BETTER IMPLANTS FOR BONE REGENERATION

COATINGS THAT MIMIC THE NATURAL SCAFFOLDING HOLDING TISSUES TOGETHER COULD IMPROVE THE EFFECTIVENESS OF ORTHOPAEDIC IMPLANTS

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Implants made of titanium are regularly used in orthopaedics, in the form of plates, pins, and rods, for example, to aid bone repair, and also to screw in dental prostheses into the jaw. Titanium is extremely strong and is compatible with biological tissues. However, one drawback is that the bare metal binds poorly to surrounding tissues such as bone and cartilage, which shortens its lifetime.

To improve the binding, current research is focusing on coating implants with suitable bioactive materials – in particular, biodegradable polymers combined to other biomolecules that enhance adhesion and bone growth. The ideal material should behave like a scaffold, mimicking the extracellular matrix that naturally provides the 'glue' holding cells together in body tissues. At the same time, the artificial coating should gradually degrade during the tissue regeneration associated with the healing process.

Hyaluronan (HA), a carbohydrate polymer that is one of the main components of the extracellular matrix, is a strong candidate coating. The HA molecules can be chemically modified so that they cross-link to form a 3D gel-like structure that mimics the physiological matrix. However to optimise adhesion with the titanium implant, as well as to induce the bone growth, extra chemical groups such as bisphosphonates (BPs) can be coupled to HA.

BPs have a natural affinity for calcium ions and a protein that naturally promotes bone growth – bone morphogenetic protein-2 (BMP-2). Due to this interaction, the protein BMP-2 can then be incorporated in the gel – so that it is delivered in the correct amounts at the correct rate to the site of regeneration. Concentrations that are too low will not have any effect, while those that are too high will lead to abnormal tissue development. It is thus essential that there is also a mechanism for removing the growth factor from the coated implant.

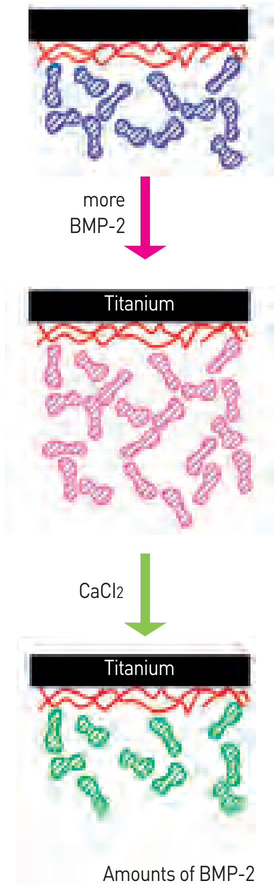
SMART COATINGS

BPs are used as drugs in the treatment of various bone diseases, such as osteoporosis, to inhibit bone loss. However, they have rarely been combined with polymers before. BPs also bind readily to titanium oxide, which always covers the titanium metal. We were particularly interested in the interaction between the growth protein BMP-2 and the HA coating – with and without bisphosphate groups.

Neutron reflectivity (p6), combined with delicate measurements (using a quartz crystal microbalance) of the mass of the surface coatings that formed, allowed us to explore in real time how well the HA gels – both with and without BP – bound to a titanium-oxide surface, and then compare the interactions of the incorporated protein in each case. We also compared the interactions with that of BMP-2 on a bare titanium-oxide surface. Of particular importance was the ease of adsorption of the protein onto the oxide surface and then its release. The latter was achieved by washing the samples with calcium-chloride solution.

The data gave us a detailed structural description of the bound polymer coatings and behaviour of the growth factor. We found that the coating containing BP anchors strongly to the titanium by chemically reacting with the oxide. It forms a thicker HA layer than that without BP. The adsorption of the protein onto the oxide surface was reversed by the presence of calcium ions when BP was present, but not from the uncoated surface. This is because the BP prefers to bind with calcium, which then weakens the binding of the BMP-2 to the coated surface.

These results, we believe, demonstrate that this HA–BP coating system is thus an effective option for ensuring the effectiveness of implants. The research group has now launched trials of similar materials for metal implants, as the next step towards transferring the results to clinical applications.



Amounts of BMP-2 introduced to a titanium surface coated with a chemically modified hyaluronan (red), when dilute (blue) and concentrated (pink), and after rinsing with calcium chloride solution (green)

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ILL INSTRUMENT USED: D17 reflectometer

REFERENCES: I. Berts *et al.*, *Advanced Engineering Materials*, 2014; DOI: 10.1002/adem.201400009