

## Electronic Supplementary Materials:

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# Biomaterial types, properties, medical applications, and other factors: a recent review

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## Data S1

### 1 Biomaterials Limitations and Uses

#### 1.1 Drug-delivery systems

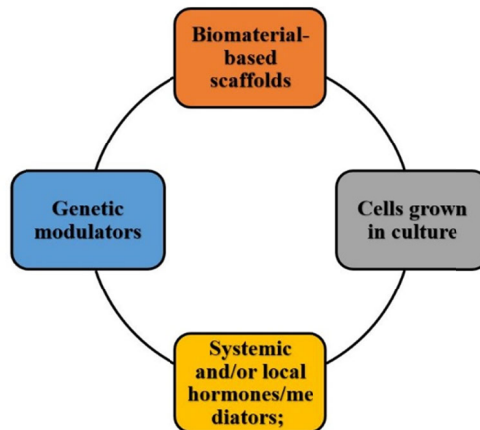
One of the fastest-growing implant areas is medication delivery devices that can be controlled and targeted to use and spread. Implanted devices with drug reservoirs have been made to deliver regulated and steady doses of medication.

#### 1.2 Carbohydrate-derived protein-resistant biomaterial

Polyether can be created by combining monomers made from natural carbohydrates. One protein-resistant, biodegradable, and functional compound is one of them. Besides the end of the chain, this can also be used. In this case, the compounds of this invention can be used to make a wide range of devices and other things.

#### 1.3 Hard tissue: biomaterial interactions

People have been using synthetic and natural biomaterials to replace and regenerate working tissues for years. Bone and cartilage can be damaged, so these materials have been used for years. Discoveries in science over the last few years have made it more likely that injured tissues can be repaired using a combination of things like those tissue engineering concepts shown in the **Figure S1**.



**Figure: S1 Tissue engineering concept**

#### 1.4 Improvements in biomaterials extracorporeal coatings require extended flow observation of blood biomaterial interaction

There are many problems with the long-term use of cardiopulmonary bypass (CPB) systems, such as thrombus formation and infection. Part of the problem is that the CPB circuitry isn't very compatible with blood. There is a lot of new ground to cover in biomaterials science when making biomaterial surfaces that are genuinely long-term hemocompatibility (Rashid et al. 2021). After a few hours of blood and biomaterial contact, it was found that it is possible to tell the difference between biomaterial coatings. Scan electron microscopy, counting platelets, and measuring myeloperoxidase were the best ways.

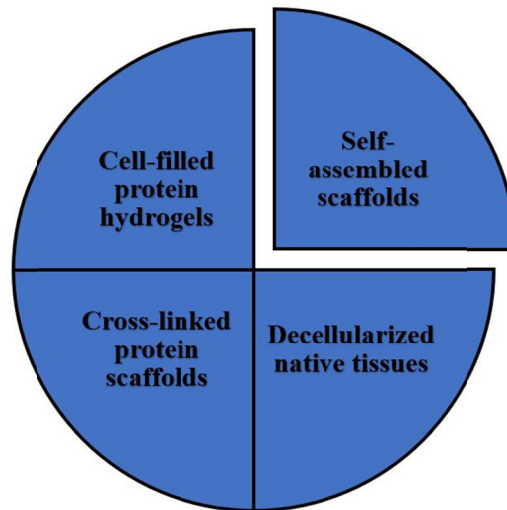
#### 1.5 Biomaterials that come into contact with blood.

Biomaterials that come into contact with blood should consider blood-biomaterial interactions, factors that affect blood response, and how to measure and evaluate these factors and interactions. How blood reacts to a biomaterial when used in a clinical setting depends on how it is made, how healthy the patient is, and what kind

of application it will be used for, among other things. They can be tested in clinical, ex vivo, in vitro, and in different ways.

### 1.6 Use of protein-based biomaterials to improve vascular tissue engineering

Blood vessel replacements that can be used in small-diameter applications drive the field of vascular tissue engineering in the real world. Because the blood vessel is so complicated, it has been hard to make engineered tissues that can be used in the real world (Kelly 2021). There are four main ways to make vascular tissue: People who do vascular tissue engineering use proteins as the primary "scaffolding" material to make living blood vessel replacements, as shown in **Figure: S2**.



**Figure: S2 Four main ways to make vascular tissue**

### 1.7 Future trends in biomaterials

As a result of biomaterials making a big difference in medicine, the first thing to think about is how drugs and polymers interact with each other, how drugs change, and how drugs spread, among other things. Vaccination and pulsatile release can be done with engineered polymers, and they can also be made to last a lot longer by making them more durable. It's also important to know how chondrocytes, osteocytes, and other connective tissue-free interfaces work to make orthopaedic biomaterials (Ray and Iroegbu 2021).

### 1.8 Biomaterials that can be used to control cell adhesion and migration.

One of the most important parts of controlling how well protein-adsorbed biomaterials work is polyethylene glycol (PEG). A group of polycarbonates made from tyrosine and PEG can make biomaterials. They have surfaces with low to medium amounts of PEG. The level of PEG stops proteins from sticking to each other, so it doesn't work either. The quantity of cell attachment changed with the amount of PEG added to the water (Kuczumow et al. 2021).

### 1.9 Systems can be affected by biomaterials and activated charcoal-based urease optimization

Biomaterials implanted into the body are usually evaluated by how the tissue is placed in response. In battles outside of their historical context, the same thing could happen. Carcinogenic, metabolic, immunological, and bacterial effects can have a wide range of possible and actual impacts on the body when they are looked at more closely (Ismail et al. 2021; Zarrintaj et al. 2021). People don't know about these effects because there aren't enough studies to support their claims. It has been used to hold urease in place to do its job of breaking down urea. It has been used to coat the enzyme support system with hexamethyl disiloxane, which is safe for living things. They used electronic spectroscopy and scanning electron microscopy to look at the finished coat and ensure it was good.

### **1.10 Biomaterials for healthcare and Bioactive specific biomaterials: present and future**

It was found that the sterile macro devices that were put in normal mini-pigs were safe for them to use (Nace et al. 2021). Because fibrosis had been caused by it, it didn't cause any inflammation or a significant change in the immune system of the outside world, even though it did. Bioactive biomaterials are synthetic polymers with certain chemical functional groups added to the macromolecular chain, making them more bioactive. These materials are meant to work with living things in a certain way. Some functional polymers may have anticoagulant properties, so they don't clog up with blood. Others have been made to interact with parts of the immune system, but they're not the only ones. They can change how cells grow and work, but not all have to change simultaneously.

### **1.11 Dental fluorinated polymers and hybrid composites**

The properties of new polymer materials don't shrink as much and have low surface energy. It took a lot of work to make new fluorinated monomers that could open rings. To make the polymers and composite resins, they first had to be made from them (Chang and Yeh 2021). Because different polymers and copolymers have other properties, it was essential to look at them. These properties include reactivity, chemical structure, thermal behaviour, and surface characteristics. Many fluorines were added to the air-polymer interface, making the air-polymer interface more fluorine rich. The air-polymer interface is more fluoride-rich. Fluorinated ring-opening monomers and crosslinkers were used to make composite resins for the teeth. Resin formulations were studied to determine what components made a resin's mechanical properties better or worse (Jatoi and Fan 2021). They also looked at its surface composition, topography, and how bacteria could attach to and grow on it. The addition of fluorinated groups significantly reduced volume shrinkage but didn't significantly affect the mechanical properties.

### **1.12 Uses for biomaterials**

Biomaterials can replace hard or soft tissues damaged or destroyed by a disease or injury. They can also make new body parts (Arif et al. 2021; Marew and Birhanu 2021; Wang et al. 2021; Li et al. 2021). Even though most people don't have cancer, they can get degenerative diseases, like fractures and infections, which can worsen over time. If the conditions are right, it may be possible to replace the diseased tissue with synthetic regenerative medicine.

#### **1.12.1 Orthopaedics**

Biomaterials are often used to make implant devices in the field of orthopaedics. These devices are made with materials that come from living things. A disease called osteoarthritis damages joints' structure to move freely. Many other things can cause arthritis in the hip, knee, shoulder, ankle, and elbow, but this is one of them (synovial). As a replacement for these joints, prostheses can be used.

#### **1.12.2 Cardiovascular applications**

Implants can fix heart valve and artery problems if considered heart parts. There are many ways to replace a damaged heart valve, which is necessary because structural changes in the heart valve make it challenging to open or close properly. Atherosclerosis is when fat builds up in the arteries, especially the coronary arteries and veins in the lower limbs.

#### **1.12.3 Ophthalmics**

Diseases and conditions can cause vision problems or even blindness when they damage the eye's tissues. Cataracts cause clouded lenses to make up for the cloudiness. A polymer-based intraocular lens can be used instead if this is not possible. Besides biomaterials, materials used in touch lenses are also called that because they touch the eye's tissues when they are used. They protect and restore eyesight in the same way as after cataract surgery.

### 1.12.4 Dental applications

It is possible to lose many teeth due to dental caries (cavities), demineralization, and tooth disintegration caused by plaque metabolic activity (a musician covering that traps bacterium on the teeth' surfaces). Teeth can be replaced or restored in their entirety or part, and various materials can be used.

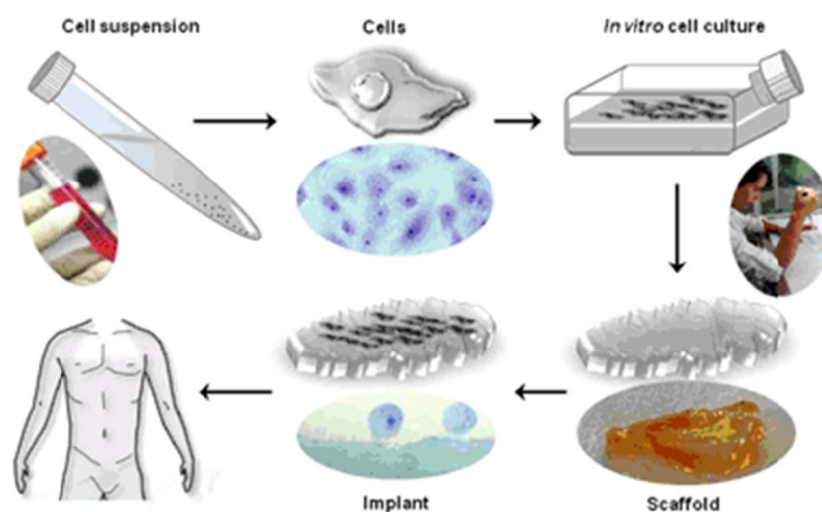
### 1.12.5 Wound healing

The use of implanted biomaterials in the closure of wounds has been around since the invention of sutures. As early as 2000 B.C., the ancient Egyptians used linen as a junction material. Polymers (the most often used kind) and a few metals are available synthetic junction materials (e.g., stainless steel and tantalum). Any device that supports the bones after breaking them is referred to as a fracture treatment device. Most orthopaedic fracture fixation devices are constructed of metals, usually, stainless steel, which is not a secret to anybody (e.g., carbon-carbon composite bone plates).

## 2 Degradable metallic biomaterials: in vitro cytotoxicity

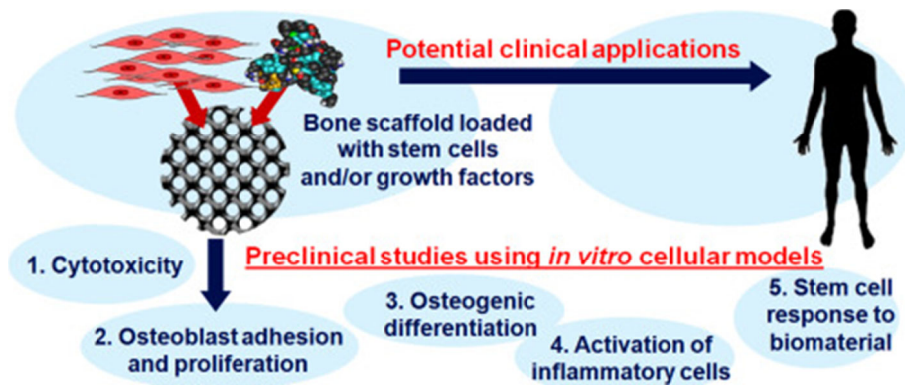
During in vivo tests, in vitro methods can't show all the body's different parts. However, they are essential for evaluating medical devices, including implants. They are necessary because they show how the new biomaterial might act when it comes into contact with living tissue (Asensio et al. 2022). This standard is only a set of suggestions, and many parameters and conditions can be changed. An extract of the sample can also be tested, called an elution test. To put it simply, during the elution test, the materials that need to be tested are placed in a liquid medium. Then, cells are exposed to the liquid medium and the extracts that come out of it. Cell viability after the exposure is looked at and compared to the control. When biomaterials of the first generation were made, they were called bioinert, which meant that the substances that came out were unsuitable. Degradable metallic biomaterials for temporary implants are getting much attention now (Mouriño 2022). In this case, the degradation is expected and necessary, and some of the conditions for in vitro testing in the standard might be too strict, which could lead to results that aren't relevant. Biomaterials can be made from polymers, ceramics, metals, and composite materials or found in nature. Polymers have been used a lot since then. It has been used to manipulate polymers to make controlled-release systems with small biomedical devices that are easy to make and use on a small scale. Make multilayer thin films with the LbL assembly by alternating the deposition of different polymers (Patil and Mehta 2022).

Researchers can use cytotoxicity data to determine how new compounds will hurt cells. These cells are called peripheral blood mononuclear cells (PBMCs). If a device is bad for blood cells, it wouldn't be suitable for medicine (Grebowski et al. 2022). In **Figure S3**, users can see how cells interact with polymeric biomaterials made of hyaluronic acid and chitosan.



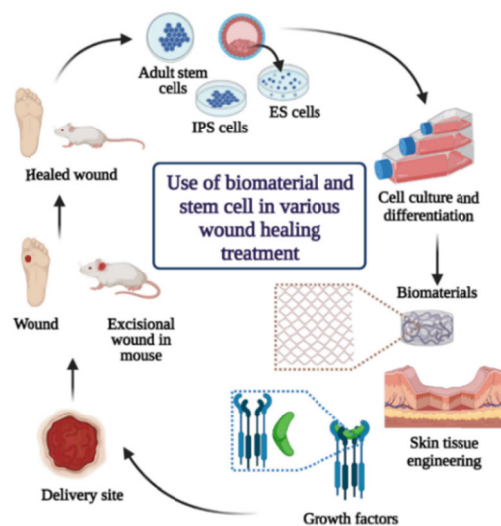
**Figure: S3** Polymeric biomaterials are made of hyaluronic acid and chitosan (Jeong et al. 2017) and reproduced from Jeong, Hyejoong et al. [2017] under the terms of the Creative Attribution Commons License 4.0 (CC-BY 4.0). <http://creativecommons.org/licenses/by/4.0/>.

Then, nanodevices should be tested to see if they harm the blood system before using them on cells. A polymer comprises three parts: cations, anions, and neutral parts. Different polymers have different electric charges: Polycations, Polyanions, and Neutral Polymers have additional electric charges. When the polymers were combined and made into films, researchers also looked at how toxic the polymers were combined and made into mixtures (DePalma et al. 2022; Saremi et al. 2022). It was called LbL assembly because polycations and polyanions were used to make the mixtures, which are called mixtures. **Figure S4** shows the first step of studying nanodevices from biomaterials used in a living body.



**Figure: S4** Study of biomaterial-based functional nanodevices in vivo (Przekora and C 2019). It is reproduced from Przekora, Agata, et al. [2019] with permission from Springer Nature.

Using co-culture systems, which are more like what happens in the real world, might be an excellent way to test biomaterials at the start. Still, they won't be able to do away with animal models completely. So, starting with cell models in the lab is best to figure out which bio interactions between cells and implantable biomaterials are most important (Tsujioka et al. 2022). Animal models can then be used to back up the results of the in vitro tests. **Figure S5** shows how biomaterial and stem cells work together to make new skin.



**Figure S5** Skin Tissue Engineering with Biomaterials and Stem Cells (Riha et al. 2021). Reproduced from Manira Maarof et al. [2021] under the terms of the Creative Attribution Commons License 4.0 (CC-By 4.0). <http://creativecommons.org/licenses/by/4.0/>.

In vitro biocompatibility testing of three-dimensional biomaterials that can be absorbed can be complex. There aren't enough ways to use in vitro cell models to look at the complex biocompatibility of materials that can be implanted, and there aren't enough ways to do this (Sanz et al. 2021; Insuasti-Cruz et al. 2022). Then they move on to animal models and tests in the real world, but they don't use all of the scientific power of in vitro models. However, the in vitro cell model's new molecular biology and biotechnology techniques have improved. These materials may keep neutrophils around for a long time and cause long-term inflammation, which leads to

scarring of the tissues around them. It can't be done in the lab to see how many different cells work together in bone regeneration (Sheridan et al. 2022; Gao et al. 2022).

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