Our Elastic Shape is Held Together by Carbohydrate Strings. Implications for The Aetiology of Osteoarthrosis

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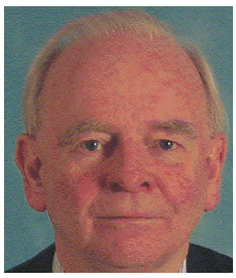

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Without reproducible permanent shapes central functions (digestive, circulatory, nervous) could not have evolved. Animal shapes are maintained by the extracellular matrix (ECM) of connective tissues. ECM shapes depend on getting collagen fibrils into the right places and keeping them there (1), held by regular, frequent and specifically located bridges or ties made of proteoglycans (PGs). These carry the anionic glycosaminoglycan (AGAG) strings that span the interfibrillar spaces, helping to maintain

ordered fibrillar matrices and hence shape. They are present throughout the animal kingdom, even in remote animals, e.g. echinoderms (1).The strings are 'spliced' aggregated chains of dermochondan, keratan and chondroitan sulphates, stabilised by hydrophobic and hydrogen bonds. In these bridges (2) (a) PG proteins attach specifically to collagen fibrils (3), (b) antiparallel chains of PG AGAGs aggregate (2) and (c) the length of the AGAG chains equals the distance between the fibrils (2). I called them 'shape modules' since they repeat regularly and hold together varied shapes of ECMs.

These structures must be elastic. I proposed 2 mechanisms (4) which endow AGAG bridges with reversible deformability;- (a) reversible cycling between conformers of L-iduronate in dermochondan polymers and (b) a sliding filament model in which specific AGAG/AGAG interactions break under stress and reform when the stress is removed. Direct proof of (a) was obtained by stretching individual AGAG molecules (5). rheoNMR showed the potential of (b).

This model has been tested against biomechanical data from specific tissues. E.g. cartilages are built of shape modules, predicting for the first time the anisotropic responses (along and at right angles to shape module axes) of articular cartilage to compressive and tensile stresses. Degradation of shape modules in osteoarthritis, the major crippling disease, would reduce these responses. Thus, loss of shape modular function in binding together collagen fibrils via decoran bridges, would result in sucking-in of water as fibrils drift apart under the swelling pressure of aggrecan,etc. Stanescu claimed loss of a decoran-like PG in osteoarthrotic cartilages. Decoran may be a primary target of the OA disease process.

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