Project description

Although treatment of rheumatoid arthritis (RA) has improved in the last years, there is still no disease modifying treatment for osteoarthritis (OA). For treatments to be effective it is considered extremely important to detect and treat these diseases early and then be able to monitor treatment efficacy early on (within weeks or months) after its initiation rather than waiting up to a year for RA and 18 months for OA. The main objective of the NanoDiaRA project is the development of nanotechnology-based diagnostic tools for easy and early detection of disease onset, progression and responses to therapy RA and OA. RA is a chronic inflammatory joint disease that involves acute and chronic synovial (joint lining) inflammation causing the erosive destruction of articular cartilages, ligaments and subchondral bone. It develops in about 1% of the population. OA, currently the main cause of disability among the middle age and elderly populations, is a degenerative arthritis involving much less synovial inflammation in most patients, with a prevalence of about 12% of the population. Debilitating symptoms such as loss of joint function, chronic joint pain and fatigue lead to frequent loss of employment, to a significant decrease of the patient's quality of life and to substantial economic burden.

Early diagnostic tools and biomarkers for the detection and determination of disease onset and for evaluating the rapidity of disease progression as well as the ability to gain rapid insight into the efficacy of therapeutic interventions are essential if we are to expedite and enable for future drug development and use. Existing diagnostic methods, namely radiographic analyses (X-rays) and magnetic resonance imaging (MRI), are not sensitive enough for the early detection of inflammatory changes such as in RA. Presently we often lack good ways of making a sufficiently early diagnosis or an effective estimation of the prognosis. Neither can we determine treatment efficacy in the short term. Therefore it is necessary to introduce new diagnostic techniques with much greater sensitivity and specificity to address these key issues. At present we detect disease outcomes by measuring structural damage. What we need is the ability to detect and measure the disease process rather than the outcome so we can see what is happening much earlier. The proposed technology, based on tissue and molecule speci?c MRI using a combination of nanotechnology, cell biology and immunology, is designed to enable the investigation of pathological processes in tissues, such as inflammation of the synovium and degradation of articular cartilage. By using MRI based molecular imaging of biological and pathological processes it should become possible to detect experimental and human arthritis onset and progression. Thereby we should be able to treat disease and monitor responses to treatment much earlier and effectively, thereby minimizing joint damage which is usually irreversible.

We are also developing new blood and urine nanotechnology-based diagnostic biomarker assays. These will detect whole body arthritic disease related changes involving joint tissues that reflect the disease process. They are designed to be very sensitive, easy to use and affordable immunoassay benchtop analytical systems for widespread clinical use.

In view of the development of this targeted nanoparticle-based technology there are also opportunities to use this tissue-targeted approach for locally controlled drug release (e.g. in joints alone/intra-articular). This way of improving drug delivery to minimize possible side effects is a long term future approach which will be examined for its feasibility during the

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term of the project. The overall project follows a personalized medicine approach and is driven by the prominent unmet clinical needs outlined above.

The NanoDiaRA project is divided into five research work packages and four supporting work packages. While the research packages deal with fundamental research, the latter are particularly addressing dissemination, publication and valorization of the research outcome, investigation of the ethical issues, training of young investigators and the administration of the project.

Please find the short description of the work packages under the titles mentioned below.

Research work packages:

- WP 1: Particle coating and functionalisation and novel equipment for coating and separation
- WP 2: Inflammation and tissue damage detection by cell and tissue tracking and molecular MRI based imaging
- WP 3a: New Biomarker/ligand and antibody detection and development: targets, antibodies and peptides
- WP 3b: New Biomarker/ligand and antibody detection and development: Clinical relevance
- WP 4: Development of bioassays
- WP 7: Toxicity

Supporting work packages:

- WP 5: Scientific Coordination and Data Management
- WP 6: Ethical, Legal, and Social Aspects, Technology Assessment (ELSI)
- WP 8: Dissemination of Results and Foreground, Communication, Education & Training
- WP 9: Management