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CET | Europe, Brussels

Proposal(s)

Motion Analysis, Multi-Omics, Novel Biosensors for Osteoarthritis Diagnosis and New Therapeutics.

Proposal acronym MANITOABA

Most relevant specific IHI objective(s) that match your proposal

SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focussing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treatment and management of diseases, meeting the needs of end-users

SO5: enable the development of new and improved evaluation methodologies and models for a comprehensive assessment of the added value of innovative and integrated health care solutions

Keywords that are most relevant to my proposal:

Non-communicable diseases | Prediction | Prevention | Detection | Diagnosis | Treatment | Digital health | Health technology

Member of an IHI industry partner?

No/not applicable

Challenges our proposal addresses

Diagnosing osteoarthritis (OA) early and accurately, along with preventing it and providing suitable treatment, poses significant challenges. The disease progresses with symptoms such as pain, swelling, loss of function and deformity. Currently, these symptoms are assessed through patient history, semi-quantitative questionnaires and imaging techniques. There is however a pressing need to quantify functional loss and metabolic changes in serum and synovial joint fluid (SJF) using advanced technologies, biosensors and novel therapeutics. This interdisciplinary proposal aims to introduce marker-less human motion analysis (MAI) technology for quantifying function in OA. MAI technology allows for the easy collection of real-life motion data from patients, bridging the gap between a sophisticated motion analysis

lab and patients' settings. The MAI platform is designed for simple use at home or office without requiring special equipment. Recent advancements in multi-omics technology enable the measurement of disease progression and treatment response. Our second objective is to collect and analyze SJF from OA patients before and after treatment. Since the metabolic activity of joint structures is reflected in SJF rather than serum, these outcomes will enhance our understanding of the disease's natural progression and validate treatment responses. Both MAI and multi-omics technologies utilize AI-driven complex software. From the multi-omics data, which includes transcriptomics, proteomics, metabolomics and lipidomics, our third goal is to develop and validate digital microfluidic and surface plasmon resonance (SPR) biosensors for anti-inflammatory, pro-inflammatory, anabolic and catabolic biomarkers of OA. These in-vitro diagnostics can be transitioned from the lab to patient care, allowing for use in outpatient settings and enabling patients to monitor their treatment responses. Finally, we will focus on developing new therapeutics, including cell-based therapies. We will test the delivery of novel regulatory nucleic acids combined with clinically approved adjuvants, such as PRP and physiotherapy, in osteochondral models to prepare for personalized medical treatments.

Short description of the proposal

Novel and quantitative OA diagnostics that will lead to the development of new biosensors and therapeutics.

Why our proposal is a good fit for IHI

As outlined in the IHI Strategic Research and Innovation Agenda (SRIA), the aging population in the EU and globally is rising. Osteoarthritis is associated with high levels of disability, co-morbidity,and increasingly mortality. The incidence of OA in Europe has surged by 54% since 1990, with a 104.9% increase in disability-adjusted life years (DALYs) from 1990 to 2016. Knee OA shows an incidence of 375 per million and a prevalence of 4,294.3 per 100,000, resulting in significant years of life lost due to disability (YLDs) and DALYs. The burden of OA is particularly pronounced in aging populations and among women. In 2019, the loss of healthy life in Western Europe amounted to approximately two million years. Furthermore, OA is becoming more common among younger individuals due to increased sports and workplace injuries. The associated pain and functional loss diminish quality of life and adversely affect mental health, leading to broader societal impacts and increasing indirect costs. The direct and indirect costs of OA due to lost productivity were estimated at €7.2 billion and €4.6 billion, respectively.

The marker-less human motion analysis (MAI) system predicts both normal and abnormal joint motion during sit-to-stand tests. This technology allows patients to use it independently from any location with a PC or smartphone. It is already available for diagnosing, monitoring disease progression, and evaluating treatment responses in OA, leveraging AI to potentially predict therapy outcomes. Quantified joint angles and balance metrics can inform adjustments to OA management and treatment.

Multi-omics encompasses transcriptomics, proteomics, metabolomics and lipidomics. Analyzing serum and SJF samples with quadrupole time-of-flight liquid chromatography-mass spectrometry (Q-TOF LC/MS) helps identify phenotypes and endotypes of OA. Given that OA manifests differently among patients and progresses through inflammation, degeneration and regeneration, our previous studies—currently under evaluation for publication—have addressed several challenges. We developed methods for separating articular joint-related lipids and proteins from serum and SJF, which enhances analysis during Q-TOF LC/MS studies. Our metabolomics research has differentiated metabolites in degenerated versus non-degenerated rotator cuff tendons. We have also examined the metabolites in leukocyte-rich and poor platelet-rich plasma, which is frequently used in OA treatment. Research on SJF in primary and secondary OA reveals significant metabolic profile differences that could lead to new molecular insights. Our team has strong expertise in SJF multi-omics studies but recognizes the need for deeper investigations

into the various genotypes, endotypes and phenotypes of OA, as a single omics approach may not apply to all patients.

Digital microfluidic and surface plasmon resonance (SPR) biosensors, previously validated for cancer diagnostics, are being adapted for OA applications in serum and SJF samples. OA patients frequently visit outpatient clinics and often seek updates on their condition and treatment effectiveness, which traditionally relies on physical and radiological examinations. Advanced techniques like ultrasound and MRI are seldom utilized unless part of a clinical trial. Implementing biosensors in outpatient settings can provide timely insights into treatment responses. The Foundation for the National Institutes of Health Biomarker Consortium's biomarkers project has identified several wet biomarkers useful for diagnosing and monitoring OA progression. Eight serum protein biomarkers have been found to differentiate knee OA patients from healthy individuals, while six serum peptides have been linked to predicting OA development and progression. Several adipokines, such as leptin and adiponectin, have also been proposed as OA biomarkers, emphasizing the need to consider co-morbidities. We aim to develop, validate and patent new biosensors informed by multi-omics findings throughout this project.

Incorporating new therapeutics into OA treatment protocols is vital. Options like nucleic acids could enhance treatment effectiveness, shorten treatment duration and improve outcomes. This approach has shown success in bone regeneration and can be applied to joint treatments in clinical settings. The safety and efficacy of nucleic acids will be assessed throughout this project, alongside evaluations of cell-based therapy options.

This proposal addresses a prevalent chronic non-communicable disease that significantly impacts morbidity and mortality rates. Osteoarthritis affects nearly half of the population, with a higher prevalence among women living in poverty. Both men and women are similarly affected in older age. The condition diminishes quality of life and independence. Alongside osteoporosis and sarcopenia, OA poses a significant health challenge for the elderly population. Currently, there are no medications or vaccines that can alter the disease's progression and while some dietary supplements are commonly used, they often provide limited relief from symptoms. Motion analysis can be effectively integrated into the diagnosis, prevention and treatment outcomes for OA. Multi-omics approaches can enhance our understanding of the inflammatory, degenerative and regenerative phases of the disease. Throughout this project, biosensors can advance from technology readiness level (TRL) 4 to TRL 6, making them suitable for production by industry after patent licensing.

Several risk factors for OA have been identified, including injuries such as fractures, strains and repetitive stress from sports or work, as well as pre-existing joint conditions like gout, metabolic disorders such as diabetes, obesity, genetic predispositions and sociodemographic factors like age and female gender. The proposal's originality lies in incorporating AI-driven motion (MAI) analysis, multi-omics data, biosensor platforms, and the development of new therapeutics, including nucleic acids, molecules, and regenerative interventions.

The anticipated impacts of the project include the ability to register OA patients across Europe into the MAI system without relying on complex motion analysis laboratory results. Multi-omics data derived from serum and SJF will offer new advancements for diagnosing and monitoring therapeutic efficacy. For example, the effectiveness of disease-modifying therapies—such as intra-articular corticosteroids, hyaluronan, hydrogels and cellular treatments—can be tracked with advanced technology. Microfluidic and SPR biosensors will be designed and tested in real-world applications.

This interdisciplinary project will involve a diverse team of medical professionals, pharmacists, analytical chemists, engineers, computer scientists and biomedical researchers. The scientific findings will be shared through congress presentations, peer-reviewed articles and book chapters, reaching a wide audience. Preference will be given to conferences that publish abstracts in renowned Web of Science (WoS)-cited media. Manuscripts will be submitted to high-impact, peer-reviewed journals, with key papers prioritized for the Open Research Europe platform. Books and chapters will also be published with established publishers.

The biosensor platforms and new therapeutics present potential for patent applications, creating both economic and technological benefits. These innovations will enable efficient screening of OA patients' disease progression and treatment response, reducing diagnostic and treatment costs. Once patents are justified, the consortium will pursue licensing opportunities. Intellectual property will be managed according to the consortium agreement, with the ultimate goal of gaining approval from regulatory bodies like the European Medical Agency, the British Standards Institution and the Turkish Standards Institution. The proposal aims to establish new standards in OA diagnosis and treatment, alleviating the disease's burden.

To maximize societal impact, close collaboration with patient advocacy groups will amplify the project's outcomes. The consortium members, who are also part of the EU-COST-CA21110 Action "NetwOArK," are working towards the establishment of the European Society for Osteoarthritis (EUSOA) and are highly mindful of environmental concerns.

The global OA therapeutics market is expanding rapidly, valued at $7.96 billion in 2023 and projected to reach $15.86 billion by 2031. The growing elderly population is a key driver, as age is a significant risk factor for OA. There is increasing demand for less invasive treatments like arthroscopy, and improved diagnostic tools, such as those proposed by NOOA, are crucial for implementing new therapies. Additionally, AI offers a promising opportunity for personalized OA treatment. Cost-effective therapies like nucleic acid delivery will be essential to scale solutions for a large patient population.

The inclusion of numerical data from MAI and multi-omics, combined with AI analysis, may offer new insights into OA diagnosis, disease progression and treatment outcomes. This approach could significantly reduce years lived with disability (YLDs) and disability-adjusted life years (DALYs). Since women are disproportionately affected by OA and tend to live longer, the target population will mainly consist of women, with a focus on promoting an independent lifestyle in older age. The MAI technology will facilitate longitudinal assessments of OA patients, such as tracking joint angle changes during sit-to-stand tests. Biosensors will enable timely intervention, and new therapeutics may not only relieve symptoms but also promote tissue regeneration.

What results/outcomes and impacts we expect our proposal to deliver

Academic outcomes are estimated to be articles, book chapters and book publication. New researchers will be educated. Patents will be obtained.

Are we part of a consortium

Yes

Partners already involved

Academia Research body

Expertise and resources we already have

This interdisciplinary project will involve a diverse team of medical professionals, pharmacists, analytical chemists, engineers, computer scientists and biomedical researchers. There are four orthopedic surgeons and two rheumatologist in the consortium from four different countries. The motion analysis technology is developed in the UK in an SME. Multi-omics studies are currently carried out in two centers and one of these centers is specialized in SJF analysis. Biosensors are studied in two centers. Currently there is an expertise in oncology biosensor, which will be transferred to OA biomarkers in the scope of this proposal. New therapeutics were previously developed for fracture healing and bone regeneration. This technology will transferred to structures of the articular joint in the context of this proposal.

Expertise and resources we are looking for

We are looking for patient societies and SMEs to join our consortium.

Experts

Feza Korkusuz

Professor, Department Chail @ Hacettepe University Faculty of Medicine, Ankara, Turkey

Hacettepe University Faculty of Medicine, Ankara, Turkey ☆

Ankara
Turkey

Website

https://www.hacettepe.edu.tr

Organisation Description

Hacettepe is a high-ranking state university located in Ankara, Türkiye. The main purpose is research, education and providing service. Hacettepe University Hospital is a reference hospital for the nation. The main campus is health related and does collaborative research at the national and international level.

Organisation Type

Academia

Cooperation we you looking for

Consortium/coordinator looking for partners

If we bring in-kind contribution to the project

No

We are a member of the following IHI industry association(s).

Not applicable

Have we already started to build a consortium?

Yes

Contact person(s)

Feza Korkusuz
Professor,
Department Chail
@ Hacettepe
University Faculty
of Medicine,
Ankara, Turkey