

SUJET DE THESE: financement UM1/REGION pour 3 ans

TITRE: Identification et rôle de microARNs liés à la sénescence et la dédifférenciation des chondrocytes durant l'arthrose <[http://www.adum.fr/as/ed/voirproposition.pl?site=cbs2&matricule\\_prop=1369](http://www.adum.fr/as/ed/voirproposition.pl?site=cbs2&matricule_prop=1369)>

RESUME:

MicroRNAs (miR) are small non-coding regulatory RNAs involved in a number of biological functions such as proliferation, apoptosis or differentiation. A recent study and our results have shown that Dicer, an essential component for biogenesis of miRs, is necessary for normal articular development. However, miR deregulation occurs in various diseases such as cancer (1). These observations suggest that miRs are important players in tissue homeostasis and may be involved in the physiopathology of osteo-articular systems. Osteoarthritis (OA) is a common chronic degenerative disorder characterized by cartilage and bone lesions affecting more than 25% of the population older than 60 years of age. The heightened risk for OA development with increasing age may be explained by age-related changes in chondrocytes. Despite active research in the field, there remain challenges to understanding the complex processes linking OA pathogenesis and aging. Indeed, identification of new regulatory pathways will help to understanding how to modify the processes involved in OA. Among these, miRs are likely to play a role in modulating the role of the numerous molecular and cellular players acting in OA cartilage. Understanding the role of MIR expression will undoubtedly help developing new therapeutic approaches. We propose the following steps: 1) Identification of miRs involved in the regulation of senescence-associated and dedifferentiation associated genes in OA cartilage, 2) in vitro validation of the functional role of miRs in OA-associated senescence and dedifferentiation, 3) identification of the targets of the selected miRs to understand the signalling pathways that are deregulated in aging chondrocytes and 4) in vivo validation of the selected miRs in OA murine models.

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