on the role of histidine-metal cross-links as sacrificial bonds in the fibrous core of the byssal thread.
Byssal threads are protein fibers, which mussels use to attach to various substrates at the seashore. These relatively stiff fibers have the ability to extend up to about 100% strain, dissipating large amounts of mechanical energy from crashing waves. Remarkably, following damage from cyclic loading, initial mechanical properties are subsequently recovered by a material-intrinsic self-healing capability. Histidine residues coordinated to transition metal ions in the proteins comprising the fibrous thread core have been suggested as reversible sacrificial bonds that contribute to self-healing; however, this remains to be substantiated in situ. The role of metal coordination bonds in the thread core was investigated using several spectroscopic methods. In particular, combined Raman and X-ray absorption spectroscopy (XAS) measurements were employed to confirm the presence of protein$-Zn^{2+}$ coordination bonds in the mussel byssus and to monitor transitions in the coordination structure during thread deformation and self-healing. Analysis of the extended X-ray absorption fine structure (EXAFS) and X-ray absorption near edge structure (XANES) suggests that tensile deformation of threads is correlated with the rupture of Zn-coordination bonds and that self-healing is connected with the re-organization of Zn-coordination bond topologies rather than the mere re-formation of ruptured Zn-coordination bonds. These findings have interesting implications for the design of self-healing metallopolymers.
The dynamic exchange of bonds plays a vital role in the mechanical behavior and self-healing in the thread core by allowing them to act as reversible sacrificial bonds. The requirements of this material can be met by the dynamic nature of the protein-metal cross-links, whereas covalent cross-linking would fail to provide the self-healing of the core. In summary, this study of the thread core serves to underline the important and dynamic roles of protein-metal coordination in the mechanical function of load-bearing protein fibers, such as the mussel byssus.

ICBB17-11
DEVELOPMENT OF AN IN VITRO RHEUMATOID ARTHRITIS (RA) MODEL AND ITS APPLICATION IN DRUG TESTING

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Rheumatoid arthritis (RA) is a common autoimmune disease that leads to progressive joint destruction. In order to understand the process of rheumatoid cartilage damage, an in vitro model consisting of an interactive tri-culture of synovial fibroblasts (SFs), LPS-stimulated macrophages and a primary chondrocyte-based tissue engineered construct was established. The tissue engineered construct closely mimicked native cartilage as it was rich in collagen type II and proteoglycans. The results generated revealed that healthy chondrocytes were activated in the presence of SFs and macrophages by displaying aberrant behaviours seen in a disease state. These behaviours include increased apoptosis, decreased gene expression for matrix components such as type II collagen and aggrecan, increased gene expression for tissue-degrading enzymes (MMP-1, -3, -13 and ADAMTS-4, -5), and upregulation of inflammatory mediators gene expression (TNF-α, IL-1β, IL-6 and IKBKB). Moreover, the inclusion of SFs and macrophages in the model enabled both cell types to more closely replicate their in vivo role in mediating cartilage destruction. This is evidenced by extensive matrix loss detected by immunostaining and biochemical analysis. Subsequent drug treatment with celecoxib indicated that the model was able to respond to the therapeutic effects of this drug by reversing cartilage damage. Taken together, this study showed that the model was able to recapitulate certain pathological features of an RA cartilage. If properly validated, this model has a great potential to be used for screening new therapeutic drugs/strategies, thereby contributing to the improvement of anti-rheumatic treatment.

ICBB17-12
IN-VIVO CELL REMOTE CONTROL: A MECANO-ELECTRO COMPUTATIONAL STUDY

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Nowadays, due to its importance for human survival, tissue and organs regeneration have received a high attention of the scientific community. For the development of this field, understanding the cell behavior is essential for *in-vivo* tissue and organs regeneration. Cell behavior can be controlled *in-vitro*, among other stimuli, by changing the extracellular matrix mechanical properties, applying external forces and/or electrical field. Controlling these stimuli *in-vivo* is not trivial. Therefore, in this work, to remotely control the local cell environment, we consider a microsphere of cell size that is fabricated from a piezoelectric material and charged with nanomagnetic particles. This microsphere is integrated within an extracellular matrix, in such a way, through an external magnetic field, internal forces can be generated within the microsphere. As a result, a stiffness gradient as well as an electric field are generated around the microsphere. These cues can be controlled externally by changing the magnetic field intensity. To tune up this process and achieve the cell desired quantities, a computational numerical simulation has been developed and employed for several cell phenotypes using the commercial software ABAQUS with user subroutine UEL. The obtained results, which are in agreement with several experimental works, show that the generated stiffness gradient as well as the generated electric field within the cell microenvironment can play an outstanding role in remotely controlling the lineage specification of the Mesenchymal Stem Cells. The proposed technique can accelerate cell migration and proliferation, which open the door for new tissue regeneration methodologies. Although this 3D numerical model can successfully predict fundamental aspects of cell maturation, differentiation, proliferation, and apoptosis within a nonlinear substrate, further investigations into physical and mechanical factors such as colony size and cell shape are essential for a better understanding of the precise mechanism behind cell fate decisions.
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ADAPTABLE, AUTOMATED PLATFORM FOR MINIATURIZED CELL CULTIVATION EXPERIMENTS INCLUDING FOURIER-OPTICAL ANALYTICS

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Sophisticated cell cultivation experiments demand for dedicated experimental strategies. On the one hand, environmental conditions must be controlled within narrow confines, while on the other hand manipulation processes need to be possible to investigate cellular stimulus-response-mechanisms. For this purpose, a wide range of analysis