Introduction

Diagnosis of diseases affecting the locomotory system currently depends on physical examination, patient history and diagnostic radiography. An important component in the radiographic analysis is a decreased distance between the bone ends in the joint. Consequently, the disease process is identified only following loss of cartilage tissue. Thus, the approach is not very sensitive for those early phases of the disease that are more likely future targets for successful intervention.

New developments in MRI will most likely improve the sensitivity for detecting changes in the joint tissues at an earlier stage of the disease. Although most of today's efforts within MRI are directed towards imaging the joint to detect altered cartilage surface and thickness, it is possible that future developments will enable us to discern early structural alterations in a cartilage of normal thickness.

Over the recent ten years, however, new approaches have been developed to identify early changes in the tissues of the diseased joint. Any process in the joint structures will be reflected at the molecular level, either as fragmentation of structural molecules or as a biosynthetic response to the tissue damaging process. Studies have indeed shown that fragments of cartilage and bone macromolecules can be detected in synovial fluid as well as in the general circulation as a result of the process. These will serve as indicators of the tissue destroying process, but may also indicate tissue remodeling. At the same time presence of intact, tissue derived molecules will mark new synthesis where those molecules not incorporated in the structural framework of the tissue may be released into surrounding body fluids.

Bone and cartilage both differ with regard to their macromolecular composition with topographical site. Thus, in articular cartilage the superficial parts are different from those deeper and the region close to the cells is different from that further away. Bone composition differs between regions closer to the cartilage and cortical bone, respectively. Thus processes that start in a given compartment can potentially be selectively monitored by assaying fragments representing macromolecules with a distinct tissue distribution.

One prospect for the future is that a pattern of typical fragments and intact macromolecules found in a particular body fluid will reflect the disease process such that the stage of tissue alterations and the prognosis can be delineated at an early phase of the disease. Indeed, there are already reports on markers that predict future joint destruction in both rheumatoid arthritis and osteoarthritis.

The characteristics of the tissue destroying process may be different from the normal remodeling. Provided that different sets of proteinases are activated, it should become possible to use neoepitopes created by the cleavage of a particular protein to specifically identify those processes that lead to tissue breakdown.

One important consequence of the new technology is that it provides a new opportunity to discover changes at an early stage of the disease, when the prospects for efficient therapeutic intervention are greater. Also, monitoring the efficacy of this therapeutic intervention, when initiated before the other diagnostic procedures detect changes, will have to depend on molecular marker technology, optimally in combination with long term outcome measures. The sensitivity will improve as we develop new assays for prognostically strong markers, which will allow us to select groups at higher risk and therefore decrease the number of patients required.

It may even become possible to use a set of several markers that each indicate events in different compartments of the tissue and also provide indications of the balance between tissue breakdown and attempted repair to show reversal of the tissue destroying activity. This approach is likely to provide an outcome measure within a very short time frame.

At a time when we can see so many potentials for this new technology it is important that new information is adequately spread to all disciplines involved. These are diverse and reach from molecular biology to clinical epidemiology, with important contributions from industry in applying assays developed to larger scale analysis and wider availability. The report from this symposium on molecular markers contains information on current standing with regard to assays and how they are evaluated and correlated to traditional outcome measures.

For the editors

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