sahnish College (NHSC)
Sitting Bull College (SBC)
Turtle Mountain Community College (TMCC)
United Tribes Technical College (UTTC)

The Center for Cellular Biointerfaces in Science and Engineering (CCBSE) will use computational modeling to garner an improved interdisciplinary understanding of biological and engineered materials biointerfaces; expand expertise in novel cellular growth and analysis paradigms for mimicking the *in vivo* environment; catalyze research/computing capabilities; and, support the translation of research into use through products, partnerships, and collaborations with various stakeholders.

The reach and sustainability of CCBSE will be enhanced through a series of broader impact efforts by participants organized within the Promoting Sustainable Partnerships within Education and Research (PROSPER) network. Through PROSPER, ND-ACES provides diverse and sustainable STEM education and professional development pathways and expanded bioscience partnerships and internships designed to increase success in future federal funding and support the translation of research into use, broaden underserved (particularly rural and/or low-income students) and underrepresented (particularly American Indians, Hispanics, women, or persons with disabilities) participation, and inform ND's citizens. An overview of ND-ACES is in **Error! Reference source not found.**.

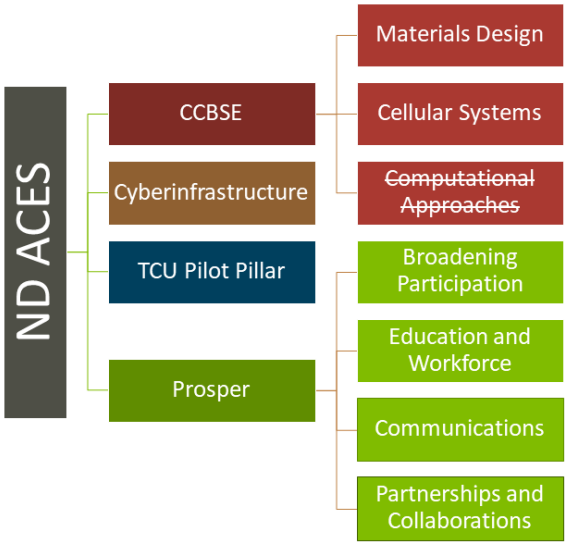

Figure 1. ND-ACES Structure (updated)

Primary Organizational Partners and Their Roles

CCBSE is fully integrated across two research Pillars: 1) Materials Design at Biointerfaces; and 2) Cellular Systems at the Materials Interface; with research expertise in Computation, Machine Learning, and Predictive Modeling embedded in each Pillar. Each CCBSE Pillar is also co-led by a NDSU and UND researcher. Collectively, the CCBSE Pillars will support the expansion of bioscience research capacity and advanced understanding of the biochemistry and cell biology of cancer cells and tumors (primary metastasis sites). A TCU Pilot Pillar/Element is being piloted starting in Year 4 to increase engagement and integration of TCU participants across all aspects of ND-ACES.

PROSPER provides education and experiences designed to build a diverse workforce, enhance partnerships and collaborations with various stakeholders, and inform the residents of ND. The four components of PROSPER are: 1) Education and Workforce Development (EWD); 2) Broadening Participation (BP); 3) Partnerships and Collaborations; and, 4) Communication and Dissemination.

The intellectual merit and broader impact efforts of ND-ACES, led by CCBSE and PROSPER respectively cross all

organizational partners.

Expected Benefits of Project to the Jurisdiction including the Jurisdiction's Academic Research and Education Infrastructure

The ND-ACES logic model (Table 1) outlines how the investments ND-ACES makes in existing and new personnel, high performance computing (HPC)/cyberinfrastructure (CI) systems, workforce, and partnerships will drive outcomes and create lasting jurisdictional impact. Key investments include equipment purchased by the ND EPSCoR Office prior to the start of the award (from state, non-match dollars) and Research Universities' commitment to provide the funding necessary to hire two new faculty associated with the CCBSE Materials Design at Biointerfaces Pillar (a need identified in the proposal development and outlined in more detail within Appendix D). ND- ACES investments provide the ability to conduct new research and outreach activities (outlined in the Project Implementation section of this document) designed to produce short-term outcomes within the five years of this RII Track-1 cooperative agreement. These efforts have been carefully designed to provide longer-term outcomes with sustained jurisdictional impacts that will help ND expand its economy and reach beyond commodity-based investments.

Table 1. ND-ACES Logic Model

	Investment	Activities	Participants	Short Term Outcome (5 yr)	Long Term Outcome (10 yr)	Impacts
Faculty/Research	Project Personnel, 2 new materials science faculty – 1 at each RU, and 2019 ND EPSCoR State Office laboratory equipment purchases at NDSU and VCSU	Synthesize, characterize materials; define 3D cell-matrix mechanisms; create large- scale cellular modeling; expand AI/ML expertise; report updates on research	Collaboration of ND-ACES team, seed grant awardees, joint RU biomedical/ engineering and other students, EAB, State Steering, medical/ health community	Create new knowledge that expands ND's bioscience research, capacity, and expertise; catalyze ND's research/ computing capabilities; increase success in federal funding; support translation of research into use; inform citizens	Effect sustainable engagement and support of project participants Inform local/ nationa research and stakeholder, community, and public	Northern Plains leader in new and sustainable biosciences technology advances
HPC/CI	Project HPC investments inHPC/CI system purchases at both RUs prior to ND-ACES	Train researchers, build state-wide access to equipment/HPC/ CI systems	ND-ACES, new CI facilitators at RUs, and CI campus staff		Expanded use of HPC/CI in PUI/MCU/TCU research and education	Sustainable, competent, and diverse state biosciences and bio- technology workforce from A.A. through Ph.D.
Woorkforce	Commitments made to bioscience/ STEM education and developing a diverse workforce pool	Strengthen bio-science/STEM ecosystem through mentoring; teacher professional development in rural/tribal/ underserved; training in research; NATURE; student teaching	Senior ND- ACES faculty to mentor early career faculty, graduate/ undergraduate students; rural/ underserved/ tribal K-12 teachers	Establish diverse and sustainable bioscience/ STEM education and professional development pathways; seek to broaden the participation of under- represented communities	Foster the ongoing development of a skilled, diverse workforce Positively impact state economy Supply research outcomes for growing/ new bioscience ventures and partners	Growing economic sector in bioscience industry with new partners, growing businesses, and expanded workforce opportunity
Partnerships	Investing in partnerships	Leverage/ recruit partners to expand research impact; add contract/ collaborative opportunities, and internships	ND-ACES personnel and ND/regional industry/ medical partners	Impact beyond the project with partnerships and expanded internships		
Communication and assessment throughout all elements						

ND-ACES milestone activities and metrics (outlined in the Project Implementation section) provide a pathway to ND-ACES outcomes that produce changes in the knowledge and capacities of the state (Table 5. CCBSE Timeline Activities, Milestones, Metrics and Anticipated Outcomes) and sustained positive impacts and growth as a result of these changes (Table 5. CCBSE Timeline Activities, Milestones, Metrics and Anticipated Outcomes). The outcomes of ND-ACES are the beneficial impacts on ND that will affect sustainable engagement, inform stakeholders, support ND's growing biosciences sector, and advance the development of a skilled workforce. The short- and long-term outcomes summarized within the ND-ACES logic model will improve the local economy for the citizens of ND, leading to jurisdictional impacts within the Northern Plains' growing biosciences sector.

Jurisdiction-wide impacts will be the result of the achievement of short-term and long-term outcomes all along the education and workforce continuum. ND-ACES will prepare the Northern Plains to be a leader in new and supportable biosciences technological developments. This commercial growth will impact the state by providing expanded workforce opportunities in a new industry.

Project Implementation

ND-ACES personnel will work collaboratively within and across the two CCBSE Research Pillars, the TCU Pilot Pillar, and the four PROSPER broader impact components (Figure 2). The RU HPCs, shown between the CCBSE and PROSPER groups, are instrumental to the operational work conducted in the areas of computation, machine learning, and predictive modeling; have training/outreach responsibilities to the MCU, PUIs, and TCUs; and, will play a role in expanding the STEM pathway through the hiring of CI interns.

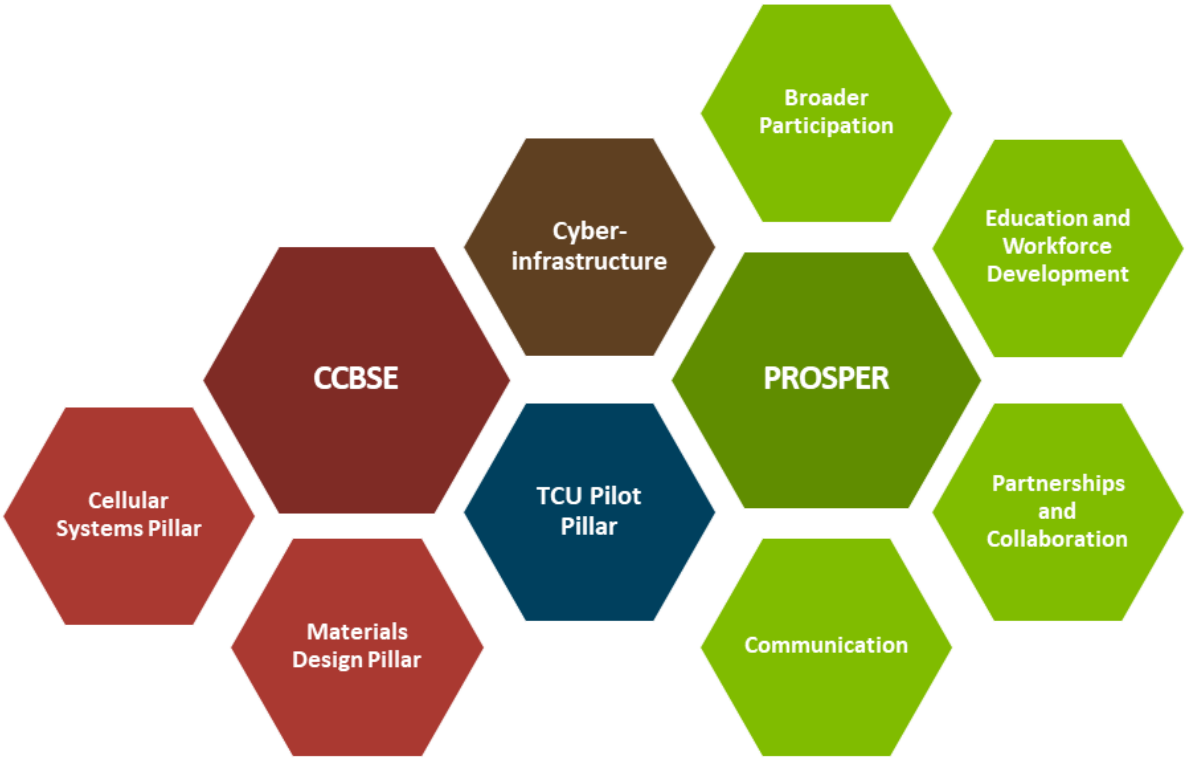

Figure 2. Interrelationship of project components

The ND-ACES overall work plan will be implemented along five integrated tracks:

1) Interdisciplinary and transdisciplinary research in biointerfaces (the interface between engineered and biological materials) that uses advanced research computing as a conduit for intellectual and translational advances.
2) Workforce training and broadened participation programming at all campuses to support North Dakota's biosciences industry.

3) Regional industry and medical entity partnerships that facilitate bioscience sector sustainability.
4) Advanced research computing to increase North Dakota researchers' expertise, with the research universities serving as solution providers.
5) Elevated public understanding of the economic impact of growing North Dakota's biosciences sector through strategic research investments as a result of data-sharing, communication, and outreach.

Overall CCBSE Implementation

The CCBSE activities link to ND-ACES tracks 1, 2, 3, and 4 and support the center's core goal of expanded bioscience research capacity in improved soft tissue and bone-mimetic scaffolds and models that create and increase the knowledge and advanced understanding of the biochemistry and cell biology of cancer cells and tumors. To broaden application of the foundational knowledge gained on metastasized cancer/tumors, the team will pursue developmental research to increase capacity and knowledge in the area of nanoparticle-based delivery systems (secondary goal; links to ND- ACES tracks 1, 2, 3, and 4). This secondary goal will provide a solid foundation for the future development of new therapeutic solutions (mid- to long-term outcome; outside the scope of this proposal) to address bone metastasized cancer. The CCBSE researchers collaborate across multiple disciplines of materials science engineering, cellular biology, and scientific computing.

The CCBSE goals will be reached by employing five Strategies:

1) Construct innovative 3D biocompatible structures of hard and soft tissues (core goal).
2) Design novel cell culture paradigms to accurately model *in vivo* tumor cell biology (core goal).
3) Provide a fundamental understanding of biointerfaces that adapts to biomedical and biotechnology research and translates to industry (core and secondary goals).
4) Use iterative computational learning to establish models capable of predicting cell responses on 3D biointerfaces (core goal).
5) Develop an understanding of polymer nanoparticles as a surrogate for vascular transport of effector molecules (secondary goal).

Each Pillar has a set of Pillar-specific goals and objectives, which when successfully addressed will lead to achieving CCBSE's core and secondary goals. CCBSE's success will be enabled by old and new investments, multidisciplinary coordination among nine institutions, and transdisciplinary growth of expertise and research capacity across each pillar.

CCBSE Materials Design Pillar

The Materials Design Pillar is focused on designing bio-inspired materials (hard and soft tissue) as platforms for the growth of cancer cells in the primary tumor site (soft tissue) and a metastatic bone site (hard tissue). The three goals of this Pillar are outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 2). The goals emphasize the foundational design principles of tissue-mimetic materials and nanoparticles. The results from the Cellular Systems Pillar and embedded computational approaches researchers will allow iterative improvement of the design principles for the materials research under this Pillar. Hence, the goals for the Materials Design Pillar are not hypothesis-driven.

This team will use three Tactics aligned with CCBSE Strategies 1, 3, 4, and 5 to successfully meet its Pillar-specific goals and objectives: 1) design novel soft materials that mimic tissues through layered chitosan-alginate systems (primary site of cancer) and hard materials that mimic bone through amino acid modified clays (secondary site - metastatic; Strategy 1); 2) develop a system for vascular surrogacy in 3D cocultures (Strategy 5); and, 3) integrate with the Cellular Systems Pillar and the embedded computational approaches researchers to produce a high throughput format for rational design of increasingly functional materials through the use of Pillar Liaisons (Strategies 3 and 4).

The workflow will follow an iterative cycle: 1) biosimilar and biocompatible materials will be selected for hard and soft tissue matrix designs; 2) polymer nanoparticles will be designed for vascular-like transport of effector molecules into the dense 3D cell cultures; 3) scaffolds and polymeric nanoparticles will be delivered to the Cellular Systems Pillar for assessing the effects of released effector molecules on the heterogeneous 3D culture

phenotypes for comparison to in vivo growth (studies from literature); 4) Cellular Systems Pillar feedback will be integrated with computation predictions; and, 5) predictive model output from the embedded computational researchers will direct modifications for specific material pore size, shape, organization, elasticity, and degradability over time for subsequent iterations.

Materials Design Pillar Goal 1.1: The team will develop porous bone-mimetic scaffolds to create interfaces with breast and prostate cancer cells and collaborate with the Cellular Systems Pillar to study the effects of the materials using cell phenotyping. Specifically, this goal is the selection of optimal hard materials as porous bone-mimetic scaffolds.

- **Materials Design Pillar Objective 1.1a:** Design and optimize nanoclay scaffolds.
- **Materials Design Pillar Objective 1.1b:** Characterize the scaffolds and demonstrate cancer cell growth

Materials Design Pillar Goal 1.2: The team will develop soft, polymeric scaffolds for the growth of prostate and breast cancer cells. Scaffold mechanics will be optimized using steered molecular dynamics (SMD) modeling efforts of the Computation team to help optimize the stress-strain characteristics of the scaffold material. As a result, the combined model outputs will inform the modulation of the concentrations of chitosan, (Chi) sodium alginate (Alg), and polygalactouronic acid (pgA) to achieve characteristics that support cancer cell cultures and enable the mechanical stability of the scaffold system. Specifically, this goal is the selection of optimal polymeric materials as soft tissue-mimetic scaffolds.

- **Materials Design Pillar Objective 1.2a:** Design and optimize soft polymeric scaffolds.
- **Materials Design Pillar Objective 1.2b:** Characterize the scaffolds and demonstrate cancer cell growth.

Materials Design Pillar Goal 1.3: The team will prepare polymersomes responsive to the hypoxic microenvironment of the 3D cultures of the cancer cells, and development of polymer- based fluorescent nanoparticles for cancer cell imaging. In collaboration with the Cellular Systems Pillar, the developed nanomaterials will be used to investigate the biochemical changes and apoptosis of the cancer stem cells in the hypoxic niches of the 3D cultures after exposure to a gene transcription (small organic molecule) inhibitor to inhibit the stemness.

- **Materials Design Pillar Objective 1.3a:** Design and develop stimuli-responsive polymeric materials as nanocarriers.
- **Materials Design Pillar Objective 1.3b:** Design and develop silicon quantum dots (QDs) and polymer-QDs hybrids for bioimaging.
- **Materials Design Pillar Objective 1.3c:** Design and test polymer nanoparticles for vascular surrogacy for use in 3D cocultures.

Table 2. Materials Design Pillar Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

Materials Design Pillar - Timeline of Activities Goal 1.1					
Objective 1.1a	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Prepare nanoclay scaffolds with amino acids for cancer cell growth	Prepare scaffolds based on prior studies	Optimize amino acid structure based on modeling, the loading amount, prepare two additional scaffolds, provide scaffolds to nanomaterials sub-group and Cellular Systems Pillar	Provide feedback to the embedded computational approaches researchers, optimize scaffold materials, provide the scaffolds for nanomaterials testing	Continue to prepare the optimized scaffold, provide them to Cellular Systems Pillar	Continue to prepare the optimized scaffold
Activity 2: Assist non-RU campuses involved in Activity 1 with compliance protocols	Assist with the initiation of conversations between non-RU faculty and RU campuses for the administration of necessary compliance protocols (IBC, MTAs)	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses
Activity 3: Prepare hard scaffolds with vascularization mimics using three different routes and select optimized methodology			Prepare hard scaffolds with 3 different routes to mimic vascularization	Continue prepare hard scaffolds with 3 different routes to mimic vascularization	Continue to prepare the “vascularized” hard scaffolds and select optimized scaffold
Objective 1.1b	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Characterize the scaffolds and culture of breast and prostate cancer cells	Mechanical characterization, biocompatibility testing, nanomechanics, metastatic breast and prostate growth	Continue with characterization, optimize cell spheroid growth, nanomechanics	Optimize scaffold and cancer cell growth conditions, nanomechanics	Continue to prepare the optimized scaffolds with cancer cells and patient-derived samples	Continue to prepare the optimized scaffolds with cancer cells and patient-derived samples

Materials Design Pillar - Timeline of Activities Goal 1.2					
Objective 1.2a	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Prepare soft scaffolds from Chi, Alg, and PgA, characterize the scaffolds	Prepare soft material scaffolds from two polymers	Optimize the scaffolds by altering the polymer composition and molecular weights, provide feedback to embedded computational approaches researchers and scaffolds for nanomaterials testing and Cellular Systems Pillar	Based on the feedback from the computational researchers, and Cellular Systems Pillars, optimize scaffold materials, provide scaffolds for nanomaterials testing and Cellular Systems Pillar	Continue to prepare the optimized scaffolds, provide scaffolds for nanomaterials testing and Cellular Systems Pillar	Continue to prepare the optimized scaffolds, provide scaffolds for nanomaterials testing and Cellular Systems Pillar
Activity 2: Assist non-RU campuses involved in Activity 1 with compliance protocols	Assist with the initiation of conversations between non-RU faculty and RU campuses for the administration of necessary compliance protocols (IBC, MTAs)	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses
Activity 3: Prepare a small combinatorial library (24-48) of soft scaffolds from natural, synthetic, or hybrid polymers			Prepare 24 soft scaffolds from cross-linked polymers or layer-by-layer assembly of linear polymers	Continue to prepare the three optimal scaffolds or prepare another set of 24 new scaffolds (if necessary)	Continue to prepare the three optimal scaffolds
Activity 4: Prepare soft scaffolds with vascularization mimics				Modify the three optimal scaffolds for selective polymer hydrolysis or photodegradation	Continue to prepare the “vascularized” scaffolds
Objective 1.2b	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Determine mechanical properties, cell viability in the scaffolds, analyze gene expression profiles	Mechanical characterization, nanomechanics, biocompatibility testing, breast and prostate cancer cell growth	Continue with characterization, optimize tumoroid growth, nanomechanics	Optimize scaffold and cancer cell growth conditions, nanomechanics	Continue to prepare the optimized scaffolds with cancer cells	Continue to prepare the optimized scaffolds with cancer cells
Activity 2: Assist non-RU campuses	Assist with the initiation of conversations between	Ensure that all necessary compliance protocols are	Ensure that all necessary compliance protocols are	Ensure that all necessary compliance protocols are	Ensure that all necessary compliance protocols are

involved in Activity 1 with compliance protocols	non-RU faculty and RU campuses for the administration of necessary compliance protocols (IBC, MTAs)	in place at the non-RU campuses	in place at the non-RU campuses	in place at the non-RU campuses	in place at the non-RU campuses
Activity 3: Determine breast and prostate cancer cell growth in the scaffolds			Determine which scaffolds are supporting cancer cell growth for 7 days	Determine the three optimal soft scaffolds for breast cancer cells and three for prostate cancer cells and transfer them to Cellular Studies Pillar for detailed biochemical studies	Continue to prepare the three optimal scaffolds for biochemical studies and nanoparticle testing

Materials Design Pillar - Timeline of Activities Goal 1.3					
Objective 1.3a	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Investigate pH responsive properties	Identify poly(silyl ether)s as pH-responsive materials	Modify and improve polymer structure and nanoparticles (NPs) properties	Make light- responsive polymeric materials for controlled release and optimize NPs fabrication	Prepare lanthanide binding polymeric materials and fabricate NPs	Prepare multi- responsive polymeric materials and fabricate NPs
Activity 2: Test biocompatibility	Fabricate and characterize NPs	Test toxicity of the polymers and NPs	Test the cell survival rate when the light-responsive polymer	Test biocompatibility of the lanthanide binding polymer NPs	Evaluate polymer- NPs biocompatibility *in vitro*
Activity 3: Examine cell culture usage		Determine optimal hard and soft scaffolds in *in vitro* studies	Determine optimal cancer cell identification using the polymer NPs in 3D cells	Image 3D hard and soft scaffolds using the prepared NPs	Determine cellular applications of the NPs in soft and hard scaffolds
Objective 1.3b	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Selection of the best precursor	Selection of precursors for making silicon quantum dots (QDs)	Modify quantum dot surface through chemical reactions	Selection of polymer to improve quantum dot's quantum yield	Making quantum dot and polymer hybrids	Prepare the optimized hybrid of quantum dots-polymer in 3D scaffold
Activity 2: Testing feasibility	Optimization of QD's optical signals in cancer cells	Test toxicity and biocompatibility of the QDs	Test the selected polymers in bioimaging	Test the biocompatibility of hybrids in 3D cell Culture	Identification of intra cellular reactions using the hybrids in soft and hard scaffold

Activity 3: Cancer cells imaging	Application of the QDs in cancer cell imaging	Application of the QDs for cancer cell identification	Application of the polymers in cancer cell imaging	Application of the hybrids in 3D cell culture	Application of the hybrids in 3D cell culture
Objective 1.3c	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Design, preparation, and testing of hypoxia- responsive polymer nanoparticles	Synthesize a set of diblock copolymers	Optimize release properties of anticancer drugs using cancer cells on hard and soft material scaffolds	Select the optimal nanoparticle, demonstrate tumor targeting and tumor penetration on the hard and soft material scaffolds	Determine the effects of the released drugs on the cancer cells, mechanistic studies	Based on the mechanistic studies, select and demonstrate the efficacy of the optimal variant
Activity 2: Design, preparation, and testing of pH-responsive polymer nanoparticles	Synthesize a set of triblock copolymers with conjugated anticancer drugs	Optimize pH- mediated release of the anticancer drugs	Select the optimal nanoparticle, demonstrate tumor targeting and penetration on the hard and soft scaffolds	Mechanistic studies on the pH-triggered drug release from polymer backbone, cellular effects of the released drugs	Based on the mechanistic studies, select and demonstrate the efficacy of the optimal variant

Materials Design Pillar - Milestone metrics					
Materials Pillar	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 1.1a	Prepare 3 different biocompatible scaffolds	Develop 2 nanoclay scaffolds incorporating the amino acids and evaluate additional one hard scaffold	Select one optimal scaffold (critical)	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3
Objective 1.1b	Complete characterizations on the scaffolds prepared in 1.1a. Demonstrate growth of MCF7 and PC3a cells	Demonstrate growth of MDA-MB-231 and PC3 cells and compare with MCF 7 and PC3a cells	Demonstrate tumoroid formation (critical)	Time evaluation of tumor growth on optimized scaffolds	The tumors on the scaffold are genetically and morphologically similar
Objective 1.2a	Prepare 3 different biocompatible scaffolds	Prepare 3 different biocompatible scaffolds	Select 1 optimal scaffold (critical)	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3 (nanomaterials testing)	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3
Objective 1.2b	Complete characterizations on the scaffolds prepared in 1.1a.	Demonstrate growth of MDA-MB-231 and PC3 cells	Demonstrate tumoroid formation (critical)	Time evaluation of tumor growth on optimized scaffolds	The tumors on the scaffold are genetically and morphologically similar

	Demonstrate growth of MCF7 and PC3a cells	and compare with MCF 7 and PCa			
Objective 1.3a	Prepare 5 different PSEs and characterize nanoparticles	Demonstrate drug release in the tumoroids cells in scaffolds	The nanoparticles release drugs within desirable time in scaffolds (critical)	Prepare 3 different polymers, demonstrate imaging in the tumor cells in 3D scaffolds	Released drugs kill majority of cancer cells in scaffold/models
Objective 1.3b	QDs with stable signal in cells	Demonstrate good biocompatibility with cancer cell lines	Identify two polymers (critical)	Make two polymer-SiQD hybrids	Demonstrate optimized imaging
Objective 1.3c	Prepare 3 polymers with different hypoxia-responsive units, characterize nanoparticles	Prepare two additional polymers, demonstrate drug release in the tumoroids on hard and soft scaffolds	The nanoparticles release drugs within 2 hours in the hard and soft scaffolds (critical)	Release drugs kill at least 80% of the breast and prostate cancer cells on the scaffolds (critical)	Released drugs kill at least 80% of the cancer cells in the patient-derived model
	Prepare 3 polymers, characterize nanoparticles	Demonstrate drug release in the tumoroids on hard and soft scaffolds	The nanoparticles release drugs within 2 hours in the hard and soft scaffolds (critical)	Release drugs kill at least 80% of the breast and prostate cancer cells on the scaffolds (critical)	Released drugs kill at least 80% of the cancer cells in the patient-derived model

Anticipated Outcomes of Materials Design Pillar		
Across this Pillar	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Goal 1.1	Create new knowledge that expands ND's bioscience research, capacity, and expertise; increase success in federal funding; support translation of research into use.	Effect sustainable engagement and support of project participants; foster the ongoing development of a skilled, diverse workforce.
Goal 1.2	Create new knowledge that expands ND's bioscience research, capacity, and expertise; increase success in federal funding; support translation of research into use.	Effect sustainable engagement and support of project participants; foster the ongoing development of a skilled, diverse workforce.
Goal 1.3	Create new knowledge that expands ND's bioscience research, capacity, and expertise; increase success in federal funding; support translation of research into use.	Effect sustainable engagement and support of project participants; foster the ongoing development of a skilled, diverse workforce.
Overall Outcomes	Increase success in federal funding; support translation of research into use.	Supply research outcomes for growing/new bioscience ventures and partners; positively impact state economy

CCBSE Cellular Systems Pillar

The Cellular Systems Pillar is focused on increasing the capacity and expertise of the CCBSE researchers in basic and translational use of *in vivo*-like 3D cell cultures, which will ultimately (long-term outcome) allow the team to partner with regional health care providers to serve as a resource for personalized medicine approaches to cancer. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 3). The goal empathizes the creation of innovative models of heterogeneous, multi-cell 3D research cultures using multiple soft and hard material scaffolds designed by the Materials Design Pillar and refined by embedded computational approaches researchers. Hence, the goals for the Cellular Systems Pillar are not hypothesis-driven.

This team will focus on three strategies to successfully meet its objectives: 1) validate multiple soft and hard tissue scaffolds as appropriate for *in vivo*-like 3D cultures (Strategy 2); 2) generate heterogeneous multicellular 3D cultures with improved *in vivo*- like tissue by sequential addition of cell types (macrophages, fibroblasts, etc.) with the cancer cell lines (Strategy 3); and, 3) model patient-derived organoid (PDO) systems and compare with the commonly used and commercially available mouse patient-derived xenograft (PDX) systems to develop a high throughput system that combines materials and modeling to create an improved culture paradigm for human *in vivo* relevance.

The workflow will initially focus on prostate and breast cancer cell lines grown in both soft and hard tissue biomaterial scaffolds is designed to grow different cell types and tuned to optimize adhesion, porosity, and stiffness or evaluation of cellular response. These tests will allow better definition of the role of biointerfaces and 3D structures including those of a hypoxic nature, on complex multi-cell behaviors such as *in vitro* cell growth and differentiation, cancer growth/ metastatic progression, and multicellular tissue engineering. Research will then focus on creating innovative models of heterogeneous, multi-cell 3D research cultures using multiple soft and hard material scaffolds designed by the Materials Design Pillar and refined by embedded computational approaches researchers.

Cellular Systems Pillar Goal 2.1: The team will use various biomaterial formulations (test scaffolds) developed by the Materials Design Pillar to develop a robust pipeline for both morphometric and molecular analysis for the purpose of validating whether characteristics of the test scaffolds are biocompatible and can be used to answer fundamental questions about cancer cells' behavior in response to different microenvironmental inputs. Then, using systematic analysis, the team will determine which materials have the most potential for high throughput content testing and, in conjunction with embedded computational approaches researchers feed computation-driven models to optimize the materials design of the scaffolds. Specifically, this goal is to create innovative models of heterogeneous, multi-cell 3D research cultures.

- **Cellular Systems Pillar Objective 2.1:** Increase CCBSE capacity/expertise in basic and translational use of *in vivo*-like 3D cell cultures, which will ultimately (long-term outcome) allow the team to partner with regional health care providers to serve as a resource for personalized medicine approaches to cancer.

Table 3. Cellular Systems Pillar Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

Cellular Systems Pillar - Timeline of Activities					
Objective 2.1	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Validate multiple soft and hard tissue scaffolds	Standardize validation protocols using existing materials and compare to 2D culture Create protocol database Establish common reagent database Preliminary validation of 1st generation materials (viability, hypoxic responses, EMT/MET status) Submit data to Materials Design Pillar and embedded computational approaches researchers	Secondary validation of 1st generation materials (migration, adhesion, surface contact analysis) Preliminary validation of 2nd generation materials (viability, hypoxic responses, EMT/MET status) Update SOPs and reagents database Submit data to Materials Design Pillar and embedded computational approaches researchers	Tertiary validation of 1st generation materials (focal adhesion, migration, Transcriptomics) Secondary validation of 2nd generation materials (migration, adhesion, surface contact analysis) Update SOPs and reagents database Nanomaterial delivery assessment Submit data to Materials Design Pillar and embedded computational approaches researchers	Quaternary validation of 1st generation materials (chromatin accessibility and modification assays) Tertiary analysis of 2nd generation materials Nanomaterial delivery assessment Submit data to Materials Design Pillar and embedded computational approaches researchers Update SOPs and reagents database	Quaternary validation of 2nd generation materials (chromatin accessibility and modification assays) Nanomaterial delivery assessment Submit data to Materials Design Pillar and embedded computational approaches researchers Update SOPs and reagents database
Activity 2: Generate heterogeneous multicellular 3D cultures with improved *in vivo*-like tissue	Establishment of viable co-culture conditions of tumor cell lines and macrophages or fibroblasts Preliminary validation of 1st generation materials (viability, hypoxic responses, EMT/MET status) Data exchange with Materials Design Pillar and embedded computational approaches researchers Create protocol database	Comparison of co-cultures to tumors Establishment and maintenance of inter-cell contact sites between seeded populations Morphometric analysis Submit data to Materials Design Pillar and embedded computational approaches researchers Update SOPs and reagents database	Continued establishment and maintenance of inter-cell contact sites between seeded populations (via microscopic evaluation) Continued Morphometric analysis Submit data to Materials Design Pillar and embedded computational approaches researchers Update SOPs and reagents database	TAM analysis Gene expression profiling Nanocarrier assessments Continued Submit data to Materials Design Pillar and embedded computational approaches researchers Update SOPs and reagents database	Continued gene expression profiling Continued Nanocarrier assessments, including interruption of TAM/TAF/Cancer cell interactions Submit data to Materials Design Pillar and embedded computational approaches researchers Update SOPs and reagents database

	Establish common reagent database Submit data to Materials Design Pillar and embedded computational approaches researchers				
Activity 3: Develop a high throughput system that combines materials and modeling to create an improved culture paradigm for human *in vivo* relevance	Procure and maintain PDX models of breast and prostate cancer from commercial sources. Isolation of PDX tumors and establishment of growth as organoids (XOs) in culture Preliminary comparisons of XO tissues using viability assessments, and determination of phenotypes between 2D, scaffold, and *in vivo* maintenance conditions Establish clinical partnerships to obtain additional patient materials for organoid establishment Submit data to Materials Design and embedded computational approaches researchers Update SOPs and reagents database	Detailed analysis of XO tissues in maintaining viability and proliferative capacity of explanted tissue when maintained upon the next- generation scaffolds. Establishing long- term (greater than 1 month) viable patient-derived organoid (PDO) lines. Optimization of standard procedures as needed Preliminary PDO assessments and testing success in maintaining viability and proliferative capacity of explanted tissue (greater than 1 month) when maintained upon the next- generation scaffolds Submit data to Materials Design Pillar and embedded computational approaches researchers Update SOPs and reagents database	Continued XO explant grafting and comparison between scaffold and *in vivo* phenotypes Hypoxia- acidification analysis of XO scaffold cultures XO growth in the absence and presence of TAM/TAF seeding, comparative growth analysis Detailed analysis of PDO tissues in maintaining viability and proliferative capacity of explanted tissue when maintained upon the next- generation scaffolds Submit data to Materials Design and embedded computational approaches researchers Update SOPs and reagents database	Continued TAM/TAF seeding and comparative analysis of XO behavior to purified cell cultures Preliminary assessment of nanocarrier mediated pharmacologic interventions on TAMs-PDO communication Continued organoid assessments and testing success in maintaining viability and proliferative capacity of explanted tissue (greater than 1 month) when maintained upon the next-generation scaffolds Microenvironment assessments of XO and PDO scaffold cultures Submit data to Materials Design and embedded computational approaches researchers Update SOPs and reagents database	Gene expression profiling comparisons of XO/PDO cultures to *in vivo* growth conditions Continued assessment of nanocarrier mediated pharmacologic interventions on TAMs-PDO communication Submit data to Materials Design and embedded computational approaches researchers Update SOPs and reagents database
Activity 4:	Assist with the initiation of conversations between non-RU faculty and RU	Ensure that all necessary compliance protocols are in place	Ensure that all necessary compliance protocols are	Ensure that all necessary compliance protocols are	Ensure that all necessary compliance protocols are

Assist non-RU campuses involved in Activity 1 with compliance protocols	campuses for the administration of necessary compliance protocols (IBC, MTAs)	at the non-RU campuses	in place at the non-RU campuses	in place at the non-RU campuses	in place at the non-RU campuses

Cellular Systems Pillar - Milestone metrics					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 2.1	Activity 1: Validation SOP creation using existing materials and 2D culture Protocol database creation based on validation Reagent database creation based on validation Completion of preliminary evaluation of provided first generation materials (baseline viability and growth, initial hypoxic response and EMT/MET signatures) e.g., 85% similar to 2D and matrigel cultures Data exchange with Materials Design and embedded computational approaches researchers	Activity 1: Completion of secondary validation on provided 1st generation materials Completion of preliminary validation on provided 2nd generation materials Continued data exchange with Materials Design and embedded computational approaches researchers	Activity 1: Completion of tertiary validation, provided 1st generation materials Completion of secondary validation, provided 2nd generation materials Completion of preliminary nanomaterial delivery assessments Continued data exchange with Materials Design and embedded computational approaches researchers	Activity 1: Completion of quaternary validation, provided 1st generation materials Completion of tertiary validation, provided 2nd generation materials Completion of secondary nanomaterial delivery assessments Continued data exchange with Materials Design and embedded computational approaches researchers	Activity 1: Completion of quaternary validation, provided 2nd generation materials Completion of tertiary nanomaterial delivery assessments Continued data exchange with Materials Design Pillar and embedded computational approaches researchers
	Activity 2: A protocol for growth of multi- cellular cultures on provided hard and soft 1st generation materials Continued data exchange with Materials Design and	Activity 2: An optimized co-culture protocol for growth on provided hard and soft 1st generation materials A co-culture protocol for growth on provided hard and soft 2nd generation materials	Activity 2: An optimized co- culture protocol for growth on provided hard and soft 2nd generation materials Establish phenotype marker criteria (e.g., morphology and proteins) for co- cultures on provided hard and soft 2nd	Activity 2: Optimized protocol for nanocarrier design and drug delivery to 3D- cultures Genomic and transcriptomic characterization of co-cultures on hard and soft materials	Activity 2: Demonstration of nanocarrier-mediated drug delivery effects on co-culture viability and the established cellular phenotype markers Genomic and transcriptomic characterization of nanocarrier-mediated drug

	embedded computational approaches researchers	Establish phenotype marker criteria (e.g., morphology and proteins) for co-cultures on provided hard and soft 1st generation materials to compare to *in vivo* tumors Continued data exchange with Materials Design and embedded computational approaches researchers	generation materials to compare to *in vivo* tumors Protocol for nanocarrier design and drug delivery to 3D- cultures Continued data exchange with Materials Design and embedded computational approaches researchers	Continued data exchange with Materials Design and embedded computational approaches researchers	delivery to co- cultures on hard and soft materials Continued data exchange with Materials Design and embedded computational approaches researchers
	<u>Activity 3</u>: Successful establishment of PDX colonies as source of test materials Establishment and maintenance of PDX explant tissues (XOs) in scaffold cultures with greater than 1-month viability Development of standard protocols for sustained growth of XO tissues on next generation material scaffolds Continued data exchange with Materials Design and embedded computational approaches researchers	<u>Activity 3:</u> Complex Analysis of phenotypic criteria indicating XO tissues on scaffolds exhibit growth and gene expression characteristics similar to *in vivo* conditions Faster and more efficient growth of XO tissues under scaffold conditions when compared to *in vivo* maintenance Successful growth of PDO on the next-generation scaffolds Continued data exchange with Materials Design and embedded computational approaches researchers	<u>Activity 3:</u> Response to hypoxia/acidification by XO/scaffolds that mimics the *in vivo* tumor environment Development of a standard protocol for successful co-culture of XO with TAM/TAF on scaffolds Complex Analysis of phenotypic criteria indicating PDO tissues on scaffolds exhibit growth and gene expression characteristics similar to *in vivo* conditions Faster and more efficient growth of PDO tissues under scaffold conditions when compared to *in vivo* maintenance Continued data exchange with Materials Design and embedded computational approaches researchers	<u>Activity 3:</u> Successful long-term culture of PDO with TAM/TAF on scaffolds Presentation of miniature tumor microenvironment by PDO/TAM/TAF on scaffolds that is similar to TME of PDX tumor Continued data exchange with Materials Design Pillar and embedded computational approaches researchers	<u>Activity 3:</u> Changes in PDO/scaffold growth behavior, genetics, and morphology upon the intervention of TAM- PDO communication Presentation of drug resistance characteristics by explanted tumoroids that maintain similar properties to those observed *in vivo* Continued data exchange with Materials Design Pillar and embedded computational approaches researchers

Anticipated Outcomes of Cellular Systems Pillar		
Across this Pillar	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Goal 2.1	We will establish an interdisciplinary collaborative team across the state engaging faculty, graduate, and undergraduate students at NDSU, UND, the PUIs, and TCUs focused on developing our expertise in use of cell line and patient-based organoid cultures.	The established interdisciplinary partnerships will expand to include faculty, industry, and institutions beyond the initial ND- ACES. New programs, departments, or centers will formalize based upon the established expertise.
Overall Outcomes	Create new knowledge that expands ND's bioscience research, capacity, and expertise; catalyze ND's research/ computing capabilities; increase success in federal funding; support translation of research into use; inform citizens; establish diverse and sustainable bioscience/STEM education and professional development pathways; seek to broaden underserved participation; and impact beyond the project with partnerships and expanded internships.	Effect sustainable engagement and support of project participants; inform local/national research and stakeholder community, and public; expanded use of HPC/CI in PUI/MCU/TCU research and education; foster the ongoing development of a skilled, diverse workforce; positively impact state economy; supply research outcomes for growing/new bioscience ventures and partners.

CCBSE Computational Approaches Pillar

In response to the NSF Site Visit in Year 4, a decision was made to integrate the computational approaches researchers into the Materials Design and Cellular Systems Pillars. The metrics, milestones and outcomes associated with the Computational Pillar will remain in this section of the Strategic Plan to simplify tracking.

The Computational Approaches Pillar is focused on developing computational predictive models to provide useful design rules for creating biointerfaces. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 4). The goal emphasizes the development of an *in-silico* platform to predict tumor growth through the enhancement of connected learning, knowledge, and application across multiscale modeling, machine learning platforms, and experimental biomaterials and cellular data.

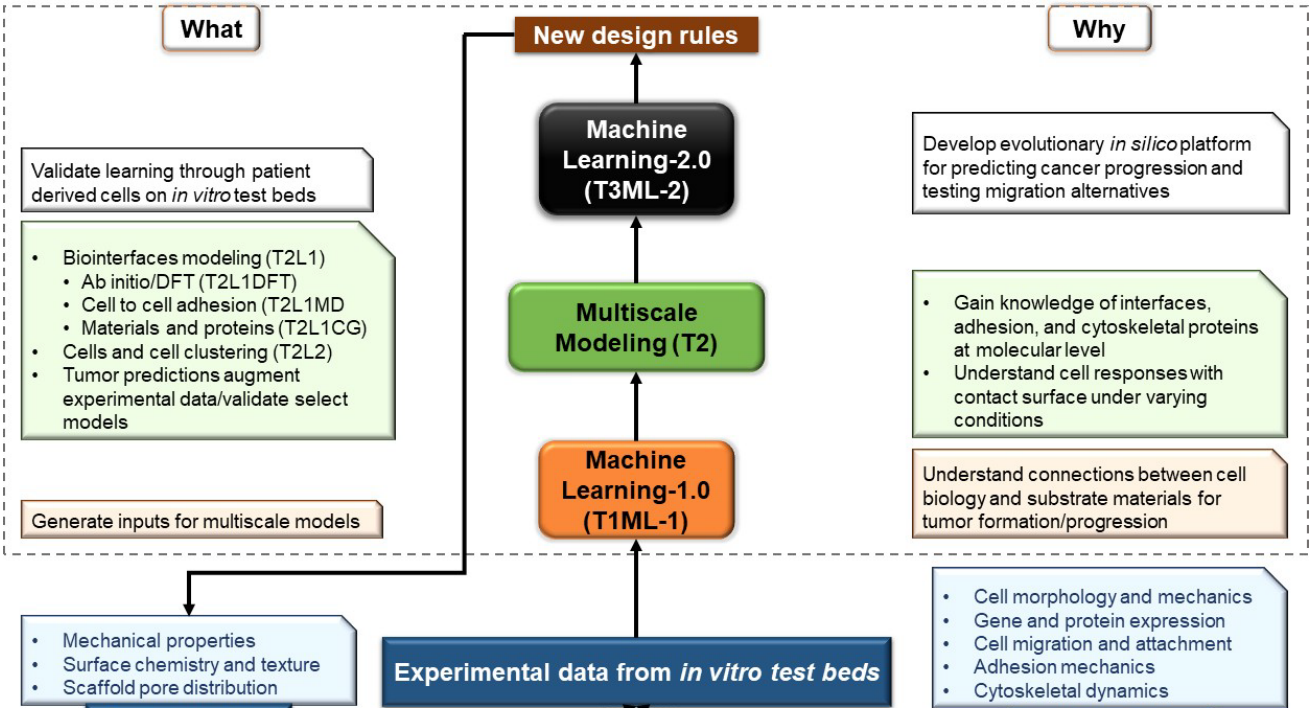

Figure 3. Iterative Tactics of Computational Activities

This team will use four interdependent Tactics (Figure 3) aligned with CCBSE Strategies 1, 3, and 4 to successfully meet the objective of the Pillar. *Due to the intricate interdependencies of these Tactics, the activity milestones in this section are presented with additional detail*:

1) Machine learning-1 (T1ML-1) to understand connections between cellular biology and substrate materials.
2) Multiscale modeling (T2 is further delineated in the next paragraph) from nano- to macroscale.
3) Machine learning-2 (T3ML-2) that will use the data from T1ML-1 and T2 to developthe *in-silico* platform.
4) Computationally-driven materials design (T4).

The workflow will follow an iterative cycle (Figure 3)) and research will be informed, via a reciprocal cycle of modeling of the cancer progression from the initial stages of cell attachment (primary site), to tumor formation, migration to secondary site (metastasis), and growth in *in vitro* testing. The computationally created design rules can provide fundamental information to enhance the predictability of the cellular responses to various material

surfaces and characteristics. The team, assisted by CI personnel, will build a collaborative research framework and proof-of-concept machine learning platform trained by experimental data gathered from cancer cell behavior on soft and hard tissue testbeds and computer simulations, resulting in multiscale models to predict disease progression.

Computational Approaches Pillar Goal 3.1: Conduct interdisciplinary/transdisciplinary research in biointerfaces (the interface between engineered and biological materials) that uses advanced research computing as a conduit for intellectual and translational advances.

Specifically, this goal is the development and enhancement of computational approaches in the prediction of breast and prostate cancer tumor growth.

- **Computational Approaches Pillar Objective Pillar 3.1**: Enhance connected learning, knowledge, and application across multiscale modeling, machine learning platforms, and experimental biomaterials and cellular data, which will result in an evolutionary in-silico platform to predict tumor growth.

Table 4. Computational Approaches Pillar Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

Computational Approaches Pillar- Timeline of Activities					
Objective 3.1	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Machine learning to understand cellular and materials connections	C7-ML Bone Site Image recognition of cancer cells and bone cells based on existing databases and validate with 2D experiments C8-ML Primary Site Image recognition of cancer cells from other cells in tissues from databases and validate with 2D experiments	C7-ML Bone Site Image recognition of cell migration, lustering and tumor formation Role of material formulation on cellular growth in 3D C8-ML Primary Site Image recognition and prediction of cell migration, clustering and tumor formation Role of material formulation on cellular growth in 3D Build Machine learning capacity at a PUI and determine Y3-5 PUI researcher activity	C7-ML Bone Site Identification of patterns in gene, protein expressions and other assay data and their relationship to tumor formation. Role of material properties formulation on cellular growth in 3D C8-ML Primary Site Identification of patterns in gene, protein expressions and other assay data and their relationship to tumor formation Role of material Properties formulation on cellular growth in 3D and prediction of optimal properties Build Machine learning capacity at a PUI. Actively collaborate with ML researchers at NDmage recognition of cell migration, clustering, and breast cancer tumor formation. Identify the role of material formulation on cellular growth in 2D Develop new methods to Interpret trained deep	Identification of patterns in the gene, protein expressions, and other assay data and their relationship to breast cancer tumor formation. Role of material properties formulation on cellular growth in 2D	

			neural networks used for cancer image recognition and characterization. Propose AI-based pathfinding algorithms that could be used to quantify interactions between biological entities in an environment		
Activity 2: Multiscale modeling with Materials Design Pillar	M1-Ab-initio/DFT 10 unnatural amino acids-evaluation of partial charges. Evaluation of interactions with clay composite. Evaluation of interactions with two polymers M2-Ab-initio/DFT MD model for primary site composite: evaluation of partial charges and binding sites M3-Molecular Dynamics MD and SMD simulations of existing PCN: Evaluation of mechanical properties at the molecular scale M4-Coarse Graining Development of CG model for PCN and evaluation of mechanical properties	M1-Ab-initio/DFT Computational evaluation of additional/designer modifier molecules Evaluation of interactions with clay composite Evaluation of interactions with two polymers M2-Ab-initio/DFT MD model for primary site composite with up to three formulations and densities: evaluation of partial charges and binding sites M3-Molecular Dynamics MD and SMD simulations of PCNs using second candidate amino acid: Evaluation of mechanical properties at the molecular scale M4-Coarse Graining Development of CG model for PCN with second candidate amino acid with varying polymer characteristics	M1-Ab-initio/DFT Computational evaluation of additional/ designer modifier molecules Evaluation of interactions with clay composite Evaluation of interactions with two polymers M2-Ab-initio/DFT MD model for primary site composite with up to three additional formulations and densities: evaluation of partial charges and binding sites M3-Molecular Dynamics MD and SMD simulations of PCNs using third candidate amino acid: Evaluation of mechanical properties at the molecular scale M4-Coarse Graining Development of CG model for PCN with third candidate amino acid with varying polymer characteristics		

	M4-Coarse Graining Development of CG model for PCN and evaluation of mechanical properties M5-Finite Element Modeling FEM model of PCN and evaluating constitutive responses M6-Computational Fluid Dynamics CFD models for scaffolds with degradation	M4-Coarse Graining Development of CG model for PCN with second candidate amino acid with varying polymer characteristics M5-Finite Element Modeling FEM model of PCN with second candidate amino acid. Evaluating constitutive responses M6-Computational Fluid Dynamics CFD models for scaffolds with new formulations, synthesis parameters and degradation characteristics	M4-Coarse Graining Development of CG model for PCN with third candidate amino acid with varying polymer characteristics M5-Finite Element Modeling FEM model of PCN with third candidate amino acid. Evaluating constitutive responses M6-Computational Fluid Dynamics CFD models for scaffolds with new formulations, synthesis parameters and degradation characteristics		
Activity 3: Multiscale modeling with Cellular Systems Pillar	C1-Ab-initio/DFT Bone site Identification and characterization of Integrin domains interacting with clay. Identification and characterization of a representative Integrin-domains interacting with polymer. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C1-Ab-initio/DFT Bone site Identification and characterization of cell-cell adhesion molecule (E-Cadherin) domains at cadherin junctions and at the cell anchor site	C1-Ab-initio/DFT Bone site Identification and characterization of representative Integrins (covering 4 classes)-domains interacting with clay Identification and characterization of representative Integrins (covering 4 classes)-domains interacting with polymer. Evaluating the charge redistribution/ transfer over the substrate-protein interface		C1-Ab-initio/DFT Bone site Studies on the influence of various ions on the adhesion of integrins with clay. Studies on the influence of various ions on the adhesion of integrins with polymers. Evaluating the charge redistribution/ transfer over the substrate-protein interface

	C2-Ab-initio/DFT Primary site Identification and characterization of a representative Integrin-domains interacting with polymers 1 and 2. Identification and characterization of Integrin domain interacting with composites. Evaluating the charge redistribution/transfer over the substrate-protein interface	C2-Ab-initio/DFT Primary site Identification and characterization of cell-cell adhesion molecule (E-Cadherin) domains at cadherin junctions and at the cell anchor site.	C2-Ab-initio/DFT Primary site Identification and characterization of representative Integrins (covering 4 classes)-domains interacting with polymers 1 and 2 Identification and characterization of representative Integrins (covering 4 classes)-domains interacting with composites. Evaluating the charge redistribution/ transfer over the substrate-protein interface.	C2-Ab-initio/DFT Primary site Identification and characterization of additional Integrins (covering 4 classes) - domains interacting with polymers 1 and 2 Identification and characterization of additional Integrins (covering 4 classes)-domains interacting with composites. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C2-Ab-initio/DFT Primary site Studies on the influence of various ions on the adhesion of integrins with polymers. Evaluating the charge redistribution/ transfer over the substrate-protein interface
	C3-Molecular Dynamics Mechanics of Actin and actin dynamics Model construction of representative Integrin	C3-Molecular Dynamics Mechanics of Actin and actin dynamics with polymerization/depolymerization genes. Mechanics of representative Integrin on PCN and polymers	C3,C9,C10-Molecular Dynamics Mechanics of E-Cadherin junctions Mechanics of representative Integrin molecules on PCN and polymers	C3, C9, C10-Molecular Dynamics Mechanics of additional Integrin molecules on PCN and polymers	
	C4-Coarse Graining CG model of multiple integrins with PCN: evaluation of the mechanics of the interphase	C4-Coarse Graining CG model of multiple integrins with primary site polymers: evaluation of the mechanics of the interphase	C4-Coarse Graining CG model of six integrins with bone site and primary site polymers: evaluation of the mechanics of the interphase	C4-Coarse Graining CG model of additional six integrins with bone site and primary site polymers: evaluation of the mechanics of the interphase	
	C5-Finite Element Modeling Development of cancer cell model on PCN	C5-Finite Element Modeling Simulations of experiments to evaluate cell substrate adhesion	C5-Finite Element Modeling Simulations of experiments to evaluate cell substrate adhesion, incorporating actin		

			properties from MD and updated properties of interphase obtained from CG, to develop continuum adhesion models. Development of FEM models for Cell-Cell adhesion	C11-Multibody dynamics simulations integrated with Finite Element Modeling of cell migration on substrates	C11-Multibody dynamics simulations integrated with Finite Element Modeling Modeling of cell clustering on substrates
Activity 4: Machine learning to develop the in-silico platform	C6-Computational Fluid Dynamics CFD models for scaffolds with cellular growth of MSCs	C6-Computational Fluid Dynamics CFD models for scaffolds with cellular growth of MSCs cocultured with prostate cancer cells	C6-Computational Fluid Dynamics CFD models for scaffolds with cellular growth of MSCs cocultured with breast cancer cells	C6-Computational Fluid Dynamics Parametric studies on scaffold and bioreactor geometry using CFD models with cellular growth of MSCs cocultured with prostate and breast cancer cells to aid in the development of scaffold pore geometry and bioreactors	C6-Computational Fluid Dynamics CFD models and simulations for cell transport to and through scaffolds to mimic cancer cell adhesion during metastasis
			C12, C14, C15, C16, C18-ML Bone Site Development and training of ML system with cancer progression (cell- cell adhesion and cell-substrate adhesion) data, biointerface parameters from multiscale modeling and experimental data (images and gene/protein expressions, material properties) from Cellular	C12, C14, C15, C16, C18-ML Bone Site Training of ML system with cancer progression (cell- cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data (images and gene/protein expressions, material properties) from Cellular Systems Pillar and	C12, C14, C15, C16, C18-ML Bone Site Additional training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data (images and gene/protein expressions, material properties) from Cellular

			Systems Pillar and Materials Design Pillar	Materials Design Pillar (e.g., material properties, surface characteristics, chemistry, porosity, 3D confinement, adhesion proteins, interacting protein domains, ECM characteristic). Evaluate accuracy of predictions with separate datasets	Systems and Materials Design Pillars. Evaluate accuracy of predictions with separate datasets
			C13, C14, C15, C16, C18-ML Primary Site Development and training of ML system with cancer progression (cell- cell adhesion and cell-substrate adhesion) data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars	C13, C14, C15, C16, C18-ML Primary Site Training of ML system with cancer progression (cell- cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars. Evaluate accuracy of predictions with separate datasets	C13, C14, C15, C16, C18-ML Primary Site Additional training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars. Evaluate accuracy of predictions with separate datasets Primary site: Development and training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars

Activity 5: Design Rules				C17, C12, C13, C14, C15, C16, C18- Formulation of draft design rules for materials and scaffolds Interrogating the ML system to develop design rules for materials and scaffolds used for cancer progression experiments	C17, C12, C13, C14, C15, C16, C18- Formulation of updated design rules for materials and scaffolds Interrogating the ML system along with feedback from experiments using rules from previous iteration to develop design rules for materials and scaffolds used for cancer progression experiments

Computational Approaches Pillar - Milestone metrics					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 3.1	Activity 1: Bone site - Classification Accuracy >=0.4 Primary site - Datasets generation from composite data sources for ML model training & identification of best performing ML algorithms for image recognition of the 4 types of cancer cells on bone stem cells	Activity 1: Bone site - Classification Accuracy >=0.5 Primary site - 1) Datasets generation for the cellular growth-material formulation using data from experimentalists and other collaborators Identification of high performing ML algorithms on image recognition for cell migration and clustering	Activity 1: Bone site – Classification Accuracy >=0.6 Primary site - Determination of patterns & optimal properties via ML		
	Activity 2: M1-Ab-initio/DFT- Obtain binding interface information at the atomistic level	Activity 2: M1-Ab-initio/DFT - Obtain binding interface information at the atomistic level	Activity 2: M1-Ab-initio/DFT - Obtain binding interface information at the atomistic level		

	M2-Ab-initio/DFT - Building atomistic models to understand interfaces	M2-Ab-initio/DFT - Building atomistic models to understand interfaces	M2-Ab-initio/DFT - Building atomistic models to understand interfaces		
	M3-Molecular Dynamics - Successful model development	M3-Molecular Dynamics - Successful model development; compare mechanical properties with nanoindentation with results within an order of magnitude	M3-Molecular Dynamics - Successful model development; compare mechanical properties with nanoindentation with results within an order of magnitude		
	M4-Coarse Graining - CG model of clay developed; CG model of polymer developed; CG force field validated	M4-Coarse Graining - CG model of clay developed; CG model of PCN developed; CG force field validated	M4-Coarse Graining - CG model of clay developed; CG model of PCN developed; CG force field validated		
	M5-Finite Element Modeling - Successful model development	M5-Finite Element Modeling - Successful model development. Elastic modulus within an order of magnitude of nanoindentation/ macroscale experiments	M5-Finite Element Modeling - Successful model development. Elastic modulus within an order of magnitude of nanoindentation/ macroscale experiments		
	M6-Computational Fluid Dynamics - Range of model parameters for degradable scaffold established; Models for cell interaction and migration developed	M6-Computational Fluid Dynamics - Range of model parameters for degradable scaffold established; Models for cell interaction and migration developed	M6-Computational Fluid Dynamics - Multi- resolution CFD model for scaffold developed; Local distribution of shear stresses in complex geometries validated		
	Activity 3: C1-Ab-initio/DFT Bone site - Creation of reduced models for integrin domains, nanoclays, and polymers	Activity 3: C1-Ab-initio/DFT Bone site - Validation and improvement of reduced models for nanoclays and polymers interacting with Integrin domains	Activity 3: C1-Ab-initio/DFT Bone site	Activity 3: C1-Ab-initio/DFT Bone site	Activity 3: C1-Ab-initio/DFT Bone site
	C2-Ab-initio/DFT - Building atomistic models to model bio-interfaces	C2-Ab-initio/DFT - Building atomistic models to	C2-Ab-initio/DFT Primary site - Building atomistic models to model bio interfaces	C2-Ab-initio/DFT Primary site	C2-Ab-initio/DFT Primary site - Building atomistic models to

		represent/model bio-interfaces			represent/model bio-interfaces
	C3-Molecular Dynamics - Successful model development of actin and integrin. Obtaining mechanical properties of actin from SMD	C3-Molecular Dynamics - Successful model development of actin and depolymerization genes; integrin on surfaces; Obtaining mechanical properties of actin and integrin from SMD	C3, C9, C10-Molecular Dynamics - Determine the mechanical properties of E-Cadherin junctions; Determine the mechanical properties of the integrin molecules on PCN and polymers	C3, C9, C10-Molecular Dynamics - Determine the mechanical properties of the additional six integrin molecules on PCN and polymers	
	C4-Coarse Graining - CG model of integrins developed; Integrins-PCN interfacial interactions captured by CG modeling	C4-Coarse Graining – Continued	C4-Coarse Graining - Mechanical properties of interphases obtained with CG modeling for six integrins and varying interfacial design parameters	C4-Coarse Graining - Mechanical properties of interphases obtained with CG modeling for additional six integrins with extended interfacial design parameters	C11-Multibody dynamics simulations integrated with Finite Element Modeling - Successful development of multibody dynamics simulations model for cell migration
	C5-Finite Element Modeling - Successful development of FEM cell model	C5-Finite Element Modeling – Successful development of FEM cell model on substrate; incorporation of adhesion parameters from C1 through C4; calibration with experiments	C5-Finite Element Modeling - Successful development of FEM cell model on substrate and Cell-Cell adhesion model; incorporation of adhesion parameters from C1 through C4; calibration with experiments		
	C6-Computational Fluid Dynamics - Continuum representation of actin networks in cell membrane developed; Cell adhesion model developed and validated	C6-Computational Fluid Dynamics - Models for cell migration on a clay substrate developed and validated	C6-Computational Fluid Dynamics - CFD simulations of flows around groups of cancer cells populated on a substrate	C6-Computational Fluid Dynamics - Using measures such as cell density and alignment to validate CFD models for cellular migration on the surface of scaffold	C6-Computational Fluid Dynamics - Full- scale simulation of cell migration in a bio- reactor. Resolution provides from millimeter to micrometer (three order of magnitudes). Flow distribution and shear stresses will be provided in all pores of the scaffold

	Activity 4: NA	Activity 4: NA	Activity 4: C12, C14, C15, C16, C18-ML Bone Site - Obtain the knowledge to construct preliminary rules of designing new scaffold materials for bone site. Classification Accuracy >=0.6	Activity 4: C12, C14, C15, C16, C18-ML Bone Site - Obtain the knowledge to construct fundamental rules of designing new scaffold materials for bone site; Classification Accuracy >=0.7; Generate simulated datasets under perturbed conditions and use those datasets to build ML models for cell migration; ML predictive models derived; ML model predictions validated against modeling and experiments	Activity 4: C12, C14, C15, C16, C18-ML Bone Site - Accuracy >=0.8; ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for bone site
				C12, C14, C15, C16, C18-ML Bone Site - ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for bone site	
			C13, C14, C15, C16, C18-ML Primary Site - Obtain the knowledge to construct preliminary rules of designing new scaffold materials for primary site. Statistical and reduced order models will be developed to predict where cancer cells migrate and grow	C13, C14, C15, C16, C18-ML Primary Site - ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for primary site	C13, C14, C15, C16, C18-ML Primary Site - Accuracy >=0.8; ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for primary site
	Activity 5: NA	Activity 5: NA	Activity 5: NA	Activity 5: C17, C12, C13, C14, C15, C16, C18- Parameter-structure-property relationships drawn	Activity 5: C17, C12, C13, C14, C15, C16, C18-

				for design of materials; optimized design parameters identified; develop design rules (geometry, material properties) for fluid flows in degradable scaffolds	Formulation of updated design rules for materials and scaffolds - Parameter-structure-property relationships refined for design of materials; materials design parameters finalized; validate design rules and establish optimized ranges of parameters

Computational Approaches Pillar - Anticipated Outcomes		
Across this Pillar	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Goal 3.1	Build capacity - researchers and students in computational areas of multiscale modeling and machine learning targeted towards biomedical research. Development of robust computational models spanning multiple length scales for tissue engineered scaffolds and cells seeded on scaffolds. This will lead to enhanced understanding of cell adhesion mechanisms on materials and the understanding of mechanisms that influence mechanical properties of materials and scaffolds. Development of ML tools/processes to predict cellular behavior on tissue engineering materials and scaffolds leading to proof of concept for using ML for predicting cancer progression in *in vitro* systems.	Increased workforce in the region trained in leveraging computations for discoveries and design in biomedical fields. Increased graduate student enrollment in programs such as biomedical engineering, materials and nanotechnology, computer science with research focus in biomedical areas. New research center(s) such as ERCs, MERSECs focused on translational biomedical research driven by computations. Support biomedical companies (startups and existing) with technologies, IP and workforce. Collaborate with physicians to validate and revise predictive models and findings with patient data for potential deployment for real world applications.
Overall Outcomes	Enhanced understanding of biointerfaces via computations and their role on cellular response and development of design rules for materials design.	Predictive tools for cancer progression.

CCBSE - Overall Summary

As previously stated, the core goal of the CCBSE is to expand bioscience research capacity in improved soft tissue and bone-mimetic scaffolds and models that create and increase the knowledge and advanced understanding of the biochemistry and cell biology of cancer cells and tumors. This goal will be accomplished through the successful completion of the Materials Design Pillar, Cellular Systems Pillar, and embedded computational approaches (previously Computational Approaches Pillar) metrics outlined above in Tables 2, 3, and 4. Additional CCBSE outcomes that will be obtained through the combined efforts of the three Pillars are outlined in Table 5. Success of the core goal lays the foundation for the secondary goal to increase capacity and knowledge in the area of nanoparticle-based delivery systems by pursuing developmental research, which is a long-term goal for the CCBSE and not a part of the ND-ACES project.

Core Goal: Expand bioscience research capacity in improved soft tissue and bone-mimetic scaffolds and models that create and increase the knowledge and advanced understanding of the biochemistry and cell biology of cancer cells and tumors

Secondary Goal: Increase capacity and knowledge in the area of nanoparticle-based delivery systems by pursuing developmental research.

Table 5. CCBSE Timeline Activities, Milestones, Metrics and Anticipated Outcomes

CCBSE **Specific milestones – Core Goal**					
CCBSE Strategies	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Strategy 1: Construct innovative 3D biocompatible structures of hard and soft tissues	Successful completion of Materials Design and embedded computational approaches (previous Computational Approaches Pillar) yearly activities and metrics				
Strategy 2: Design novel cell culture paradigms to accurately model *in vivo* tumor cell biology	Successful completion of Cellular Systems Pillar yearly activities and metrics				
Strategy 3: Provide a fundamental understanding of biointerfaces that adapts to biomedical and biotechnology research and translates to industry	Successful completion of Materials Design, Cellular Systems, and embedded computational approaches (previous Computational Approaches Pillar) yearly activities and metrics				
Strategy 4: Use iterative computational learning to establish models capable of predicting cell responses on 3D biointerfaces	Successful completion of Materials Design, Cellular Systems, and embedded computational approaches (previous Computational Approaches Pillar) yearly activities and metrics				

CCBSE **Specific milestones –Secondary Goal**					
CCBSE Strategies	Year 1	Year 2	Year 3	Year 4	Year 5
Strategy 4: Use iterative computational learning to establish models capable of predicting cell responses on 3D biointerfaces	Outside the scope of ND-ACES. However, knowledge gained in ND-ACES (Years 1-5) will serve as the basis for this long-term strategy				
Strategy 5: Develop an understanding of polymer nanoparticles as a surrogate for vascular transport of effector molecules	Outside the scope of ND-ACES.				

Overall milestone metrics for CCCBSE, in addition to those outlined in Tables 3, 4, and 5	
Number of new hires	2
Total number of peer-review publications	140
Number of collaborative products/outputs (one senior author from two or more ND-ACES institutions)	70
Total number of conference presentations by CCBSE senior personnel	90
Total number of submitted research proposals (PI/Co-PI from two or more ND-ACES institutions)	50
Number of submitted collaborative proposals	25
Number of CAREER proposals submitted	2-4
Total external research funding (million $) – 5-year total is cumulative	$25M
Number of projects funded with private sector partners	12
Number of graduate students trained (some may be counted in multiple years)	140
Number of conference presentations by graduate students (oral and poster)	120
Number of undergraduate students trained (some may be counted in multiple years)	70
Number of conference presentations by undergraduate students (oral and poster)	80
Seed Funding: seed funding support of $60,000 in Translational Research Initiative Project and an additional $101,655 in other research opportunity support – 5-year total is cumulative	$161,655
Number of CCBSE research participant meetings (10 - 12 / year depending on need)	50

Anticipated Outcomes of CCBSE		
Across the CCBSE	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Meet CCBSE's Core Goal	Create new knowledge that expands ND's bioscience research, capacity, and expertise; catalyze ND's research/ computing capabilities; increase success in federal funding; support the translation of research into use; and have impact beyond the project with partnerships and expanded internships.	Effect sustainable engagement and support of project participants and supply research outcomes for growing/new bioscience ventures and partners.

PROSPER Implementation

Expanding North Dakota's emerging biosciences capacity through a STEM-enabled, well- trained workforce positions ND-ACES as North Dakota's leading scientific and educational resource and will signify successful completion of this important work. PROSPER efforts incorporate both faculty and students at the 11 participating institutions in collaborative research, early career development, education enhancement, and outreach to increase the abilities of early career faculty, increase advanced scientific computing capabilities, and broaden the participation and number of STEM undergraduate and graduate students. North Dakota's K-12 sectors are also crucial to a sustainable ND STEM pathway; thus, another key component will be education and outreach in rural and tribal K-12 schools. Teachers, particularly those in grades 6-12, will engage in professional development activities where they will learn about tools to expose and engage their students in biosciences inquiry. Additionally, to bring the new knowledge and companion products to industry, focused activities will build or expand on existing collaborative industry/medical partnerships. Finally, a suite of communication activities will engage, inform, and educate ND stakeholders and citizens, as well as national audiences about ND-ACES scientific and outreach efforts. PROSPER is comprised of four sections/elements: 1) EWD; 2) BP; 3) Partnerships and Collaborations; and, 3) Communication and Dissemination.

PROSPER Education and Workforce Development (EWD)

EWD will facilitate a variety of activities that grow knowledge, motivate innovation, and develop talent in materials engineering, cell biology, and computational sciences with special emphasis on the inclusive excellence of underrepresented groups (e.g., women, and racial and ethnic minorities) along the education/career continuum. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 6).

Working in close conjunction with all ND-ACES participants, this initiative supports faculty professional development, student training, and K-12 student bioscience, engineering, and computational exposure. This group's efforts link to ND-ACES tracks 2, 4, and 5 (which are adopted as the Strategies for EWD) and integrate with the CCBSE goals.

EWD Element Goal 4.1: Strengthen North Dakota's bioscience/STEM ecosystem by building a diverse pool of competitive researchers, skilled workers, effective educators, and engaged students.

- **EWD Element Objective 4.1a:** Retain/advance CCBSE's early-career faculty and graduate students in bioscience/STEM careers and disciplines, particularly those from underrepresented groups (e.g., women, and racial and ethnic minorities).
- **EWD Element Objective 4.1b:** Engage/develop K- 16 student interest in bioscience/STEM careers and disciplines, particularly those from underrepresented groups (e.g., women, and racial and ethnic minorities).

Table 6. EWD Element Timeline of Activities, Milestones, Metrics, and Anticipated Outcomes

EWD Element - Timeline of Activities					
Objective 4.1a	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Early Career Faculty Mentoring Program	Set baseline for Early Career Faculty professional/ technical skills, self- efficacy, persistence intentions, retention, sense of belonging and scholarly productivity. Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. Gather information from ECF about their mentorship and professional development needs. Identify mentor training materials and/or programs	Two new faculty will be hired. Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. PROSPER personnel (at least 2) will engage in training and/or independent study in mentorship best practices via the CIMER Project (https://cimerproject.org/) (Summer-Fall 2021). CIMER Project Trained PROSPER personnel will then train 25% ND ACES CBBSE Faculty in mentorship best practices	Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. CIMER Project Trained PROSPER personnel will then train 25% ND ACES CBBSE Faculty in mentorship best practices	Hold regular Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty	Hold regular Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty
Activity 2: Early Career Faculty Professional Development Activities	Identify or develop in-person and Web- based ECF professional development activities	Continued	Continued	Continued	Continued
Activity 3: Student Research Training Groups (RTG)	Establish student mentor-mentee relationships and train students in research and technical scientific	Student mentor-Mentee relationships will be revisited, creating new relationships for new	Continued	Continued	Continued

	communication skills & set baselines for student professional/ technical skills, self-efficacy, persistence intentions, retention, sense of belonging, and scholarly productivity	students and revising ones that necessitate changes, and transitioning graduate students from mentee to mentor as appropriate			
Activity 4a: Graduate Student Cyber-Infrastructure	Graduate students will receive CI training and support	Continue to provide CI support to graduate students and conduct a Cyberinfrastructure (CI) Needs Survey of the ND-ACES CCBSE pillar (Computational, Materials, and Cellular) senior personnel (CCBSE researchers) and their graduate students	Continue to provide CI support to graduate students and based on the results of the Y2 survey and input from the CCBSE Computational Approaches Pillar Leads, CCAST (NDSU's HPC center) and CRC (UND's HPC center) will: 1) each develop a new, or customize an existing, CI workshop, which will be offered a min of at least once per year and 2) provide CI training to CCBSE faculty researchers and graduate students	Continued	Continued
Activity 4b: STEM Teaching Assistantship		Doctoral and/or Masters students receive and complete teaching assistantships at TCUs/PUIs/MCU	Continued	Continued	Continued
Objective 4.1b	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**

Activity 1: Distributed Research Experience for Undergraduates (dREU)	Distributed REU students placed. IRB will be written	Continued	Continued	Continued	Continued
Activity 2: Engage grade 6-12 students in Nature/Sunday Academy	Set baselines for Grade 6-12 students (i.e., Nature/Sunday Academy participants) beliefs and attitudes about, interests in, and intentions to pursue bioscience/STEM disciplines	Increased numbers over baseline	Increased numbers over prior year		
Activity 3: Training of Rural and tribal K-12 teachers in the use of PROSPER bioscience modules	Plan and start developing PROSPER bioscience modules	Module 1 implemented, Module 2 developed, and K-12 teachers trained	Module 1 refined, Module 2 implemented, and K-12 teacher training continued	Module 1 disseminated, Module 2 refined, and K-12 teacher training continued	Modules 1 and 2 disseminated and K- 12 teacher training continued
Activity 4: Pre- service STEM teachers will engage in rural/tribal student teaching experiences	Establish pilot program that places preservice student teachers in rural/ tribal schools in the Spring 2021	Expand program to all pre-service teacher candidates at ND-ACES affiliated RUs, PUIs, and MCU in Fall 2021. Place two Preservice Student teachers in rural/tribal schools in Fall 2021 and Spring 2022	Continued	Continued	Continued

	EWD Element - Milestone metrics				
Across this Element	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 4.1a	Activity 1: ECFs retained. Set baselines.	Activity 1: ECFs retained. 1 new faculty member hired at NDSU and 1 new faculty	Activity 1: ECFs and new hires retained. Meet/ exceed baselines. Monthly Pillar	Activity 1: ECFs and new hires retained.	Activity 1: ECFs and new hires retained.

	Monthly Pillar meetings held between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. Information gathered from ECF about their mentorship and professional development needs	member hired at UND. Meet/ exceed baselines. Monthly Pillar meetings held between CCBSE research leads and faculty. Minimum of two EWD Personnel trained and prepared to facilitator training for all ND-ACES CCBSE faculty in mentorship best practices (Summer- Fall 2021). Train 25% ND ACES CBBSE Faculty in mentorship best practices by June 30, 2022	meetings held between CCBSE research leads and faculty. Train an additional 25% of ND-ACES CCBSE Senior Faculty in mentorship best practices by June 30, 2023	Meet/exceed baselines. Regular Pillar meetings held between CCBSE research leads and faculty	Meet/exceed baselines. Regular Pillar meetings held between CCBSE research leads and faculty
	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 2 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 3 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 3 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 3 PD activities); track engagement with PD activities with goal that participation rates meet or exceed the rates of the previous year	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 2 PD activities); track engagement with PD activities with goal that participation rates meet or exceed the rates of the previous year
	Activity 3: 10 mentor/mentee pairs will be established; mentor/ mentee pairs will meet monthly; mentee individual development plan created; 50% of RTG students present work at one regional/national meeting; set baselines	Activity 3: 10 mentor/ mentee pairs will be maintained or established; mentor/ mentee pairs will meet monthly; mentee individual development plan created; 80% of students present work at one regional/national meeting; 75% of students publish (first author) paper	Activity 3: 10 mentor/ mentee pairs will be maintained or established; mentor/ mentee pairs will meet monthly; transition from mentee to mentor for graduate students progressing; mentee individual development plan created; 80% of students present work at one regional/national meeting;	Activity 3: Maintain central communication site for Interaction between students across the state. Develop list of professional development activities available and disseminated to students on a monthly basis (alternatively develop and implement 6 PD activities); track engagement with PD activities	Activity 3: 1Maintain central communication site for Interaction between students across the state. Develop list of professional development activities available and disseminated to students on a monthly basis (alternatively develop and implement 6 PD activities); track engagement with PD activities.

		prior to graduation; meet/ exceed baselines	75% of students publish (first author) paper prior to graduation; meet/exceed baselines	Track Students presenting work at regional/national meetings; student's authorship on papers	Track Students presenting work at regional/national meetings; student's authorship on papers
	Activity 4a: 30% of the total participants are trained	Activity 4a: 80% response from CCBSE researchers and graduate students to the CI Needs Survey	Activity 4a: 2 (1 from CCAST and 1 from CRC) new or customized CI workshops developed Both workshops offered at least once during Y3	Activity 4a: 2 (1 from CCAST and 1 from CRC) new or customized CI workshops developed Both workshops offered at least once during Y4	Activity 4a: 2 (1 from CCAST and one from CRC) new or customized CI workshops developed Both workshops offered at least once during Y5
			10% of CCBSE researchers and graduate students participate in the Y3 workshop or other CI training programs	10% of CCBSE researchers and graduate students participate in the Y4 workshop or other CI training programs	10% of CCBSE researchers and graduate students participate in the Y5 workshop or other CI training programs
	2 CI assistantships offered; 2 CI GRAs hired	2 CI GRAs hired	2 CI GRAs hired	2 CI GRAs hired	2 CI GRAs hired
	Activity 4b: THIS PROGRAM HAS BEEN MOVED TO Y2 DUE TO COVID-19	Activity 4b: Explore virtual options for doctoral student assistants Reallocate unused funding to additional TCU/PUI/MCU faculty time.	Activity 4b: 1-2 GTAs hired Incorporate virtual options into the program	Activity 4b: 1-2 GTAs hired Continued	Activity 4b: 1-2 GTAs hired Continued
	Activity 5: N/A	Activity 5: 95% of participants presenting	Activity 5: 95% of participants presenting	Activity 5: Meet/exceed previous year's percentage of participants presenting	Activity 5: Meet/exceed previous year's percentage of participants presenting
Objective 4.1b	Activity 1: 6 dREU students complete research, and present at the state conference and undergraduate research showcase	Activity 1: 12 dREU students complete research and present at the state conference and undergraduate research showcase	Activity 1: 12 dREU students complete research, and present at the state conference and undergraduate research showcase	Activity 1: Track post experience (STEM Career/Graduate School) of dREU students who complete research, and track number of dREU students who present at undergraduate research	Activity 1: Track post experience (STEM Career/Graduate School) of dREU students who complete research, and track number of dREU students who present at undergraduate research

				showcase or appropriate conference.	showcase or appropriate conference.
	Activity 2: Baselines set	Activity 2: Meet/exceed baselines	Activity 2: Meet/exceed prior year's numbers		
	Activity 3: Module 1 developed	Activity 3: Baselines number of teachers reached set via Module 1. Module 2 developed	Activity 3: Meet/exceed prior year's training numbers via Lesson plan 1 and 2	Activity 3: Meet/exceed prior year's training numbers	Activity 3: 100 total teachers trained over 5- year period
	Activity 4: 2 pre- service teachers trained and placed in Spring 2021 semester	Activity 4: 2 pre-service teachers trained each semester (Fall/Spring); 2 pre-services teachers placed each semester	Activity 4: 2 pre-service teachers trained each semester; 2 pre-services teachers placed each semester	Activity 4: 2 pre-service teachers trained each semester; 2 pre- services teachers placed each semester	Activity 4: 2 pre-service teachers trained each semester; 2 pre- services teachers placed each semester

	EWD Element - Anticipated Outcomes	
Across this Element	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Objective 4.1a	Establish diverse and sustainable bioscience/STEM education and professional pathways for early career and graduate students in ND-ACES, particularly those from underrepresented groups (e.g., women and racial ethnic minorities) and establish CI and college teaching opportunities for STEM graduate students.	Foster ongoing development of skilled and diverse bioscience/STEM workforce in the state of North Dakota through continued engagement and support of early career faculty and graduate students and expand use of cyberinfrastructure across the state through continued training of graduate students in this area.
Objective 4.1b	Establish diverse and sustainable bioscience/STEM education and professional pathways for K-16 students throughout the state of ND, particularly those from rural and tribal communities.	Foster ongoing development of skilled and diverse bioscience/STEM workforce through sustained engagement and support of K-16 students and K-12 teachers in North Dakota.
Overall Outcomes	Establish mentoring programs and professional development activities as a means of improving early career faculty and graduate students' professional/technical skills, self-efficacy, intentions to persist in the field, actual retention in the field, sense of belonging and scholarly productivity; establish research training experiences that bolster K-16 students' interests in bioscience/STEM with hopes of broadening their participation in	Impact the state's economy and expand bioscience research and education to schools beyond the RUs

	bioscience/STEM education and career opportunities, particularly those from underrepresented groups; establish student teaching experience in rural and tribal communities that promotes bioscience/STEM activities and increases the number of qualified STEM teachers in these communities; establish professional development opportunities for rural and tribal K-12 teachers focused on increasing their proficiency in bioscience/STEM education.	

PROSPER Broadening Participation (BP)

The BP initiative includes all ND-ACES participants in supporting American Indians and other underserved groups along the bioscience's pathway.

The team will increase the participation of underrepresented/underserved groups engaged in bioscience education and disciplines. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 7).

This group's efforts link to ND-ACES tracks 1, 2, 4, and 5 and integrate with the CCBSE goals.

BP Element Goal 5.1: Open pathways in North Dakota's bioscience sector for increased interest, access, and contribution by underrepresented/underserved groups.

- **BP Element Objective 5.1:** Increase the participation of all groups engaged in bioscience education and careers.

Table 7. Broadening Participation Element Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

Broadening Participation Element - Timelines of Activities					
Objective 5.1	Year 1	Year 2	Year 3	Year 4	Year 5
Activity 1: TCU bioscience students will conduct outreach in their local K-12 schools via bioscience lesson plans	Establish a library of K-12 STEM Lesson plans from NATURE Sunday Academy STEM Modules-	Continued 6-12 grade STEM teachers identified for Y3 and TCU student involvement planned or post-associate assistantships	Continued Fall 2022 and Spring 2023 TCU students identified and introduced to 6-12 grade STEM teachers 6-12 grade STEM teachers track the number of TCU student/6-12 grade student interactions 6-12 grade STEM teachers provide feedback on TCU student involvement 6-12 grade STEM teachers identified for Y4 and TCU student involvement planned based on prior year's feedback		
Activity 2: Support engagement in biosciences at the B.S. level (particularly for AI)	Engagement in biosciences at the B.S. level.	Continued	Continued	Continued	Continued
Activity 3: TCU bioscience faculty will be offered	Enhanced interdisciplinary collaborations and	Continued	Continued		

research techniques and equipment training	increased retention and advancement of faculty				
Activity 4: TCU camps for middle and high school kids at the four partnering TCUs	TCU NATURE coordinators will conduct summer camps at the four partnering TCUs	Continued	Continued	Continued	Continued
Activity 5: Sunday Academies for middle and high school kids at the four partnering TCUs	TCU NATURE coordinators will be site coordinators for Sunday Academy bioscience learning modules conducted at four TCUs	Continued	Continued	Continued	Continued
Activity 6: Bridge camps for graduating high school seniors at the four partnering TCUs	TCU NATURE coordinators will be site coordinators for bridge camps at the four partnering TCUs	Continued	Continued		
Activity 7: University Summer Camp for participants from the four partnering TCUs	NDSU and UND will have site coordinators for the University Summer Camps	Continued	Continued	Continued	Continued

Broadening Participation Element - Milestone metrics					
Across this Element	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 5.1	2 TCU students deliver the bioscience lessons to 40 students	Activity 1: 5 additional ND-ACES related STEM lesson plans 2 TCU students deliver STEM lessons to 60 students.	Activity 1: 5 additional ND-ACES related STEM lesson plans 2 TCU students deliver STEM lessons to 60 students.	.	

	3 NATURE students matriculating into STEM degrees (either AS or above)	4 NATURE students completing STEM degrees.	4 NATURE students completing STEM degrees		
	Activity 2: Plan research assistantships for juniors and seniors.	Activity 2: 2-3 students will have received research assistantships as juniors and seniors or post-associate assistantships	Activity 2: 2-3additional students will have received research assistantships as juniors and seniors and 1 student will have completed their B.S. degree or post-associate assistantships	Activity 2: 2-3additional students will have received research assistantships as juniors and seniors or post-associate assistantships and 1 additional student will have completed their B.S. degree	Activity 2: 7-10 students will have received research assistantships as juniors and seniors or post-associate assistantships and 3 of those will have completed their B.S. degree over 5 years
	Activity 3: One TCU faculty will visit CCBSE collaborators and learn a research technique/learn a HPC technique/expand knowledge in a Pillar area	Activity 3:	Activity 3: One additional TCU faculty will visit CCBSE collaborators and learn a research technique/learn a HPC technique/expand knowledge in a Pillar area		
		Survey for TCU STEM faculty re: training preferences developed and distributed	Continued		
		Preferences prioritized	Continued		
		Collaborating institutions' faculty requested to provide training in selected areas	Continued		
		One training video produced and released to TCU faculty	Continued		
	Activity 4 120 participants	Activity 4: 140 participants	Activity 4: 140 participants	Activity 4: 140 participants	Activity 4: 680 participants over 5 years
	Activity 5: 350 participants	Activity 5: 350 participants	Activity 5: 350 participants	Activity 5: 350 participants	Activity 5: 1,750 participants over 5 years

	Activity 6: 10 participants Activity 7: 20 participants	Activity 6: 15 participants Activity 7: 20 participants	Activity 6: 15 participants Activity 7: 20 participants	Activity 7: 20 participants	Activity 7: A total of 100 participants over 5 years

	Anticipated Outcomes of BP Element	
Across this **Element**	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Goal 5.1	More diverse and sustainable bioscience/STEM education and professional development pathways.	Increased numbers of underserved/underrepresented groups in bioscience degree programs and careers. Increased bioscience research activity at the TCU/MU/PUIs.
Overall Outcomes	Increased institutional commitment to BP at all participating institutions.	A culture of increased BP at all participating institutions.

PROSPER Partnerships and Collaborations

The Partnerships and Collaborations initiative builds research infrastructure and strengthens ND's research competitiveness through industry partnerships and other collaborations. Team members include the Pillar leads.

The team will facilitate a variety of activities that assist CCBSE researchers in forming partnerships and collaborations (particularly with industry in ND and the wider region) and promote ND's research competitiveness, innovation, and bioscience pathway development. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 8).

This group's efforts link to ND-ACES tracks 1, 3, and 4 (which are adopted as the Strategies for Partnerships and Collaborations) and integrate with CCBSE goals.

Partnerships and Collaborations Element Goal 6.1: Ensure sustained educational and economic impact beyond the project through partnerships and internships.

- **Partnerships and Collaborations Element Objective 6.1a:** Expand the intellectual reach of the CCBSE by building stronger collaborations with other academic institutions and federal labs.
- **Partnerships and Collaborations Element Objective 6.1b:** Create pathways for translating research results into commercially viable end products by expanding existing and forging new bioscience partnerships with business economic development entities, and developing intellectual property (IP) and commercialization.

Table 8. Partnerships and Collaborations Element Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

Partnerships and Collaborations Element - Timelines of Activities					
Objective 6.1a	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Determine and build upon the baseline	Survey senior personnel to establish the baseline collaborations	Build/extend baseline collaborations	Continued	Continued	Continued
Activity 2: Support participant interactions with external collaborators with travel funding			1-3 trips to external collaborators and 1-3 external collaborators coming to campuses	Continued with 2- 6 total visits	Continued with 2-6 total visits
Activity 3: Support interactions with e collaborators			Fund at least one seed award between CCBSE and an external collaborator	Continue to fund one seed award per year	Continued
Objective 6.1b	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Determine and build upon the baseline for partnerships	Survey campus industry relations offices and participants to establish the baseline for partnerships	Build/extend from baseline partnerships	Build/extend from prior year's partnerships baseline	Continued	Continued
Activity 2: Support Partnerships	Plan for Y2 communication efforts and determine measures of engagement	Provide support for current and identify next year's communication e	Continued	Continued	Provide support for and identify ongoing communication sustainability efforts
Activity 3: Identify ND companies using tools like NAICS	e	Following the April 2022 EAB meeting, together with CCBSE and Pillar leads, begin to develop a CCBSE prospectus for cultivating partnerships and exploring potential funding possibilities (Bio ND, EDA, SHARPhub/I-Corp, Innovate ND, Main Street, SBIR, STTR)	Finalize a CCBSE prospectus	Update CCBSE prospectus	Continued
Activity 4: Identify partnership opportunities		Begin to identify opportunities and	Continue to identify opportunities and	Continue to identify opportunities and	Continued

		determine whether actionable by CCBSE leads	determine whether actionable by CCBSE leads	determine whether actionable by Pillar leads	
Activity 5: Identify IP protocols at all 10 institutions	Work with campuses to identify IP protocols	Continue to work with campuses to identify IP protocols and determine how joint IP will be handled	Make necessary changes protocol document and joint IP agreement as necessary	Continued	Continued
Activity 6: Understand how tribal laws impact IP disclosures	Work with TCU campuses located in ND to identify impacts	Continue to work with TCU campuses located in ND to identify impacts and determine whether to survey other AIHEC campuses	If determined in Y2, survey other AIHEC campuses	If determined in Y2, compile survey data from other AIHEC campuses	If determined in Y2, publish results from other AIHEC campuses
Activity 7: Identify commercialization protocols at all 10 participating institutions	Work with campuses to identify commercialization protocols and enroll participants in SHARPhub	Continue to encourage CCBSE participants to enroll or take part in SHARPhub/I-Corps activities, work with campuses to identify commercialization protocols and enroll participants in SHARPhub/I-Corps In Spring 2022, meet with the ND SHARPhub/I-Corps coordinator to determine next steps	Updated campus commercialization protocols, as necessary, continue to encourage CCBSE participants to enroll in I-Corps activities, and assistance with IP disclosures	Continued	Continued
Activity 8: Identify workshops / conferences to attend and mentoring opportunities (I-Corps, USPTO, SBIR, etc.	Identify initial workshops related to typical processes (e.g., NDSU and UND IP offices, Holly e Trademark Searching) for participants to discuss IP	Continue to identify workshops related to typical processes for participants to discuss IP	Continued	Continued and host 1 CCBSE workshop or conference	Continued
Activity 9: Based on other activities, determine potential funding possibilities with other I-Corps EPSCoR states	N/A	After Spring 2022 meeting with the SHARPhub/I-Corps coordinator and April 2022 EAB meeting, together with CCBSE and Pillar leads and the UND I-Corps coordinator /trainer to explore potential conversations with other	Begin conversations with other EPSCoR states with bioscience research agendas, including those that previously participated in SHARPhub	Based on conversations with other EPSCoR states, determine and engage in action Items	Engage in action items and determine sustainable potential of action items

		EPSCoR states participating in SHARPhub			

Partnership and Collaborations Element - Milestone metrics					
This Element	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 6.1a	Activity 1: Baseline established	Activity 1: 20% increase in meaningful collaborations over prior year	Activity 1: 20% increase in meaningful collaborations over prior year	Activity 1: 20% increase in meaningful collaborations over prior year	Activity 1: 20% increase in meaningful collaborations over prior period
	Activity 2: N/A	Activity 2: Meeting the numbers outlined	Activity 2: Meeting the numbers outlined	Activity 2: Meeting the numbers outlined	Activity 2: Meeting the numbers outlined
	Activity 3: N/A	Activity 3: N/A	Activity 3: Meeting the number outlined	Activity 3: Meeting the number outlined	Activity 3: Meeting the number outlined
Objective 6.1b	Activity 1: Baseline established using CDAs, MTAs, other efforts (grant applications, etc.)	Activity 1: Increase in partnership engagement or partner activities over baseline - measured by the provision of valuable resources (as defined in 4.7, Tactic 2)	Activity 1: Increase in partnership engagement or partner activities over the prior year - measured by the increased provision of valuable resources	Activity 1: Increase in partnerships or partner activities over prior year and continued evidence of provision of valuable resources	Activity 1: Increase in partnerships or partner activities over prior year and continued evidence of provision of valuable resources
	Activity 2: Identification of Y2 support efforts based on baseline data and determination of measures [# participants (if event), # of inquiries following communication effort, etc.]	Activity 2: Increased engagement by meeting of prior year's identified support efforts	e	Activity 2: Increased engagement by meeting of prior year's identified support efforts	Activity 2: Increased engagement by meeting of prior year's identified support efforts
	Activity 3: N/A	Activity 3: Completed prospectus	Activity 3: Prospectus updated		
	Activity 4: N/A	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable

	Activity 5: >50% protocols identified	Activity 5: 100% protocols identified; Collaborative decision made regarding the handling joint IP and updated protocol document	Activity 5: Up to date protocol document and joint IP agreement	Activity 5: Up to date protocol document and joint IP agreement	Activity 5: Up to date protocol document and joint IP agreement
	Activity 6: 50% identified	Activity 6: 100% identified	Activity 6: Survey developed and released	Activity 6: Survey results compiled	Activity 6: Results published
	Activity 7: >50% protocols identified and 25% of participants enrolled in SHARPhub	Activity 7: 100% protocol identified	Activity 7: Updated protocol document, and 1 invention disclosure	Activity 7: Updated protocol document, 3+ invention disclosures, and 2+ provisional patents	Activity 7: Updated protocol document, 3+ invention disclosures, 2+ provisional patents, and 2+ patent
	Activity 8: 1+ workshop or conference attended by >40% CCBSE participants	Activity 8: 1+ workshop or conference attended by >60% CCBSE participants.	Activity 8: 1+ workshop or conference attended by >75% CCBSE participants	Activity 8: 1+ workshop or conference attended by 75%+ CCBSE participants and 1 CCBSE workshop or conference attended by 80% CCBSE participants	Activity 8: 1+ workshop or conference attended by 85%+ CCBSE participants and 1 CCBSE workshop or conference attended by 80% CCBSE participants
	Activity 9: N/A	Activity 9: N/A	Activity 9: List of action items for other EPSCoR states	Activity 9: States continue to be engaged	Activity 9: 1-3 sustainable goals for at least 3 states

	Anticipated Outcomes of Partnerships and Collaborations Element	
Element	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Goal 6.1a	Existing external collaborations become more meaningful; as evidenced by increased conference, journal, and proposal co-authorship among project participants, and between project participants and external organizations; joint working papers; regularly established interactions that may lead to the submission of an article/proposal, increased use of facilities and equipment (i.e., increased use of CCAST and CRC by MCU/PUI/TCU researchers [and internal collaborators]; and increased use of Extreme Science and Engineering Discovery Environment [XSEDE] by all participating institutions [an external collaboration]). New external collaborations are built to produce meaningful outcomes/impacts.	Sustained, meaningful external collaborations with other academic institutions and federal labs.
Goal 6.1b	Existing partnerships make more provisions of valuable resources (student internships, collaborative research opportunities, insight into needs and future direction of ND and regional industry [Inc. stakeholder advisory groups], sharing/commercialization of IP). New partnerships are built with an expectation of the provision of resources.	Sustained partnerships that positively impact North Dakota's economy.
Overall Outcomes	Impact beyond the project with partnerships and internships expanded by 50%.	Foster the ongoing development of a skilled, diverse workforce; positively impact state economy; supply research outcomes for growing/new bioscience ventures and partners; and open new research avenues.

PROSPER Communication and Dissemination

The ND-ACES- wide initiative of Communication and Dissemination keeps all stakeholders informed, supports the harmonious interactions of all ND- ACES groups, assists research and programmatic participants in disseminating their work to legislative, scientific, and citizen stakeholders, and develops materials for consumption by lay audiences. Team members include all senior personnel.

The team will increase awareness of the CCBSE's role in developing the state's bioscience ecosystem from education to economic diversification. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 9).

This group's efforts link to ND-ACES tracks 1, 3, and 4 (which are adopted as the strategies for Partnerships and Collaborations) and integrate with CCBSE goals.

Communication and Dissemination Element Goal 7.1: Develop an elevated public understanding of the economic impact of growing North Dakota's bioscience sector through strategic research investments as a result of data-sharing, communication, and outreach.

- **Communication and Dissemination Element Objective 7.1a:** Provide clear communication between all participants.
- **Communication and Dissemination Element Objective 7.1b:** Inform and educate stakeholders.
- **Communication and Dissemination Element Objective 7.1c:** Contribute to a scientifically informed citizenry.

Table 9 . Communication and Dissemination Element Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

Communication and Dissemination Element - Timelines of Activities					
Objective 7.1a	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Facilitate communication through regular meetings	Attending CCBSE meetings, and PROSPER meetings	Continued	Continued	Continued	Continued
Activity 2: Facilitate communication across the by providing updates	Providing team updates (newsletter/ web/social media), writing support for new funding	Continued	Continued	Continued	Continued
Activity 3: Facilitate Communication by providing communication	Technical training in MS Teams provided for leadership on internal team communication. Annual evaluation of MS Teams based internal communication practices	Continued	Continued	Continued	Continued
Objective 7.1b	Year 1	Year 2	e	e	e
Activity 1: Populate website and social media with relevant public-facing content	Measure dissemination website/social media/newsletter	Continued	Continued	Continued	Continued
Activity 2: Assist team members from CCBSE and PROSPER with creating public-facing communication products	Offer individual consulting sessions for presentation preparation and PR/public dissemination strategies	Continued	Continued	Continued	Continued
Activity 3: Disseminate project milestones and talking points to stakeholders and decision makers in the state	Press releases drafted for submission to regional/national news as well as NDUS PR offices. Talking points sent to key	Continued	Continued	Continued	Continued

	decision makers and legislators				
Objective 7.1c	Year 1	Year 2	Year 3	Year 4	Year 5
Activity 1: Offer workshop opportunities for faculty and graduate students	Plan ND EPSCoR-sponsored communicating science workshop to develop better skills in disseminating their work/public engagement	Host ND EPSCoR-sponsored communicating science workshops to develop better skills in disseminating their work/public engagement	Continued	Continued	Continued
Activity 2: Include public engagement opportunities as part of the annual conference	ND EPSCoR will host an annual conference, provide skill-building resources to participants - COVID-19 permitting	Continued	Continued	Continued	Continued
Activity 3: Ensure that we have a diverse representation of science and scientists on website, to help engage all publics		Scoring by external evaluation firm's diversity rubric		Responsiveness to Y2 scoring	
Activity 4: Engage with local publics about the value and the benefits of the science	Support science cafes - *COVID-19 permitting	Continued	Continued	Continued	Continued

Communication and Dissemination Element - Milestone metrics					
Across this Element	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 7.1a	Activity 1: Meeting attendance	Activity 1: Meeting attendance	Activity 1: Meeting attendance	Activity 1: Meeting attendance	Activity 1: Meeting attendance
	Activity 2: At least monthly outreach to participants, stakeholders, and citizens	Activity 2: At least monthly outreach to participants, stakeholders, and citizens	Activity 2: At least monthly outreach to participants, stakeholders, and citizens	Activity 2: At least monthly outreach to participants, stakeholders, and citizens	Activity 2: At least monthly outreach to participants, stakeholders, and citizens

	Activity 3: Training offered at least quarterly	Activity 3: Training offered at least quarterly	Activity 3: Training offered at least quarterly	Activity 3: Training offered at least quarterly	Activity 3: Training offered at least quarterly
Objective 7.1b	Activity 1: Same metric framework for all: Baseline established of interaction (engagement rate)	Activity 1: ≥5% Increase in number of interactions per day divided by followers.	Activity 1: ≥5% Increase in number of interactions per day divided by followers.	Activity 1: Maintain engagement over the prior year. Maintain number of interactions per day divided by followers.	Activity 1: Maintain engagement over the prior year. Maintain number of interactions per day divided by followers.
	Activity 2: Needs research products; sessions begin in year two	Activity 2: 5 sessions per year completed	Activity 2: 5 sessions per year completed	Activity 2: 5 sessions per year completed.	Activity 2: 5 sessions per year completed.
	Activity 3: 2+ press releases	Activity 3: 4+ press releases; Updating stakeholders on project milestones (quarterly)	Activity 3: 4+ press releases; Updating stakeholders on project milestones (quarterly)	Activity 3: 4+ press releases; Updating stakeholders on project milestones (quarterly)	Activity 3: 20 press releases over the 5- year period. Updating stakeholders on project milestones (quarterly)
Objective 7.1c	Activity 1: 2 workshops planned annually. Workshops begin year 2	Activity 1: 40+% attendance by ND-ACES participants	Activity 1: 55+% attendance by ND- ACES participants	Activity 1: 75+% attendance by ND- ACES participants	Activity 1: 90% of ND- ACES participants will have attended at least 1 workshop over the 5-year period
	Activity 2: 2021 Annual conference with attendees from each of the participating campuses.	Activity 2: 2022 Annual conference with attendees from each of the participating campuses.	Activity 2: 2023 Annual conference with attendees from each of the participating campuses.	Activity 2: 2024 Annual conference with attendees from each of the participating campuses.	Activity 2: 2025 Annual conference with attendees from each of the participating campuses.
		Activity 3: Scoring by external evaluation firm's diversity rubric		Activity 3: Scoring by external evaluation firm's diversity rubric	
	Activity 4: Science cafes planned annually. Science cafes begin year 2	Activity 4: 1-2 science cafes supported	Activity 4: 2 science cafes supported.	Activity 4: 2-3 science cafes supported	Activity 4: 2-3 science cafes supported

Anticipated Outcomes of Communication and Dissemination Element		
Across this Element	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Goal 7.1a	Facilitate communication and collaboration across the research Pillars and broader impacts elements.	Contribute to a shared understanding across disciplines.
Goal 7.2b	Increase the awareness of the research that expands ND's bioscience research, capacity, and expertise.	Foster the ongoing awareness of the research that expands ND's bioscience research, capacity, and expertise.
Goal 7.3c	Engage the public in scientific research.	Contribute to a more scientifically informed citizenry.
Overall Outcomes	Communication and dissemination efforts will increase awareness of the role of the CCBSE in developing the state's bioscience ecosystem from education to economic diversification.	Develop a robust understanding of the importance of the communication of science among all participants and contribute to a more scientifically informed citizenry.

PROSPER – Overall Summary

As previously stated, the goal of PROSPER is to broaden the impact of the CCBSE within the jurisdiction. This goal will be accomplished through the successful completion of the Education and Workforce Development, Broadening Participation, Partnerships and Collaborations, and Communication and Dissemination metrics outlined above in Tables 6,7, 8, and 9. Additional CCBSE outcomes that will be obtained through the combined efforts of the PROSPER elements are outlined in Table 10.

Table 10.Overall PROSPER Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

PROSPER Specific milestones					
PROSPER Strategies	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Expand ND's biosciences capacity through a STEM- enabled, well-trained workforce	Successful completion of Education and Workforce Development Element yearly activities				
Increase advanced scientific computing capabilities	Successful completion of Education and Workforce Development and Broadening Participation Element yearly activities and metrics				
Broaden the participation and number of STEM undergraduate and graduate students	Successful completion of Broadening Participation Element yearly activities and metrics				
Provide professional development to rural and tribal K-12 teachers and outreach to K-12 students	Successful completion of Education and Workforce Development and Broadening Participation Element yearly activities and Metrics				
Solicit industry- focused activities that build or expand on existing partnerships	Successful completion of Partnerships and Collaborations Element yearly activities and metrics				
Create a suite of Communication activities will engage, inform, and educate	Successful completion of Communication and Dissemination Element yearly activities and metrics				

Overall milestone metrics for PROSPER, in addition to those outlined in Tables 6, 7, 8, and 9	
Meet annually with TCU presidents to report on the impacts of the collaboration efforts between CCBSE, PROSPER, and the TCUs. Report also on the numbers of American Indian students who are involved in ND-ACES programming	5
Meet annually with MCU and PUI presidents to report on the impacts of the collaboration efforts between CCBSE, PROSPER and those campuses. Report also on the numbers of their students who are taking advantage of the programming	20
Number of TCU visits (some of these visits will be virtual due to COVID-19)	20
Number of MCU and PUI visits (some of these visits will be virtual due to COVID-19)	20
Number of legislator visits	10
Number of annual conferences (some of these conferences will be virtual due to COVID-19)	5
Number of External Advisory Board meetings (combination virtual and in-person; 1 meeting per year in Years 4 and 5)	8
Number of ND-ACES Management meetings (to be scheduled monthly Years 1-3; 6 per year in Years 4 and 5)	48
Number of ND-ACES Leadership meetings (to be scheduled quarterly/revised and now part of Management mtg)	15
Number of ND-ACES All-Participant meetings (to be scheduled twice annually)	10
Number of CCBSE and PROSPER meetings (to be scheduled every other month)	25-30

Number of undergraduate students trained (some may be counted in multiple years)	70
Number of conference presentations by undergraduate students (oral and poster)	80
Seed Funding: seed funding support of $60,000 in Translational Research Initiative Project and an additional $101,655 in other research opportunity support – 5-year total is cumulative	$161,655
Number of CCBSE research participant meetings (10 - 12 / year depending on need)	50

Anticipated Outcomes of PROSPER		
Across PROSPER	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Meet PROSPER's Goal	Expand North Dakota's emerging biosciences capacity through a STEM-enabled and well-trained workforce. to broaden the impact of the CCBSE.	Effect sustainable engagement and position ND-ACES as North Dakota's leading scientific and educational resource.

TCU Pilot Pillar Implementation

As part of the response to the 2023 Site Visit Report, ND-ACES will pilot an emergent TCU Pilot Pillar/Element, coordinated by the ND EPSCoR Tribal Partnerships Director, with an eye to what a TCU Core might look like for the jurisdiction in a future NSF EPSCoR E-CORE proposal. North Dakota has more tribal colleges than any state other than Montana, and the only statewide Tribal College System, so there are longer-term opportunities to build out supporting infrastructure jurisdiction-wide.

The proposed TCU Pilot Pillar will be comprised of activities:

- Reflecting contextually and culturally relevant programming
- Increasing opportunities for TCU students to engage with ND-ACES programming including professional development
- Increasing research opportunities for TCU faculty and students

Planned activities within the TCU Pilot Pillar will be compromised of both existing and new activities. Examples of activities are included in Figure 4.

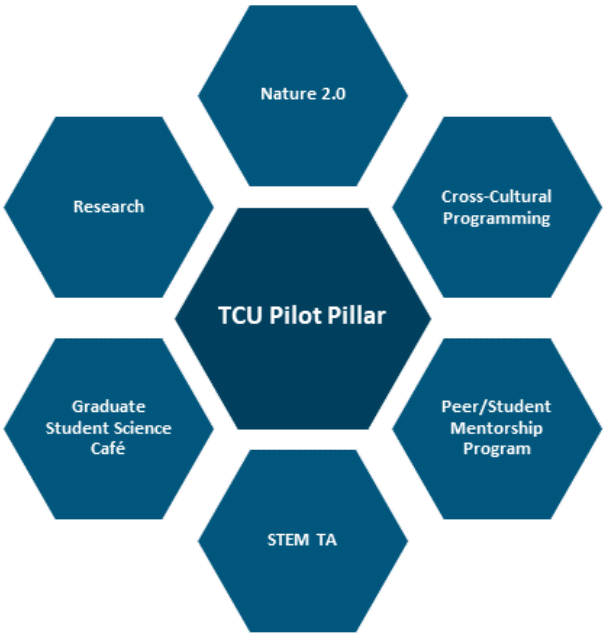

Figure 4. Overview of TCU Pilot Pillar activities.

TCU Pilot Pillar Goal 8.1: Establish a TCU Pilot Pillar to better engage with and facilitate TCU participation in ND-ACES

- **TCU Pilot Pillar Objective 8.1a:** Continue to improve dialogue with TCU leadership regarding ND-ACES project to continue to build trust and accountability while assessing the needs and strengths within each TCU and its community.
- **TCU Pilot Pillar Objective 8.1b:** Develop mentorship and professional development opportunities for TCU students.
- **TCU Pilot Pillar Objective 8.1c:** Provide professional development opportunities for ND-ACES participants at RUs and PUIs to develop equitable and sustainable partnerships with TCUs and emphasize the importance providing STEM education in a contextually and culturally relevant manner.
- **TCU Pilot Pillar Objective 8.1d**: Expand research opportunities for TCUs as part of ND-ACES.

Table 11. TCU Pilot Pillar Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

TCU Pilot Pillar - Timelines of Activities					
Objective 8.1a	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Facilitate communication through regular meetings with ND TCS.				Regular attendance at ND Tribal College System meetings providing updates and requesting input, as needed.	Continue
Objective 8.1b	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Identify and implement a mechanism to share professional development and training opportunities developed as part of ND-ACES with TCU students.				Identify a mechanism to share existing and new professional development/training resources with TCU students in an asynchronous manner. Work with NATURE coordinators to identify ways to include TCU students in synchronous activities.	Continue
Activity 2: Explore peer mentoring opportunities.				Tribal Partnerships Director will work with NATURE coordinators to identify opportunities for peer mentoring (e.g. engaging NATURE graduates as mentors at summer camps).	Continue
Objective 8.1c	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Realignment of NATURE programming (University Summer Camp and Sunday Academy) to				Engage TCUs to provide input to revise process for identifying and reviewing program activities.	Continue

increase contextual and cultural relevance				Engage external evaluators to review proposed NATURE activities and review process to ensure they reflect best practices and are appropriate for ND.	Continue
Activity 2: Provide professional development training to ND-ACES participants at RU and PUI/MCU related to the development of equitable and sustainable partnerships with TCUs.				Develop training modules Provide training prior to University Summer Camp in June	Continue
Objective 8.1d	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Activity 1: Explore opportunity for UTTC to join ND-ACES				Continue discussions with UTTC about joining ND-ACES project.	Continue
Activity 2: Increase research opportunities for TCU students				Implement foundational laboratory skills course as part of University Summer Camp Support TCUs interested in expanding research activities under ND-ACES	Continue

Anticipated Outcomes of TCU Pilot Pillar		
Across this Element	**Short-term (5 Years) (changes in knowledge or capacities)**	**Long-term (10 Years) (changes in actions or conditions)**
Goal 8.1a	Facilitate communication and build more equitable collaborations across ND-ACES.	Contribute to a shared understanding across disciplines.

ND-ACES – Overall Impacts

The jurisdictional impacts (listed in Table 12) of meeting the ND-ACES outcome metrics for CCBSE, PROSPER, and the TCU Pilot Pillar are to fulfill the mission of ND-ACES to contribute to cancer research in ways that have state, national, and international ramifications and underpin sustainable activities for a trained and diverse workforce and informed populace.

The changes implemented as part of the NSF Site Visit in Year 4 will establish stronger connections between the participating institutions and create additional linkages across the creating greater opportunities for faculty and students building networks and connections that will be sustained beyond the current project.

Figure 5. Conceptualization of connections and linkages between TCU Pilot Pillar and existing ND-ACES structure.

Table 12. Jurisdictional Impacts

Across ND-ACES Jurisdictional Impacts
North Dakota will become the Northern Plains leader in new and sustainable biosciences technology advances.
North Dakota will have a sustainable, competent, and diverse state biosciences and bio- technology workforce from A.A. through Ph.D.
North Dakota's bioscience industry will have grown into a major economic sector with new partners, growing businesses, and expanded workforce opportunity.

Risk Management Plan

During the Strengths, Weaknesses, Opportunities, and Threats (SWOT) Analysis Meetings (synchronous and asynchronous) and the Strategic Planning Meeting, senior personnel were asked to consider all potential risks to the ND-ACES project and associated consequences. This exercise also included the consideration of three NSF-facilitator driven scenarios related to COVD-19: 1) back to normal, 2) some hybrid between back to normal and continued restrictions, and 3) full restrictions (i.e., virtual). A description of the SWOT analysis meetings and strategic planning meeting schedules/overview are included in Appendix E.

Table 13 summarizes the deliberations around normal risks (those that ND-ACES would need to address independent of COVID-19). Risks specifically associated with COVID-19 are listed in Table 14.

Table 13. Normal Risk Mitigation Matrix

No.	Potential Risks	Consequences	Impact	Likelihood	Mitigation
1	Team is very large and diverse with many complex collaborative tasks to complete in a limited time-frame.	Delay in meeting ultimate project goals.	High	Medium	Redesign/adjust composition of project; project leadership to communicate frequently with project management about concerns impacting project success. All senior personnel have adopted our Collaboration Agreement (Appendix C).
2	Cyberinfrastructure resources are not equal on all campuses and in all communities.	Barrier to collaborative work.	Medium	High	Work with the TCUs, MCU, and PUIs to develop additional accessibility options and alternative lines of access whenever necessary.
3	Obstacles inevitable in our complex research plan that will require the team to be very adaptable.	Barrier to collaborative work.	Medium	Low	Quarterly review process will identify areas in need of attention/change. Mitigating strategies will be developed, in conjunction with our program officer, as necessary.
4	Interruptions in ND-ACES activities due to COVID-19.	Potential to halt all activities.	High	High	Multi-scenario mitigation plan developed and updated quarterly or as events change, in conjunction with our program officer, as necessary
5	Inability to recruit new faculty hires.	Reduced expansion into new areas of materials science. Inability to meet this programmatic condition.	High	Low	Revisit and revise the hiring plan (Appendix D), addressing whatever the cause for failure. If the failure is the inability (e.g., financial) to complete the hire, then the mitigation plan might be to turn to one of the other campuses to see if one of them can complete the hire or return to negotiation with our program officer if no hire is possible
6	Decline or discontinuation of state support during the 2021, 2023, or 2025	Decline in the ND EPSCoR state cash commitment.	High	Low	Turn to the RUs to provide the required match.

	legislative sessions.				
7	A researcher becomes unable to contribute to project due to illness, overload, or departs university.	Unable to meet Metrics.	Medium	Medium	Shift work to another peer investigator, hire an additional investigator through a seed grant proposal; or initiate a new faculty search for a replacement, if needed and possible.

Table 14.COVID-19 Scenario Planning

Scenario	**Implications**	**Impact**	**Likelihood**	**Mitigation**
New normal	Project activities continue without accommodations.	Low	Medium	Conform to institutional safety protocols.
Some hybrid between back to normal and continued restrictions	Potential slowdown of research, outreach, and education occur in a hybrid model.	High	Medium to High	In-person research and outreach will conform to institutional safety protocols. Research - It may be necessary to limit the number of people allowed in lab spaces at one time, augmented cleaning protocols, increase work on virtual platforms, etc. Each activity and circumstance will be evaluated by co-leads on a case-by-case basis as required. Accommodations will seek consistency across campuses if possible; alternatively, work may be shifted from one campus to another if possible and necessary to keep the project on pace. Outreach – it may be necessary to develop online/virtual activities that students can do at home. Summer 2020 NATURE programs will be used as a template for the creation of virtual outreach activities.
Full restrictions (i.e., virtual)	Outreach in person is not possible; restricted access to facilities impedes research.	High	Medium	Research – activities may be postponed or modified to occur remotely; use of core services may be outsourced on a fee-for-service basis. Frequent communication with our program officer will occur. Outreach – online/virtual activities that students can do at home will be developed. Summer 2020 NATURE programs will be used as a template for the creation of virtual outreach activities.

Succession Plan

The NSF Track 1 award to the North Dakota jurisdiction is administered by NDSU under the Office of Research and Creative Activity. Colleen Fitzgerald serves as the Vice President for Research and Creative Activity. Jolynne Tschetter is the ND EPSCoR Executive Director.

John Warford, a member of the North Dakota University System State Board of Higher Education, chairs the ND EPSCoR Steering Committee. ND ACES leadership staff are also located at both UND (Co-PI: John Mihelich, Interim Vice President for Research and Economic Development) and NDSU (Executive Director: Jolynne Tschetter, ND EPSCoR).

Management Structure: The NDSU PI (Fitzgerald) and Co-PI (Mihelich), together with the ND EPSCoR Executive Director (Tschetter), will oversee the implementation of ND-ACES. They will work with the sub-awardee/campus PIs and the ND-ACES leads/co-leads to ensure timely execution of project components and delivery of outcomes and outputs. The ND EPSCoR unit coordinates project management, data gathering for reports, and global event planning. The leads/co-leads ensure that the strategic priorities of the cooperative agreement are met.

Succession Plan: The purpose of the Succession Plan (Table 15) is to ensure that the leadership and management of the program are in place for the duration of the project. The succession plan will be reviewed and updated annually.

Table 15.Succession Plan

Position	**Strategies for Succession**
PI/PD	e
Co-PIs	Co-PIs will inform the PD/PI as soon as possible that they will be leaving his/her position. Replacement of the UND Co-PI will be by the UND president and/or Provost. Replacement of the NDSU Co-PI/PA (Project Administrator) will be identified by the PD/PI. Once a replacement has been identified, a formal “change of Co-PI” request will be made to NSF.
CCBSE Pillar and PROSPER Section/Element Leads	Each CCBSE Pillar has designated a lead from each RU. Thus, the other assumes the full Pillar leadership role during any planned or unplanned absences of the other campus Pillar Lead. In the event that the absence is greater than one month, a second interim Pillar lead will also be named by the PD/PI in consultation with the Co-PIs and the other Pillar leads. If a Pillar Lead leaves his/her institution, a new Pillar Lead will be selected either from the faculty pool within the Pillar or through an internal campus search.
Benchmark/Activity Leads	Succession planning is not an issue as most benchmarks/activities have two individuals named for backup and collaboration between the campuses; however, in the event that the individuals named are from different campuses, the project research cluster members will assist with collaboration efforts. In the instances where just one benchmark/activity lead is named, the component lead for that portion of the project will name an interim benchmark/activity lead.

Appendix A –Teams, External Advisory Board, and ND EPSCoR State Steering Committee

Management Team is comprised of the PI/PD, Co-PI, Executive Director, Pillar Leads, Element Leads, two PUI representatives, and two TCU representatives.

ND ACES External Advisory Board is comprised of five subject matter experts, three representatives from industry/medical systems, and two representatives with expertise in broader impacts.

ND EPSCoR State Steering Committee composition is determined by its bylaws but in general includes representation from the State Board of Higher Education, legislators, private industry, K-12 education, economic development, and Higher Education (including representation from research universities, tribal colleges and universities, and primarily undergraduate institutions).

Appendix B – 2020 Strategic Planning Process and Timeline

Date	Activity
5/27	Collaboration Plan CCBSE Subgroup Session
5/28	Collaboration Plan PROSPER Subgroup Session
6/15	EPSCoR RII Track-1 Strategic Planning Webinar with NSF, PI, Co-PIs, CCBSE Leads, and ND EPSCoR Communication Manager
6/18	Full Collaboration Plan Session
6/29	Initial Strategic Planning Meeting Preparatory Meeting with NSF Facilitator, PI, Co-PIs, and ND EPSCoR Communication Manager
6/30	Researcher Preparatory Meeting with NSF Facilitator and ND-ACES Leadership Team
7/14	All-Hands Introductory Meeting and SWOT Analysis Synchronous Meeting
7/29-7/31	Strategic Planning Meeting with NSF Program Officer, NSF Facilitator, and External Evaluator (The Mark, USA)
8/14	Initial Drafts of CCBSE Pillar and PROSPER Element Implementation Sections Due from Leadership Team to ND EPSCoR
8/21	Initial Draft of Full Strategic Plan due back to Leadership Team and External Evaluators
9/1	Initial Full of Strategic Plan due from Leadership Team to ND EPSCoR
9/14	Final Draft of Full Strategic Plan due back to Leadership Team and External Evaluators
9/21	Final Full Strategic Plan due from Leadership Team to ND EPSCoR for final editing and formatting
10/1	Strategic Plan due to NSF

Appendix C – Glossary of Acronyms

CCCC	Cankdeska Cikana Community College, Fort Totten, ND
CCBSE	Center for Cellular Biointerfaces in Science and Engineering
CI	Cyberinfrastructure
DoE	Department of Energy
DSU	Dickinson State University, Dickinson, ND
HPC	High-Performance Computing
MaSU	Mayville State University, Mayville, ND
e	Minot State University, Minot, ND
NATURE	Nurturing American Tribal Undergraduate Research and Education
ND-ACES	New Discoveries in the Advanced Interface of Computation, Engineering, and Science
NDSU	North Dakota State University, Fargo, ND

NHSC	Nueta Hidatsa Sahnish College (formerly Fort Berthold Community College), New Town, ND
PROSPER	PROmoting Sustainable Partnerships in Education and Research
PUIs	Primary Undergraduate Institutions
REU	Research Experience for Undergraduates
RII	Research Infrastructure Improvement
SA	Sunday Academy
SBC	Sitting Bull College, Fort Yates, ND
TCUs	Tribal Colleges and Universities
TMCC	Turtle Mountain Community College, Belcourt, ND
UTTC	United Tribes Technical College
UND	University of North Dakota, Grand Forks, ND
VSCU	Valley City State University, Valley City, ND

Appendix D – Programmatic Terms and Conditions - Hiring Plan

NSF Jurisdiction Specific Terms and Conditions: Hiring of Faculty and other Key Personnel: The PI is responsible for ensuring that participating institutions follow through recruiting and securing all proposed hires of faculty and other key personnel as established by the original project proposal, any award conditions, or the approved RII Track-1 Strategic Plan. Any changes require prior NSF EPSCoR approval. The annual or final report must report on the status of faculty (and other key personnel) hires.

Background

Both RUs have research foci in health (biosciences/biomedical) and infrastructure (data analytics/societal infrastructure).

- NDSU's commitment to health-related bioscience includes the recent hiring of seven faculty in biomedical engineering-sensors and 3D printing; materials/ mechanobiology; computational biology; cancer biology; polymer science; and; computational chemistry (the last two were hired under the 2014-2021 NSF Track-1 [INSPIRE-ND]). NDSU has also invested in the Center for Computationally Assisted Science and Technology (CCAST), increasing its footprint, procuring additional equipment, and recruiting a research facilitator (FY18).
- UND has also committed to hiring in the biosciences/biomedical arena, with plans to hire up to six research-intensive computational faculty with expertise in data analytics, machine learning (ML), artificial intelligence (AI), and deep learning. UND's School of Medicine has invested in the growth of cellular expertise through three recent hires in cancer cell biology and the establishment of a clinical and translational research center (IDeA; Dakota Cancer Collaborative on Translational Activity, which also includes NDSU). UND has also hired faculty in integrative systems biology and computational materials chemistry and recently expanded its Computational Research Center(CRC).

To fill the gap identified in state investments to meet the vision of becoming the Northern Plain's leading scientific and educational driver in new and sustainable biosciences technology advances, ND-ACES incorporates the recruitment and hiring of two materials faculty, one at NDSU and one at UND.

Recruiting and Hiring Plan

NDSU and UND will conduct national searches for the two tenure-track faculty members. It is anticipated that each hire will be at the assistant professor level.

NDSU: The new faculty hire (depending on the background of the selected candidate) may fit within one of several colleges: Engineering; Science and Mathematics; or Agriculture, Food Systems, and Natural Resources. Thus, a cross-disciplinary search committee will be selected to include faculty from each of these colleges and

CCBSE researchers. The position will be advertised nationally and internationally, on the NDSU web page, within targeted scientific societies, and through directed emails and letters to chairs and faculty in the targeted research groups and others as well as relevant listservs.

The committee will filter applications to select a top tier list of candidates (approximately 10-12) for phone/video conference interviews. Three or four candidates will be selected as finalists for on-campus (or virtual) interviews. These interviews will take place over two days. The candidates will meet with college/department faculty, students (undergraduate and graduate), the chairs of the departments in which the faculty may fit, and deans of the three colleges. In addition, each candidate will present a public research seminar as well as teach a class lecture pertinent to the materials area (the class will be determined by the search committee). NDSU has made a significant effort to recruit a diverse faculty including members from underrepresented and underserved groups.

The NDSU faculty search will begin in fall 2021. It was originally planned to have the new faculty member in place in year two. However, COVID-19 (and the financial implications) shifted this search to the fall of year two. The intent is for the new faculty to join the team at the beginning of year three.

UND: The new faculty hire will be recruited to join the Department of Chemistry in the College of Arts & Sciences. The position in materials science will contribute to the broad area of synthetic- biological chemistry applications and focus on the development of soft-tissue-like material. The new position will strongly complement the department's existing expertise in synthesis and modeling such systems and biomedical applications. This ties in directly to the department's emphasis on biomaterials for transformational health related applications.

The faculty search will follow standard practices for hiring tenure-track faculty at UND and practice within the Department of Chemistry. Since one goal is for the position to collaborate with faculty from the Department of Biomedical Sciences in the School of Medicine & Health Sciences, the search committee will include at least one member from that department. Per UND practice, the position will be widely advertised, posted on the UND website, and distributed through relevant listservs and professional groups. UND has made concerted efforts to recruit strong and diverse candidate pools and will do so in this process. The committee will review applicants and select a small group of candidates to progress through a phone/virtual interview and further narrow the group to candidates invited for an in-person or virtual campus visit. The intent is to commence the search in year one and have the new faculty member in place at the beginning of year two.

UND hired Binglin Sui, Assistant Professor, Chemistry. His contract begins August 1, 2021.

Mentoring Plan

New faculty members at all participating institutions and other faculty members wishing to participate, will be mentored by CCBSE personnel and by faculty within his or her department or college. Each new faculty member will receive an orientation to the CCBSE or PROSPER research programs, their goals, and expected outcomes from the CCBSE or appropriate PROSPER Leads; be included in the regular team meetings; and; meet with other team members to identify collaborations as a means to integrate them into CCBSE's or PROSPER's efforts. Each faculty hire will develop an academic strategic plan that is aligned to successful CCBSE research and their programmatic research agenda.

Monthly mentoring sessions throughout each academic year will include topics such as grant writing, graduate student and postdoctoral recruitment, establishing collaborations, etc. will be available to these faculty. In addition to formal mentoring, senior faculty colleagues will aid each other in reviewing proposals and manuscripts and providing advice on issues of science and research. Each mentored faculty member will be expected to prepare a plan for their research, including goals, milestones, and collaborations with other CCBSE or PROSPER team members.

Appendix E – SWOT Analysis

During the SWOT Analysis Meetings which occurred synchronously on July 14, 2020, asynchronously throughout the month of July, and then during the Strategic Planning Meeting, senior personnel were asked to consider all potential risks to the project and associated consequences. This includes the consideration of three NSF-facilitator driven scenarios related to COVD-19: 1) back to normal, 2) some hybrid between back to normal and continued restrictions, and 3) full restrictions (i.e., completely virtual).

ND-ACES SWOT Analysis

- Strengths Identified
  - Strong team with diverse and relevant expertise, an established track record of collaborative efforts, and confidence in and belief of the importance of theproject
  - Access to expert technical resources
  - Solid research plan building on expertise and resources of team
  - Access to competent student pool
  - Increased opportunities for student participants
  - Team science approach to ensure the involvement of all Pillars
  - Institutions involved in project have good reputation incommunity/among stakeholders
  - All institutions have administrative buy-in
  - Centralized, experienced state EPSCoR office that handles a majority of the logistics
  - Cash match from the State of ND
  - One unified center will help to direct resources and guide sustainability efforts

- Weaknesses Identified
  - Team is very large and diverse with many complex collaborative tasksto complete in a limited timeframe – **see Risk Mitigation Plan #1**
  - Inability to maintain consistent research ties to TCU, MCU, & PUI faculty due to their full-time teaching schedules, travel distances, and weather
  - Technical resources are not equal on all campuses – **see Risk Mitigation Plan #2**
  - Obstacles inevitable in our complex research plan that will require the team to be very adaptable – **see Risk Mitigation Plan #3**
  - Few opportunities to expand diversity activities beyond American Indians and women
  - Inability to get time from RU industry engagement, intellectual property, research partners, and innovation center personnel
  - Social media accounts have low audience engagement/content
  - Limited experience among senior personnel in working under acooperative agreement
  - With such diverse intuitions, communication regarding administrativedeadlines can be complex

- Opportunities Identified
  - Discovery of new ways to conduct research and outreach due to COVID-19
  - Potential of ND-ACES to build research capacity, expand workforce, and stimulate industry growth in ND
  - Enhanced student and early career faculty opportunities
  - Potential to address today's research questions in this area
  - Increased focus on the importance of ND STEM's pathway
  - Members of ND-ACES external advisory board are national level experts well versed in this arena who are poised to assist the team in their ultimate goalof sustainability
  - New research subject matter to North Dakota; not commodity-based research, so chance to be received favorably by state's stakeholders

- Threats Identified
  - Interruptions in ND-ACES activities due to COVID-19 – **see Risk Mitigation Plan #4**
  - Inability to recruit new faculty hires – **see Risk Mitigation Plan #5**
  - Decline or discontinuation of state support during the 2021, 2023, or 2025 legislative sessions – **see Risk Mitigation Plan #6**
  - A researcher becomes unable to contribute to project due to illness or departs University – **see Risk Mitigation Plan #7**
  - Inability to recruit qualified students
  - Flooding shuts down campuses
  - New collaborative external proposals not funded
  - Cyberinfrastructure challenges limit distance options – **See Risk Mitigation Plan #2**
  - Limited local collaborative interest from individuals and public and private entities
  - Financial implications that may result due to COVID-19
  - New research subject matter to North Dakota; not commodity-based research, so chance to be received unfavorably by state's stakeholders

COVID-19 Impacts from Asynchronous SWOT meeting: Identified Threats

- **Threat 1**
  - The uncertainty COVID-19 creates. Normally I know what the semester looks like and how much time things take but right now nothing is sure and I do not know what is going to happen in the fall which makes incorporating research more complicated. Will I have time to properly supervise the students in their research?
  - Faculty are still working on reopening plans for the fall
  - Right now, it is uncertain how much research we can do in the fall semester.
  - Balance between teaching and research duties. Current reopening plans require more time for teaching preparation and execution.
  - Time and class schedules will be the biggest challenge and will affect how flexible faculty can be.
    - Addressing Threat 1: The senior personnel have gained experience with online academic, research, and outreach activities during the 2020 spring/summer, which will serve the project team well as we implement ND-ACES.
- **Threat 2**
  - Research slowed in late spring but has returned to a level approaching normal through the summer. Graduate students are coordinating with each other so that their time in the lab overlaps as little as possible. With no teaching activities to worry about this scheduling approach has been manageable. Lack of clarity about makes short term planning for when the summer ends a challenge.
  - The time each student can work in the lab is somewhat limited as we try to minimize overlaps between students.
  - Potential to completely stop this research - cannot be done remotely at all.
  - Potential slowdown of research due to the limited time of students and access to the core facilities.
  - Can we do experiments, period. If we close the university like we did in March experiments cannot be performed.
  - Access to buildings and materials in case we get another stay in place order. If the institution is closed can we keep the cell cultures going?
  - If TCU campuses and/or K-12 schools are closed because of the virus, will we be able to do outreach online?
  - Teaching can be flexible online - cell culture cannot,

        - Addressing Threat 2: Until a dependable treatment or vaccine is available, we can prevent uncertainty. For example, the university may have to implement a stay at home order that may move into spring making research impossible. That will affect the 5-year plan. Thus, a quarterly review should be implemented with decisions based on all the available data; including scenarios for when students cannot be on campus. **See Risk Mitigation Plan #4.**
            - Some experiments currently planned to use core services may be outsourced on a fee-for-service basis
            - What are the alternatives to performing experiments and creating valuable experiences?
            - Need to acknowledge that progress on these projects may have to halt completely
- **Threat 3**
    - COVID-19 and the visa issues are restricting access to new graduatestudents for those of us that don't have one to take on this project yet. Many graduate students will not be here to start in the fall.
        - Addressing Threat 3: A quarterly review should be implemented with decisions based on all the available data; including scenarios for when students cannot be on campus. **See Risk Mitigation Plan #4.**
- **Threat 4**
    - The state of childcare or K-12 schools will directly impact the work some are able to do.
        - Addressing Threat 4: Senior personnel will work with their Pillar/ PROSPER leads as needed.
- **Threat 5**
    - What is the protocol if the students involved get COVID-19 or if they need to quarantine because a classmate/roommate/friend is infected?
        - Addressing Threat 5: A quarterly review should be implemented with decisions based on all the available data; including scenarios for when students cannot be on campus. **See Risk Mitigation Plan #4.**
            - Use additional PPE such as masks and face shields and develop a cleaning protocol of lab spaces. Research can continue as planned except for access to core facilities. Create a protocol for social distancing with students
            - Use PPE and social distancing during outreach activities.
            - Determine PPE need, and stock in advance knowing shipping and timing limits, Limit the number of people allowed in lab spaces at one time, increase cleaning protocol, increase work on virtual platforms as able, increase times lab spaces/tools are open and available for use
- **Threat 6**
- Determine PPE needs, keep a close eye on the situation and pre plan for the worst-case scenario to make sure everyone has enough supplies. Make sure to order now, rather than waiting until no supplies are available. Implement everything mentioned in B and C - but also determine safety of continuing research in lab space

    - If TCU campuses are closed for September and October, should we postpone NATURE Sunday Academies and hope that campuses will be open starting in November or should we offer the September and October Sunday Academies online?
        - Addressing Threat 6: TCU campuses are closed and NATURE Sunday Academies have been postponed. ND EPSCoR's Tribal Colleges/Universities and NATURE Manager and the Sunday Academy Co-Coordinators are working with the TCU NATURE Coordinators to bring this program entirely online. ND EPSCoR and the TCU NATURE Coordinators did this for the 2020 TCU Summer Camps, 2020 Bridge Camp, and 2020 University Summer Camp.

Participants in those camps gave the online activities good reviews

- **Threat 7**
    - Consider alternative suppliers if reagent acquisition becomes achallenge.
        - Addressing Threat 7: Decision of each participant
- **Threat 8**
    - Given COVID-19 and the complications it brings, is it too early to ask for a supplement to achieve our original goals and seize the opportunities presented? For example, we will have to allow for the fact that we will not be able to gather people (easily) in large groups and will need to find ways to enable people to participate from their homes or local safe spots.
        - Addressing Threat 8: Quarterly budget reviews will address operational changes in the event that budget line items cannot be used. **See Risk Mitigation Plan #4.**

SWOT category	Identified Asset to Leverage	Area of Impact	Action to Leverage Asset	Responsible Parties	Timeline
Strength	Team Science approach	All	The development and continued reflection on and improvement of the collaboration plan	All participants	Immediate implementation, on-going revising
Strength	Strong team with diverse and relevant expertise, an established track record of collaborative efforts, and confidence in and belief of the importance of the project	All	Participate a networking baseline at the beginning of the project to engage in continuous improvement of collaboration across institution and specialty	All participants	Immediate baseline gathered, ongoing continuous improvement process, networking survey given annually
Strength	Access to expert technical resources	All	Networking with Computational Research Center for UND and CCAST at NDSU	Computational Approaches Pillar	Networking is on-going
Strength	Solid research plan building on expertise and resources of team	CCBSE	Research Pillars will meet and collaborate monthly, research Pillar have assigned liaisons	Materials Design, Cellular Systems, Computational Approaches Pillars	Research meetings occur monthly
Strength	Access to competent student pool	All	Active recruitment and retention efforts	EWD, All participants	Mentoring, recruitment, and retention efforts are an on-going effort
Strength	Increased opportunities for student participants	All	Active recruitment and retention efforts	BP, All participants	Implementation efforts are on-going

Strength	Institutions involved in project have good reputation in community/ among stakeholders	All	Connect to established networks, engage in cross-institution communication and public relations strategies	Communication and Dissemination	Develop baseline
Strength	All institutions have administrative buy-in	All	All institutions engage in ongoing collaboration	All participants	On-going, all participant institutions responsive to situational change
Strength	Centralized, experienced state EPSCoR office that handles a majority of the logistics	All	Retention of existing staff, workflow prioritization of ND-ACES participant logistics	NDSU	On-going
Strength	Cash match from the State of ND	All	Leverage existing relationships with legislators and prioritize legislative outreach	NDSU	On-going efforts, focused efforts leading up to legislative sessions
Strength	One unified center will help to direct resources and guide sustainability efforts	All	All researchers meet monthly to discuss resources, collaborate, and address sustainability efforts	CCBSE	Monthly CCBSE research team meetings
Opportunity	Discovery of new ways to conduct research and outreach due to COVID-19	All	Contingency planning, tolerance of ambiguity, and responsiveness	All participants	On-going, all participants are responsive to situational ambiguity
Opportunity	Potential of ND- ACES to build research capacity, expand workforce, and stimulate industry growth in ND	All	Bi-monthly PROSPER meetings and monthly research team meetings	All participants	Regularly collaborate across specializations on ND-ACES
Opportunity	Enhanced student and early career faculty opportunities	CCBSE	Student recruitment to interdisciplinary graduate programs, graduate students collaborate with PUIs and Tribal Colleges and Universities	Education and Workforce Development	on-going
Opportunity	Potential to address today's research questions in this area	CCBSE	Collaboration between researchers leading to new avenues of scientific exploration and	CCBSE, Partnerships and Collaborations	on-going

			discovery, new partnerships with outside organizations		
Opportunity	New research subject matter to North Dakota; not commodity-based research, so chance to be received favorably by state's stakeholders	All	Connect with stakeholders regularly to assess engagement	All project participants, as appropriate	On-going
Opportunity	Increased focus on the importance of ND STEM's pathway	PROSPER	Regular outreach to K- 16 stakeholders	PROSPER participants, all	On-going
Opportunity	Members of ND- ACES external advisory board are national level experts well versed in this arena who are poised to assist the team in their ultimate goal of sustainability	All	Frequent collaboration with ND-ACES external advisory board members	All project participants, as appropriate	embedded in project
Weakness	Multi-location project separated by large physical distances can make informal interaction difficult	Communication and Dissemination	Adoption of a unified communication and collaboration platform for ND-ACES	All project participants,	Immediate implementation, on-going technical support
Weakness	Team is very large and diverse with many complex collaborative tasks to complete in a limited timeframe	All	Administrative use of a unified communication and collaboration platform	All project participants,	Immediate implementation, on-going technical support
Weakness	Inability to maintain consistent research ties to TCU, MCU & PUI faculty due to their full-time teaching schedules, travel distances, and weather	TCU/PUI/MCU	Collaboration agreement and adoption of a unified communication and collaboration platform	, all participants	Immediate implementation, on-going technical support, on- going revisions
Weakness	Technical resources may not be equal on all campuses	All	On-going awareness of funding opportunities to support endeavor	All project participants,	On-going
Weakness	Obstacles inevitable in our complex research plan that will	CCBSE, Research Pillars	Monthly research team meetings	CCBSE, Research Pillars	Immediate implementation of monthly research team collaboration meetings

	require the team to be very adaptable				
Weakness	Few opportunities to expand diversity activities beyond American Indians and women	PROSPER	More research opportunities for TCU faculty, TCUs need SPOs	PROSPER; all participants	Once baseline is defined
Weakness	Inability to get time from RU industry engagement, intellectual property, research partners and innovation center personnel	Partnerships and Collaborations	Determine cause and develop action plan, for example, if interns cannot be placed due to COVID-19, determine whether interns are able to be placed with other partners	All project participants	Once baseline is defined
Weakness	Social media accounts have low audience engagement/ content	Communication and Dissemination	Focus on social media platforms that are most important to our organization and most relevant to the public we serve to effectively manage online communities	all participants	Once baseline is defined, audit annually
Weakness	Limited experience among senior personnel in working under a cooperative agreement	All	Improve productivity by providing administrative implementation support	All participants	On-going
Weakness	With such diverse intuitions, communication regarding administrative deadlines can be complex	Communication and Dissemination	Adoption of a unified communication and collaboration platform for ND-ACES	all participants	Immediate implementation, on-going technical support
Threat	Interruptions in ND-ACES activities due to COVID-19	All	Develop, implement and regularly updated multi- scenario mitigation plans	All participants	Develop multi- scenario mitigation plan immediately and update continuously
Threat	Financial implications that may result due to COVID-19	All	Be aware of funding opportunities to support endeavors	Administration	On-going
Threat	Inability to recruit new faculty hires	CCBSE, Research Pillars	Increase recruitment and retention efforts, develop new virtual approaches	All participants	Develop multi- scenario mitigation plan immediately and update continuously

Threat	Decline or discontinuation of state support during the 2021, 2023 or 2025 legislative sessions	All	Leverage existing relationships with legislators and prioritize legislative outreach	All project participants, as appropriate	On-going
Threat	A researcher becomes unable to contribute to project due to illness or departs university	CCBSE, Research Pillars	Development of clear succession and recruitment plans	All participants	Immediate plan development, on-going revision as necessary
Threat	Inability to recruit qualified students	CCBSE, Research Pillars	Develop, implement and regularly updated multi- scenario mitigation plans	All participants	Immediate plan development, on-going revision as necessary
Threat	Spring river flooding shuts down campuses	All	Develop, implement and regularly updated multi-scenario mitigation plans	All participants and their institutions	On-going plan development and revision
Threat	New collaborative external proposals not funded	All	On-going awareness of funding opportunities to support endeavor	All participants	On-going
Threat	Inability to keep data secure	All	Work with technical experts on the project within Computational Research Center for UND and CCAST at NDSU	All participants	On-going
Threat	Limited local collaborative interest from individuals and public and private entities	Communication and Dissemination	Plan coordinated communication and public relations campaigns	, Communication and Dissemination Element participants	On-going
Threat	Cyber- infrastructure challenges limit distance learning options	All	Work with technical experts on the project within Computational Research Center for UND and CCAST at NDSU	Project participants from HPC units at UND and NDSU	On-going
Threat	New research subject matter to North Dakota; not commodity-based research, so chance to be received unfavorably by state's stakeholders	All	Leverage existing relationships with stakeholders and prioritize outreach	All project participants, as appropriate	On-going