Theme 1: Smart Nanomaterials for Applications in Life Science

1. **'Biocompatible nanofertilizers for targeted delivery and programmed release of essential mineral ions in crops', DKK 60 million**

   Applicant: Søren Husted, Department of Plant and Environmental Sciences, University of Copenhagen

   Co-applicants:
   Jean-Claude Grivel, Department of Energy Conversion and Storage, Technical University of Denmark, DK

   Henning Osholm Sørensen, Department of Physics, Technical University of Denmark, DK

   Subhasis Ghoshal, Department of Civil Engineering, McGill University, Cananda

   Brief description:
   To take advantage of the most recent breakthroughs within phyto-nanotechnology, allowing exploration and production the first generation of foliar fertilizers based on smart nanomaterials, tailored to effectively penetrate the micro- and nanoporous leaf cuticle. Only a fraction of nutrients contained in fertilizers are taken up by crops, the rest are leached to the environment, trapped by minerals or immobilized by microorganisms in the soil. The poor efficiency of fertilization is an economic burden for farmers, causes pollution and contributes to climate change. The efficiency of fertilization has practically not improved for decades and consequently there is an urgent need to rethink the principles for crop fertilization. We will develop the first generation of nanoparticle (NP)-based fertilizers with smart properties, which will allow us to bypass the processes responsible for the poor efficiency of fertilization. Biocompatible NPs will be tailored to feed plants through the porous surface of leaves. The NPs will be provided with properties which will allow targeting to the specific sites where the nutrients enter metabolism. Here the NPs will be programmed to release their cargo of nutrients, right at the doorstep of where they are used.

2. **‘Nanomaterials for efficacious cancer immunotherapy: in vivo engineering of immune cells and tumor microenvironment’, DKK 37.7 million**

Applicant: Sine Hadrup, Dept. of Health Technology, Technical University of Denmark

Co-applicants:
Yi Sun, Dept. of Health Technology, Technical University of Denmark, Denmark

Maria Ormhøj, Dept. of Health Technology, Technical University of Denmark, Denmark

Hinrich Abken, Regensburg Center for Interventional Immunology, University Hospital Regensburg, Germany

Brief description:
To transform the logistically challenging, expensive and ineffective chimeric antigen receptor (CAR) T-cell therapy into an ‘off-the-shelf’ in vivo modification strategy that can easily be tailored to the patients’ need. The ambition of Center for Nano-Immune Cell-Engineering (NICE) is to transform the logistically challenging, expensive and ineffective chimeric antigen receptor (CAR) T-cell therapy into an ‘off-the-shelf’ in patient modification strategy. CAR T-cell therapy is a new type of treatment where cells of the immune system is genetically re-programed to locate and kill tumor cells. In solid tumors, this type of therapy faces multiple obstacles including a costly manufacturing process, lack of persistence, and suppression by cells within the tumor. NICE will address these obstacles by use of small structures in nanoscale size which can be designed and utilized to generate CAR T-cells in the patient (in vivo), modify the tumor environment to favor CAR T-cell activity, and provide continuous stimulation to enhance the persistence of CAR T-cells for long-term attack of the tumor. Together, these initiatives will radically transform the CAR T-cell therapy and greatly benefit cancer patients.

3. **'Ultra-sensitive Bio-Magnetometers with Macro to Nano Resolution (BIO-MAG)', DKK 60 million**

Applicant: Nini Pryds, Department of Energy conversion and storage, Technical University of Denmark

Co-applicants:
Jean-Francois Perrier, Department of Neuroscience, University of Copenhagen, Denmark

Alexander Huck, Department of Physics, Technical University of Denmark, Denmark

Peter Bøggild, Department of Physics, Technical University of Denmark, Denmark

Brief description:
Aim: To create small, biocompatible, and lightweight magnetic sensors with femtotesla sensitivity, suitable for mapping neuronal activity in living organisms at room temperature using radically new smart materials. Every nerve cell in our body produces a tiny magnetic field when it fires. If we had magnetic sensors sensitive enough to measure such faint signals – 10 million times weaker than the Earth's magnetic field – we could non-invasively study the activity of neurons inside our bodies and gain a deeper understanding of how they work together in networks. This could ultimately let us screen for and prevent neurodegenerative diseases or provide remote control signals for prosthetic limbs. In BIO-MAG we will develop two different and complementary magnetic sensing technologies that work at room-temperature based on new 2D materials: microscale extraordinary magnetoresistive (EMR) devices and nano-scale magneto-optical color centers. By combining these technologies in arrays of ultrasensitive magnetic field sensors we will gain unprecedented insight into neurons, neural networks, and the workings of the human mind.

Theme 2: Proteins for Tomorrow's Food

1. **'PROFERMENT: Solid-state fermentations for protein transformations and palatability of plant-based foods', DKK 56,3 million**

   Applicant: Dennis Sandris Nielsen, Department of Food Science, University of Copenhagen

   Co-applicants:
   Anne S. Meyer, Department of Biotechnology and Biomedicine, Technical University of Denmark, Denmark

   Han Wosten, Department of Microbiology, Utrecht University, The Netherlands

   Wender Bredie, Department of Food Science, University of Copenhagen, Denmark

   Brief description:
   A transition to a more plant-based diet is vital to feed the increasing world population while reducing greenhouse gas emissions and may also lead to better health. Replacing meat is, however, challenging as it contains high amounts of accessible quality protein, important micronutrients, and sensory attributes considered attractive by most consumers. Several meat substitutes are on the market but often characterized by being highly processed and with added emulsifiers and flavours. Traditional products exist, however, where microorganisms transform local plant material into foods with meat-like characteristics. The cross-disciplinary centre will explore this huge potential by clarifying fundamental mechanisms of fungal and Bacillus-driven transformations of plant materials. The goal is to increase plant protein bio-accessibility and quality, flavour formation and texture, thereby enabling a rational design of clean-label, nutritious, and palatable alternatives for meat consumption.

2. **‘SEEDFOOD: Functional and palatable plant seed storage proteins for sustainable foods’, DKK 55.9 million**

   Applicant: Marianne Nissen Lund, Department of Food Science, University of Copenhagen

   Co-applicants:
   Alexander Buell, Department of Biotechnology and Biomedicine, Technical University of Denmark, Denmark

   Taco Nicolai, IMMM, Mans University, France

   Lilia Ahrné, Department of Food Science, University of Copenhagen, Denmark

   Brief description:
   The project will transform plant seed protein – that today is being spent for feed – to high value food proteins, which can be used to substitute animal protein in foods, cover the future protein gap and lower the carbon food print. The project will exploit new sustainable technologies for isolation of proteins to remove components that reduce palatability and digestibility. The isolated proteins will be examined in depth by state of the art biophysical methods to achieve a molecular understanding of the seed proteins making it possible to tailor the proteins to highly functional building blocks for food applications by applying sustainable biotechnological methodologies. The properties of the protein isolates and the tailor-made protein building blocks will be explored and improved using relevant food models with focus on achieving the best functionality and palatability. The project team includes international leading scientists in food science, bioengineering and biophysics.

Theme 3: Mathematical Modelling of Health and Disease

1. **'Predictive, multi-scale, multi-factorial Mathematical modeling of Knee OsteoArthritis (MathKOA).', DKK 49.6 million**

   Applicant: Michael Skipper Andersen, Aalborg University

   Co-applicants:
   Rami Korhonen, Department of Applied Physics, University of Eastern Finland, Finland

   Hanna Isaksson, Department of Biomedical Engineering, Lund University, Sweden

   Lars Arendt-Nielsen, Department of Health Science and Technology, Aalborg University, Denmark

   Brief description:
   Osteoarthritis (OA) is a joint disease that causes degradation of the structures in the affected joint. The disease is the 6th most common cause of disability worldwide and causes mobility limitations, pain and reduced quality-of-life. OA is a multi-scale disease that is affected by factors on the body, joint, tissue and cell levels as well as pain.

   Currently, there is a lack in our understanding of this multi-scale and multi-factorial disease and treatment selection is often a trial-and-error approach, where the patient has to return to the clinic regularly. Therefore, in this project, we will develop a mathematical model of Knee OA (KOA) to describe the multi-scale and multi-factorial relationships and hereby enable computer-based investigations of how the treatment options will affect the outcome on all scales. This model will be applied to develop optimized, personalized treatments with the ultimate goal of improving patient care and reduce the associated societal costs of KOA.

2. **'Mathematical Modelling for Microbial Community Induced Metabolic Diseases (MATOMIC)', DKK 46.2 million**

Applicant: Daniel Merkle, University of Southern Denmark.

Co-applicants:
Peter Stadler, Department of Computer Science and Interdisciplinary Center of Bioinformatics, University of Leipzig, Germany

Christoph Flamm, Department of Theoretical Chemistry, University of Vienna, Austria

Martin von Bergen, Department of Molecular Systems Biology, Helmholtz-Centre for Environmental Research, Germany

Brief description:
The obesity pandemic in westernised countries calls for novel therapeutic approaches in order to improve the life of affected individuals and to lower the societal burden. Changes in the composition of the microbiome, i.e., the mixture of microorganisms that live in the intestine and help humans to digest food, have been linked to the disease. Therefore inducing changes in the microbiome composition poses a promising strategy for obesity treatment. The effects of such interventions are unfortunately far from being understood. The proposed project attacks this fundamental problem by a synergistic combination of advanced mathematical modelling techniques and wet-lab experimentation, which will culminate in a predictive model of how interventions affect the structure and composition of the microbiome. The efficacy of our approach will be tested for generating a lean phenotype in obese mice and will further be optimised in order to design a novel therapeutic tool for treating obesity.