



BIOINFORMATICS SEMINAR

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Chondro-protective Mechanism of Statin

Statins are a class of drugs prescribed to more than 25 million U.S. people to control blood cholesterol. Recent clinical trials found that use of statin is associated with lower occurrence of osteoarthritis (OA). However, clinical application of statin in OA treatment is hindered due to the lack of knowledge about its chondro-protective mechanisms. Statin is known to inhibit the mevalonate pathway in cells to reduce the cholesterol synthesis. In this study, we hypothesized that inhibition of the mevalonate pathway in chondrocytes by statins intervenes the downstream small GTPases (Rho, Ras, Rac etc.) activities, which prevents chondrocytes from entering the aberrant phenotypic shift under inflammatory attack, which protects the integrity of cartilage ECM. RNA-sequencing was performed on the cartilage to identify the important networks and gene set that were responsible for the chondro-protective effects of statin. In addition, we used the large clinical data sets available from Christiana Care Health System, where osteoarthritis is a common presenting problem and statin use is routine, to evaluate whether use of statins is associated with a lower incidence of OA. In summary, repurposing of the FDA-approved drug, statin, could be a new pharmaceutical solution for PTOA prevention. Statin inhibits the mevalonate pathway in chondrocytes, which further induces the dormancy of small GTPases activities and prevents



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