

## Challenge based learning (CBL)

### Supramolecular hydrogels for cartilage tissue engineering

**Note for teachers:** A CBL user guide can be found at [www.jandeboerlab.com/TissueEngineering](http://www.jandeboerlab.com/TissueEngineering) with instructions and tips to run an effective CBL teaching session.

#### Background and vision

Articular cartilage is a tissue with low regenerative capacity which lacks blood vessels and nerves. Therefore, cartilage tissue does not self-regenerate upon injury or as a result of age-related degeneration. Uncontrolled degeneration of articular cartilage leads to pain, inflammation and instability of the knee joint. One strategy to repair early and mid-stage degeneration of articular cartilage is the transplantation of chondrogenic cells into the defect site, in the form of either autologous primary chondrocytes or stem cell-derived chondrocytes. Tissue-engineered strategies use biocompatible cell entrapment systems (e.g. hydrogels) to deliver cells into the cartilage defect. Ideally, these materials should support and control the implanted cells throughout the regenerative process. The long-term goal of hydrogels in cartilage regeneration is to express the complex biological signals identified in native cartilage's extracellular matrix, and to closely mimic the function of native cartilage.

#### Motivation and stakeholders

Mechanical signals play an equally important role in tissue regeneration as biochemical signals. Surprisingly, matching these mechanical properties in a synthetic system remains a challenge. Incorporating proper mechanical properties into cell entrapment system like a synthetic hydrogel is of key importance to validate its clinical use in cartilage regeneration. Solutions to mitigate this problem should consider the needs, requirements and regulatory, financial and technical boundary conditions defined by stakeholders such as patients with cartilage defects and osteoarthritis, orthopedic surgeons and the material scientists and bioengineers.

#### Problem definition

Most hydrogels are composed of a single synthetic polymer chain, which form a simple network, with suboptimal mechanical and biological properties. This is in stark contrast to the extracellular matrix of cartilage that contains numerous and precisely organized natural polymers, and shows an intricate and highly complex mechanical identity. Multiple polymeric networks interact with each other via covalent and supramolecular interactions within cartilage. To this end, materials to regenerate articulate cartilage should have an adequate polymeric composition to mimic cartilage's microarchitecture and contain bio-active signals to guide the cells in the regeneration process.

#### Challenge

To incorporate the mechanical properties of the native extracellular matrix into synthetic hydrogels using supramolecular chemistry.

#### Learning scaffold

Reading the Synthetic Biomaterials and Bone/cartilage Tissue Engineering chapters and related literature will help you to understand:

1. What defines a hydrogel.
2. The descriptive terms to define the mechanical properties of a material.
3. The mechanical and histological properties of cartilage.
4. Which natural polymers contribute to the mechanical properties of articular cartilage.
5. Cartilage homeostasis and regeneration.

For a more focused examination of the challenge, read scientific literature and create a mind map to include information about the following:

6. Strategies to manipulate the properties of a hydrogel using covalent chemistry.
7. Strategies to manipulate the mechanical properties of a hydrogel using supramolecular chemistry.
8. The molecular building blocks to engineer tough and resilient hydrogels.
9. Materials and synthesis strategies to engineer tough mechanical properties into complex biomaterials.

10. The advantages and disadvantages of covalent versus supramolecular chemistry in biomaterial synthesis.

**End product**

A three-minute video explaining the solution of your challenge. Please include your motivation and the steps to execute your solution.

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