**Engineered Biomaterials as a Scaffold for Bone Regeneration**

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**The regeneration and/or replacement of bone tissue is traditionally done through surgical methods such as bone grafts. To keep up with the demand of the aging human population, more research is needed to study accessible, low cost methods to combat bone degradation and bone diseases. Bone tissue has now become a focal point for the development of new biocompatible materials and hydrogels. Just like how a scaffold is a temporary framework that aids in the repair of a structure, different materials can be used as scaffolds in the regeneration of damaged bone tissue. A study done by Obregon-Miano et al., (2019) has researched a biocompatible substance made from porcine (pig) extracellular matrix (connective tissue) that has shown great potential as a foundational material for bone regeneration. The substance demonstrated high stability, low degradation, and high cell compatibility for osteogenic cell proliferation. The material also demonstrated high compression tolerance and controlled swelling, an essential characteristic for bone regeneration. This substance can prove to be a foundational material for future in vivo testing that can eventually lead to substances that could potentially help in the regeneration of damaged bone tissue.**

**Introduction**

The current advancement of nanotechnologies alongside biocompatible materials has allowed for the expansion of novel ideas within tissue engineering and regenerative medicine. New treatments are being explored as traditional tissue donations are not able to meet the current demand for organ and tissue transplants. Novel treatments may also combat the consistent risk of immunological rejection that goes hand in hand with traditional transplants.

On the forefront of regenerative medicine is the development of biocompatible materials that could prove to be sufficient substitutes for a diverse set of damaged body tissues such as skin, liver, and even heart cells. Development of biocompatible materials may include mediums such as proteins, stem cells, and growth factors. These mediums are key into mobilizing the regeneration and/or replacement of damaged tissues. (1) One particular tissue of interest is bone tissue. With an increase in the aging human population, new materials are currently being researched to advance bone regeneration during surgical bone grafts. Substances known as polymeric hydrogels are of particular interest for bone regeneration due to their versatility and ability to combine with a wide variety of materials. However, a drawback of hydrogels is their lack of biomechanical stability, which is essential for bone tissue. A way to combat this is the introduction of two or more network polymers known as interpenetrating polymeric networks (IPN) into the hydrogel. These IPN hydrogels provide a more sturdy foundation and have been researched to be tested for their possible aid in the regeneration of bone tissue. In a study done by Obregon-Miano et al., (2019) IPN’s were used as a scaffold with proteins from porcine extracellular matrix (ECM) to generate a foundational material for bone regeneration. (2)

**Recent Progress**

While great strides have been made to further understand the biocompatibility and longevity of engineered substances for bone regeneration, there is still much research to be done before these substances can be used on humans. Part of that research includes the study done by Obregon-Miano et al., (2019) who created an injectable semi-IPN (SIPN) hydrogel through an extensive formulation of different materials and processes.

To create this SIPN hydrogel, the mandible jaw bone fragments from pig heads were collected and later pulverized into bone powder. The bone powder material was then demineralized and stripped of fat to be washed with sterile water and freeze dried for further testing. It was then mixed with pepsin and HCl to create a thick solution containing collagen. This thick substance was now referred to as porcine bone demineralized and digested extracellular matrix (pddEDM). Lastly, the pddEDM was sterilized using a pressurized gas method and mixed with polyethylene glycol diacrylate (PEDGA) to create a denser product. This mixture created a final SIPN hydrogel product. The SIPN hydrogel was tested for mass swelling, protein release, mass degradation, mechanical compression, and cell activity.

The SIPN hydrogel was microbial free and provided a non-toxic, biocompatible environment to allow for bone cell proliferation. The material also reacted well to the usual lack of structural stability of hydrogels and in turn had high stability and low degradation. The hydrogel demonstrated high cell compatibility with certain bone cells as it also allowed for osteogenic cell migration and differentiation. The material also demonstrated high compression tolerance and controlled swelling. In conclusion, the SIPN hydrogel promoted the growth of cells and shows a high potential for the material to be considered in future clinical applications through further testing as well as future in vivo testing. (2)

**Discussion**

The study done by Obregon-Miano et al., (2019) was very opportune and relevant to the current state of public health. With our current healthcare system and our aging population, it can be very difficult to provide access to treatment in the form of transplants due to donor shortages and lack of access to affordable healthcare. Patients with failing organs and/or debilitating diseases can be left to deal with diseases on their own. The emerging fields of tissue engineering and regenerative medicine are exceedingly important in finding new, affordable ways to treat damaged human tissues or ensure quick recoveries from surgeries or injuries.

 It is crucial, however, to ensure that treatments are safe for in vivo testing, and show potential for both longevity and biocompatibility. It is possible for a material to be biocompatible and promote cell proliferation while also be able degrade easily. For tissues that undergo high mechanical strain such as bones, low durability would not be acceptable. The study sought to find the right material that could promote osteogenic proliferation while also maintaining a high level of sturdiness. Using previous knowledge of IPN’s, the study successfully used porcine ECM as a scaffold to promote bone regeneration in in vitro testing. The SIPN hydrogel substance should continue to undergo further experimentation in order to determine bone mineralization rate, bone forming capacity, long-term toxicological effects, and inflammatory response when exposed to immune cells. These tests require some in vivo testing, and an adequate species to test this would be mice. It would probably be some time before this material can show promise to be tested on humans, but nevertheless, it is a start to the advancement of osteogenic regenerative medicine.

The authors suggest potential problems with this study that would require future research. It is hypothesized that macrophages would cause an inflammatory reaction inside the bone due to the presence of PEDGA. The biocompatibility of PEDGA is in question as it did show a lack of cell proliferation and this is most likely due to its tight and dense structure. Inflammation due to PEDGA may pose a potential threat to the overall reliability and effectiveness of the hydrogel material. PEDGA, as of now, is an essential part of the hydrogel as it significantly enhances the durability and degradation resistance of the material.

Overall, the SIPN hydrogel study serves as an exemplary research study for the field of regenerative medicine and tissue engineering. Future studies like this can lead to future advancements in the development of compatible biomaterials that can serve as scaffolds for the regeneration of a wide variety of human tissues, including essential organs such as heart, lung, and kidney.

**References**

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