Using tissue engineered cartilage to investigate diabetes-induced osteoarthritis

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INTRODUCTION: People with diabetes have more than double the incidence of osteoarthritis.

Despite the huge and increasing global incidences of both diabetes and osteoarthritis, research on diabetes-induced osteoarthritis (DiOA) as a specific condition is very limited, partly because neither animal models nor traditional cell culture are capable of fully replicating the disease state. We have generated a lab-grown tissue engineered human model of diabetic osteoarthritis to investigate the effects of high glucose concentrations on chondrocytes, uncover the DiOA mechanism and determine the efficacy of several interventional treatments (including ascorbic acid and aspirin) to reduce cartilage damage in people living with diabetes and hyperglycemia.

METHODS: Tissue engineered cartilage combines human chondrocytes with an agarose- or alginate-based hydrogel to support chondrocytes in a transparent matrix, recreating the actual cell density and tissue function of native adult cartilage. The TE cartilage was cultured in either 'normal' 1g/l (5mM) glucose, high (4.5g/l; 25mM) or very high (10g/l; 55mM) glucose concentrations for 21 days. Media assays were performed to determine the synthesis and secretion of collagen, glycosaminoglycans and total protein by the chondrocytes. Interventional compounds were added to the media to test the targeted protective effects of ascorbic acid and aspirin (acetylsalicylic acid) on chondrocyte ECM production.

RESULTS: Chondrocytes survived in very high glucose concentrations (>10mg/ml) with little loss in viability, but their production of collagen and other proteins over 21 days was inhibited by high glucose (fig 1 a-c). The production of glycosamino-glycans (sGAGs) was unaffected even in very high glucose-containing media (fig. 1.d). Supple-mentation with ascorbic acid (vitamin C), resveratrol and tocopherol (vitamin E) mitigated the effects of hyperglycemia, whilst high doses of acetylsalicylic acid (aspirin) were shown to completely reverse the disease phenotype and return collagen production to normal levels.

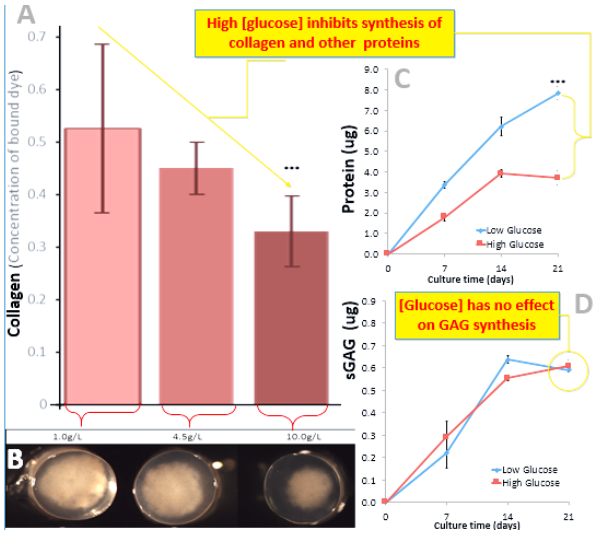

Figure 1: Collagen secretion (A) and accumulation in the tissue engineered cartilage (B) was ~40% lower in high glucose media compared to low glucose controls after 21 days. Over this time, high glucose levels of 10g/l caused a significant reduction in protein secretion in comparison to controls (C), whilst the chondrocytes secretion of sGAGs was unaffected by the excess of glucose (D). Error bars show SEM, n=6 in A, n=16 in C&D; *** $p<0.001$.

DISCUSSION & CONCLUSIONS: Diabetes-induced osteoarthritis may be a unique type of OA with a treatable cause. Our research focusses on understanding the mechanism for the condition and evaluating dietary supplements that may mitigate or reverse cartilage damage caused by persistent hyperglycaemia. The role of mitochondria as key regulators of the disease is currently under investigation.

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