Lay summary of research project grant application

1. Objective of the project

We aim to understand the mechanisms responsible for the early stages of disease development in rheumatoid arthritis (RA) in order to identify environmental and life style factors that can be modified and to design new strategies to specifically target these mechanisms. By this, prevention of RA will be achievable in the future.

2. Background

A majority of the chronic diseases results from inflammation due to the body reaction against own tissues. RA is such a disease where the abnormal body's reaction leads to formation of antibodies. We and others have shown that the lungs and the oral cavity (that are exposed to smoking and others pollutants) might be the starting point for the body's reactions in RA. In some persons (specifically in those smoking and having a sedentary life style) these reactions will lead to pain and bone loss already before disease onset. We face therefor a new clinical entity (antibody positive pain and boss loss) that requires better tools for diagnosis and offers opportunities for prevention.

1. Methods and approach

We will use clinical data and biological material obtained from persons at risk for developing RA (one of the largest follow-up programs with more than 2000 participants, either those having antibody positive joint pain or those being first-degree relatives of RA patients). We are developing better tools to identify these persons, such as e-health web based questionnaires. We will study how environmental factors interact with the body tissues (lungs and oral cavity) to give rise to disease-associated antibodies and how these antibodies contribute to pain and bone loss. This will allow each person to get more insights into the risk of developing RA and in what one can do self to minimise it.

2. Primary and secondary outcome measures

Primary outcome measures in the study population are pain and bone loss and secondary outcome is RA development.

3. Recruitment of participants

Recruitment is facilitated by an existing infrastructure to detect and follow persons at risk for developing RA.

4. Inclusion and exclusion criteria

We will include men and women, 18 years and older positive for RA-associated antibodies having or not pain but not having RA and first degrees relatives of RA patients.

5. Expected benefits for patients

The project will improve identification of persons with risk to develop RA, allowing disease prevention by a combination of (1). life-style and environmental changes (taking advantage of the patient own possibility to influence the disease outcome) and (2) specific targeting of new identified mechanisms.

6. Expected benefits for society

Early detection and better treatment will allow prevention/delay of the disease avoiding progression to a chronic phase with disability that lead to decreased work ability, impairment of life quality and high healthcare costs.

7. **Burden for patients participating in this study (if applicable: compare burden for intervention group and control group). What methods will be applied to carry out the project?**

Persons with risk for developing RA are offered the possibility to participate in a follow-up program and will be informed on the current knowledge on the risk of developing RA. No interventions are planned in the current study.

8. **Patient involvement in the design and conduct of the study**

Patient research partners have been contacted. Preliminary feedback has been obtained from the patient partner in Stockholm, and suggested changes have been integrated. We will also involve persons at risk for developing RA. Contact persons that will facilitate patient partners participation have been identified. Specifically, patient partners will be involved in developing tools for measuring patient relevant outcomes (pain), for improving recruitment (e-health tools to facilitate access to rheumatology units), for risk communication tools and for implementation of life-style changes (such as apps for quitting smoking and motivate for increased physical activity). A specific part of the budget (10%) is dedicated to facilitate patient partners participation to meetings and other research activities. We estimate the risks of the current project as low. The follow-up time (restricted to 3 years in the current project) might impact on the possibility to make definitive conclusion on RA development, but not on the primary outcomes (pain and bone loss).