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Stiftung zur Förderung der Erforschung von Ersatz- und Ergänzungsmethoden zur Einschränkung von Tierversuchen

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Project

Development of an in vitro model of rheumatoid joint destruction by using cross-linked fluorescent-labeled collagen matrices

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Development of an in vitro model of rheumatoid joint destruction by using cross-linked fluorescent-labeled collagen matrices

Rheumatoid arthritis is a common autoimmune disorder and the most frequent and severe inflammatory joint disease. Without treatment, it often leads to the destruction of affected joints and to severe disability. Mesenchymal cells within the inflamed synovial membrane, the synovial fibroblasts, play a central role in the progressive destruction of cartilage in that they firmly attach to the cartilage matrix and release matrix degrading enzymes. Of note these rheumatoid arthritis synovial fibroblasts exhibit a pattern of stable cellular activation that has been compared with that of some tumor cells, the ultimate cause of which, however, remains elusive.

To further study the activation of synovial fibroblasts in RA and to develop novel therapeutic approaches to treat rheumatoid joint destruction, well-standardized test systems are needed. So far, animal models have been used for that purpose. Current in vitro approaches that use pieces of whole articular cartilage have important limitations as intact cartilage can be kept in culture only for limited periods of time and under difficult conditions. This is mainly because natural degradation processes occur that result in poorly interpretable results even within short investigation periods. Exact quantification of matrix degradation causes additional problems.

Therefore, the present project has been initiated to develop and establish a novel in vitro assay of rheumatoid joint destruction that in its validity and reliability is comparable to animal models and, thus, may lead to a significant reduction of animal experiments. To this end, an in vitro assay will be set up and validated, in which the artificial cartilage matrix resembles important features of human articular cartilage and in which the quantification of matrix degradation is facilitated by the use of an innovative fluorescence labeling. Even if animal experiments will be inevitable for certain (approval-relevant) analyses, the availability of such an in vitro method may lead to a significant reduction of animal experiments particularly in early phases of the respective studies and even replace animal experiments in some specific questions.

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