Goebel Uta (Orcid ID: 0000-0002-1689-4999)
Stegemann Jan P (Orcid ID: 0000-0002-7989-7222)
Leach Kent (Orcid ID: 0000-0002-1673-3335)

Review

The Year 2022 in Biomaterials Research: A Perspective from the Editors of Six Leading Journals

Jan P. Stegemann[*1], William R. Wagner*[*2], Uta Göbel*[*3], Ekaterina Perets*[*4], Kam W. Leong*[*5], J. Kent Leach*[*6], Jeremy Gilbert*[*7]*

[1] Chair of the Society for Biomaterials Publications Committee, University of Michigan, Department of Biomedical Engineering, Ann Arbor, MI, USA

[2] Editor-in-Chief, *Acta Biomaterialia,* McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, PA, USA; Department of Surgery, University of Pittsburgh, Pittsburgh, PA, USA; Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA, USA; Department of Chemical and Petroleum Engineering, University of Pittsburgh, Pittsburgh, PA, USA.

[3] Editor-in-Chief, *Advanced Healthcare Materials*, Wiley-VCH GmbH, Weinheim, Germany

[4] Deputy Editor, *Advanced Materials*, Wiley-VCH GmbH, Berlin, Germany

[5] Editor-in-Chief, *Biomaterials*, Department of Biomedical Engineering, Columbia University, New York, NY, USA; Department of Systems Biology, Columbia University Medical Center, New York, NY, USA

[6] Editor-in-Chief, *Journal of Biomedical Materials Research Part A*, Department of Orthopaedic Surgery, School of Medicine, UC Davis Health, Sacramento, California, USA; Department of Biomedical Engineering, University of California Davis, Davis, California, USA

[7] Editor-in-Chief, *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Clemson University – MUSC Bioengineering Program, Charleston, South Carolina, USA

Correspondence

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jbm.a.37529

This article is protected by copyright. All rights reserved.

Author Manuscript

Jan P. Stegemann, University of Michigan, Department of Biomedical Engineering, Ann Arbor, MI, USA
Email: jpsteg@umich.edu

William R. Wagner, McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, PA, USA
Email: wagnerwr@upmc.edu

Uta Göbel, Wiley-VCH, Boschstraße 12, 69469 Weinheim, Germany
Email: ugoebel@wiley.com

Ekaterina Perets, Wiley-VCH GmbH, Rotherstr. 21, 10245 Berlin, Germany
Email: eperets@wiley.com

Kam W. Leong, Department of Biomedical Engineering, Columbia University, New York, NY, 10027, USA
Email: kam.leong@columbia.edu

J. Kent Leach, Department of Orthopaedic Surgery, School of Medicine, UC Davis Health, Sacramento, CA 95817, USA
Email: jkleach@ucdavis.edu

Jeremy L. Gilbert, Clemson University – MUSC Bioengineering Program, Charleston, SC, USA.
Email: jlgilbe@clemson.edu

Author Manuscript

Author Manuscript

Abstract

The field of biomaterials science is highly active, with a steadily increasing number of publications and new journals being founded. This article brings together contributions from the editors of six leading journals in the area of biomaterials science and engineering. Each contributor highlights specific advances, topics, and trends that have emerged through the publications in their respective journal in the calendar year 2022. It presents a global perspective on a wide range of material types, functionalities, and applications. The highlighted topics include a diversity of biomaterials; from proteins, polysaccharides, and lipids to ceramics, metals, advanced composites, and a variety of new forms of these materials. Important advances in dynamically functional materials are presented, including a range of fabrication techniques such as bioassembly, 3D bioprinting and microgel formation. Similarly, several applications are highlighted in drug and gene delivery, biological sensing, cell guidance, immunoengineering, electroconductivity, wound healing, infection resistance, tissue engineering, and treatment of cancer. The goal of this paper is to provide the reader with both a broad view of recent biomaterials research, as well as expert commentary on some of the key advances that will shape the future of biomaterials science and engineering.

Author Manuscript

1. Introduction (Jan P. Stegemann, Chair of the SFB Publications Committee)

This special contribution in the *Journal of Biomedical Materials Research Part A* (JBMR A), was commissioned by the Publications Committee of the U.S. Society for Biomaterials (SFB) with the intent of providing an expert summary of developments in the fields of biomaterials science and engineering during the 2022 calendar year. It contains concise contributions from thought leaders in biomaterials science, who have each provided commentaries that highlight recent scientific progress and trends. The field of biomaterials has continued to evolve and expand over the past decades, through both incremental and disruptive advances that have improved the quality of life and health care around the globe. The consistently increasing number of publications in the field, and the founding of new journals to cover its broad range of endeavor, attest to the global growth and impact of biomaterials science. The goal of this paper is to provide the reader with both a broad view of biomaterials research that was published in the past year, as well as expertly curated descriptions of some of the key highlights that will shape the future of the field moving forward.

This article contains contributions from the editors of six most widely read and impactful journals in the field of biomaterials: Bill Wagner (Editor-in-Chief of *Acta Biomaterialia*), Uta Göbel (Editor-in-Chief of *Advanced Healthcare Materials*), Ekaterina Perets (Deputy Editor of *Advanced Materials*), Kam Leong (Editor-in-Chief of *Biomaterials*), Kent Leach (Editor-in-Chief of the *Journal of Biomedical Materials Research Part A*, JBMR A), and Jeremy Gilbert (Editor-in-Chief of the *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, JBMR B). Each of these experts has surveyed the articles published in their respective journals over the past year, and they have each provided a perspective on the trends and progress that are shaping the field, as reflected by the publications that appeared in their journals during the previous year. In some cases, specific scientific advances are highlighted and the potential implications on human health are examined. In other contributions, publication trends and their impacts are discussed, with an emphasis on the increasing globalization and access to information in the field. Each of the editors has distilled a very busy year of research publications into a short contribution that describes their perspective on the status and direction of the field. The contributions in this paper will also be presented and discussed during a panel session of the editors at the 2023 Annual Meeting of the Society for Biomaterials in San Diego (April 19-22, 2023).

The depth, breadth, and potential impact of the advances in biomaterials science that are presented in this article are truly impressive. The highlighted topics cover a wide range of biomaterials from proteins, polysaccharides, and lipids to ceramics, metals, advanced

Author Manuscript

composites, and a variety of new forms of these materials. Important advances in dynamically functional materials are presented, including a range of fabrication techniques such as bioassembly, 3D bioprinting and microgel formation. Similarly, several applications are highlighted in drug and gene delivery, biological sensing, cell guidance, immunoengineering, electroconductivity, wound healing, infection resistance, tissue engineering, and treatment of cancer. The research presented originates from around the globe and reflects the intense energy that is being devoted to making progress in this very exciting field. It should be noted that the research that is highlighted in this article represents only a cross-section of a very diverse discipline. While some key papers from the past year are mentioned explicitly, the reader should realize that the journals in question contain a deep repository of further information on these and other advances in biomaterials science. Taken together, we hope that these expert contributions provide a comprehensive yet curated view of the current landscape and trends in biomaterials science, and will provide the reader with an impression of the tremendous progress and potential in the field.

2. *Acta Biomaterialia* (William R. Wagner, PhD, Editor-in-Chief)

At *Acta Biomaterialia*, the perspective comes from the materials science side of the table, with a structure-property-function emphasis on biomaterials advances. In 2022, the papers published in the journal reflected how diverse the field has become in terms of geography, collaboration, materials employed, pathologies targeted, and strands of scientific knowledge integrated. Much of the excitement and promise is based upon the possibilities opened as molecular biology and biomedical science uncover mechanistic knowledge that the biomaterials scientist can combine with materials science and engineering principles to create technologies targeting disease in heretofore unanticipated ways.

With respect to research, we are firmly in the era of functional biomaterials, ranging from surfaces designed for specific cellular interactions to triggered release from local environmental cues to controlled mechanics and structures driving tissue responses. One area receiving growing attention is that of electroactive biomaterials. Building upon knowledge of electroactive tissue function and repair, new biomaterials are being developed for regenerative medicine applications as well as for application with cells and tissues not traditionally thought to be electroactive. The integration of sensors and actuators with tissue has also advanced in this topic area. In response to this dynamism, *Acta Biomaterialia* published a special issue in 2022, “Conductive and Electroactive Biomaterials and Bioelectronics”, expertly assembled and edited by Professors Mehdi Nikkhah at Arizona State University (Phoenix, USA) and Jonathan

Author Manuscript

Rivnay at Northwestern University (Chicago, USA). The issue was coordinated by *Acta Biomaterialia* editor, Sarah Heilshorn at Stanford University (Palo Alto, USA).

Acta Biomaterialia volume 139, 2022, has become one of the most downloaded and cited issues of the past year and offers a broad range of reviews on electroactive biomaterials to bring the reader up to speed with the latest advances, as well as cutting-edge research reports. In the cardiac area, three reviews from thought leaders in the field [1-3] (Guest Editor, Mehdi Nikkhah et al.; Su Ryon Shin et al., Harvard, Cambridge, USA; and Li Shen, Zhongshan Hospital, Fudan University, Shanghai, China) broadly cover the design and application of electroconductive biomaterials in efforts to mitigate the negative tissue remodeling following myocardial infarction, as well as progress in creating functional in vitro cardiac tissues. The value of conductive substrates versus non-conductive materials is explored. Approaches to biomaterial design are summarized, as are considerations of mechanical properties, cell interactions and micro- and nano-scale property control. Complementing these reviews is a report from the group of Pinar Zorlutuna (University of Notre Dame, USA) [4] on 3D printing of Ti3C2Tx MXene-PEG composites for cardiac tissue engineering, and from the labs of Xiaohui Zhang and Dengfeng Gao (Xi'an Jiaotong University, China). [5] on anisotropic conductive matrices for treatment of the post-infarct ventricle. These articles together give the reader an appreciation for the complex challenge of repairing or regenerating myocardial tissue with its orchestrated electrical and mechanical behavior that must continuously operate in synchrony. The drive to integrate reparative scaffolds and tissue constructs into this active environment is an ongoing need driven by the growing global impact of cardiac failure.

Neural tissue repair has historically been a target for electroactive biomaterial development, particularly as scaffolds to regenerate tissue across regions of damage in the peripheral nervous system and the spinal cord. A collaborative review between John G. Hardy (Lancaster University, UK), Jae Young Lee (Gwangju Institute of Science and Technology (GIST), Republic of Korea.) and Christine E Schmidt (University of Florida, Gainesville, USA) [6] and an overview by Emi A Kiyotake, Michael D Martin, and Michael S Detamore (all at University of Oklahoma, USA) [7] capture the state-of-the-art in terms of organic materials for the regeneration of a range of neural tissues, and for the potential for these materials in the emerging field of regenerative rehabilitation, respectively. In the latter case, the potential for conductive biomaterials is well-placed within current clinical approaches in treating spinal cord injury. Manousiouthakis et al. [6] note the growing interest in degradable conductive materials for scaffolds in regenerative medicine approaches. Across the field of neural tissue engineering the literature has witnessed the tandem growth of increasingly sophisticated materials approaches

Author Manuscript

often coupled with advances in stem cell-based strategies. Two research reports [8-10] focused on such interactive approaches, coupling electrical stimulation and biomaterial design to promote neural stem cell growth and differentiation [8] (by the teams of Xiaowei Yang, Renjie Chai, and Mingliang Tang at Tongji University, Shanghai, Southeast University, Nanjing, and Soochow University, Suzhou, China), and mesenchymal stem cell differentiation and maturation into Schwann-like cells [9] (from Bin Duan University of Nebraska-Lincoln, USA), while Dongmei Li and Ren-Ke Li et al. (Capital Medical University, Beijing, China and University of Toronto, Canada) [10] developed a photoactive polymer capable of opto-electrical stimulation to enhance neuronal differentiation. Related to the employment of electrical field in neural tissue engineering, the lab of Sarah H Cartmell (The University of Manchester, UK) [11] showed that electrical stimulation of titanium could promote osteogenesis.

An area of electroactive biomaterials that has seen widespread efforts and success in clinical translation is implantable electrodes. As the field has advanced, so has the need for increasingly robust electrodes with greater spatial resolution and sensitivity. Oldroyd and Malliaras (University of Cambridge, UK) [12] have provided an authoritative review on thin-film electrodes for neurostimulation and summarize the substantial challenges remaining to overcome both material-centered failure mechanisms as well as those precipitated by the foreign body response and failure at the tissue-material interface. As is widely appreciated by the biomaterials community, orchestrating a functional, robust integration between material and tissue would advance technologies in brain-machine interface and a broad array of biosensing and actuation. Much work remains to be done. In terms of advances in electronic material development for biomedical applications, Jian Liu et al. (Soochow University, Suzhou, China) [13] review bio-inspired electronics for “smart electronic skin” applications with an exciting coverage of the possibilities. Along these lines, Zhou et al. (Polytechnique Montréal, Canada) [14] report a self-healing hydrogel that is adhesive and mechanically appropriate for skin application. Rylie Green and coworkers (Imperial College London, UK) [15] review how additive manufacturing can be better employed in the processing of conductive polymers through material design and highlight the challenges in achieving processability, activity and biocompatibility.

These are some of the highlights of the special issue on electroactive biomaterials this past year in *Acta Biomaterialia,* which has garnered strong interest in the community. The journal, part of the family of journals from the non-profit organization, Acta Materialia Inc., will continue to explore new ways to support and advance the biomaterials community through its

Author Manuscript

publishing and service mission. We appreciate the essential support of those who have authored, reviewed, and served as special content editors in the past year.

3. *Advanced Healthcare Materials* (Uta Göbel, PhD, Editor-in-Chief)

For the purpose of this "Year in Review" article, I am looking at the most downloaded articles published in 2022, as well as those articles, that have already received a few early citations within the same year. This provides you with an overview of the most impactful areas in biomaterials research published in 2022 in *Advanced Healthcare Materials* (AHM).
Most importantly, AHM has published a few special issues to drive exciting developments in the field, most of which also include articles gaining attention throughout the year. Importantly the journal honored two giants in the biomaterials field with dedicated Special issues: Nicholas Peppas and Buddy Ratner. Nicholas Peppas was honored in a Special issue published in April 2022, edited by Kristi S. Anseth (University of Colorado, Boulder, USA) and Younan Xia (Georgia Institute of Technology and Emory University, Atlanta, USA) [16]. The issue for Buddy Ratner, edited by Younan Xia alone, was published in May 2022 [17].

The Nicholas Peppas special issue features a few articles written by collaborators and previous students that stand out in terms of downloads and showcase significant developments in the field. First, an article by Ehsan Toyserkani (University of Waterloo, Canada), Ali Khademhosseini (Terasaki Institute for Biomedical Innovation, Los Angeles, USA) and colleagues reports on a template-enabled biofabrication technique creating perfusable macrochannels for the purpose of creating large tissue constructs [18]. The authors employ cell-laden hydrogels that could be precisely patterned via water-soluble gelatin templates that are constructed by economical extrusion 3D printed plastic templates. Secondly, the groups of Ratchaneewan Aunpad (Thammasat University, Thailand) and Mark W. Tibbitt (ETH Zurich, Switzerland) report on a novel biopolymer nano-network for antimicrobial peptide delivery [19]. This material is made of electrostatically encapsulated peptides within positively and negatively charged nanoparticles made of chitosan and dextran sulfate without further chemical modification.

These articles certainly already highlight biofabrication as a key development within the field, as well as the use of polymeric materials for drug delivery. Another example of the latter is a well-read perspective article, by the group of Omolola Eniola-Adefeso (University of Michigan Ann Arbor), covering "PLGA's Plight and the Role of Stealth Surface Modification Strategies in Its Use for Intravenous Particulate Drug Delivery" [20].

Author Manuscript

Also in the field of biofabrication, a contribution by Liliang Ouyang et al. (now at Tsinghua University, Beijing) and work conducted in the lab of Molly Stevens (Imperial College London, UK) certainly stands out. This work reports on a new tunable microgel-templated porogel (MTP) bioink [21]. Gelatin microgels are first fabricated with varied sizes and mixed with photo-crosslinkable formulations to make composite MTP bioinks. The addition of microgels significantly enhances the shear-thinning and self-healing viscoelastic properties and thus the printability of bioinks with high cell densities.

Within 2022 the journal also saw a rising number of submissions in the field of microgels. An indicator for this is AHM's most cited review article in 2022 on "Translating Therapeutic Microgels into Clinical Applications" written by Yonca Kittel, Alexander J. C. Kuehne, Laura De Laporte from the DWI – Leibniz Institute for Interactive Materials, Aachen, Germany, which seems to be an important reference article for the use of microgels and their unique properties [22].

AHM also received an increasing number of submissions on the use of extracellular vesicles and exosomes, either within biomaterials or as biomaterials themselves. To reflect this trend AHM commissioned a Special issue on "Extracellular Vesicles — A Versatile Biomaterial" edited by Juliane Nguyen (University of North Carolina at Chapel Hill, USA) and Gregor Fuhrmann (Friedrich-Alexander-University Erlangen-Nürnberg, Germany) [23]. Examples of the most accessed articles in this issue are the review by Anika Nagelkerke et al. (University of Groningen, The Netherlands) on liposomes and extracellular vesicles as drug delivery systems [24] and the application of those as siRNA delivery vehicles, employing extracellular vesicle – liposome hybrid nanoparticles, reported by the group of Pieter Vader (University Medical Center Utrecht, The Netherlands) [25]. In the same area, but not in this special issue was also the article from the group of Patrick S. Doyle (MIT, Harvard Medical School, Boston) which shows quantitative and multiplex detection of extracellular vesicle-derived MicroRNA using rolling circle amplification within encoded hydrogel microparticles [26].

By far the most cited article of the year (while only published in April 2022) was written by the group of Baolin Guo (Xi'an Jiaotong University, China) which describes the creation of a supramolecular thermo-contracting adhesive made of a poly(N-isopropylacrylamide) hybrid hydrogel dressing composed of quaternized chitosan-graft-β-cyclodextrin, adenine, and polypyrrole nanotubes prepared via host–guest interaction and hydrogen bonds [27]. This was then applied to both full-thickness skin incision and excision wound models, where wound closure was achieved after 24 h post-surgery for acute and methicillin-resistant *Staphylococcus aureus*-infected wounds. Furthermore, on the topic of wound healing, Xiaodong Guo's group

at Huazhong University of Science and Technology, Wuhan, China, report on a black phosphorus hydrogel with antibacterial and antioxidant properties [28].

Further key developments in the biomaterials field are the clinical use of microrobots as well as the use of machine-assisted tools for regenerative medicine applications, exemplified by two representative, well-received articles: Hongsoo Choi et al. (DGIST, Republic of Korea) propose an electromagnetically controllable microrobotic system which can help medical practitioners optimally manipulate interventional devices such as guidewires for the treatment of cardiovascular diseases. The system can be teleoperated, protecting medical staff from ionizing radiation [29]. Last, but not least, Adam J. Gormley (Rutgers, The State University of New Jersey, USA) and Michael A. Webb (Princeton, NJ, USA) report on the combination of robotics and machine learning used to design complex copolymers that thermostabilize chondroitinase ABC [30]. This enzyme is known to degrade the side chains of chondroitin sulfate proteoglycans and promote tissue regeneration after central nervous system injuries. Thus, further machine learning tools are on the horizon, not only for applications in spinal cord injury but also others within biomaterials research.

4. Biomaterials research in *Advanced Materials* (Ekaterina Perets, PhD, Deputy Editor)

The year 2022 has brought many breakthroughs in the Biomedical field and many of those impactful articles were featured in *Advanced Materials* within tissue engineering, regenerative medicine, medical devices, and cancer therapy.

In tissue engineering, Jennifer A. Lewis et al. from Harvard University (Cambridge, USA) [31] have successfully biofabricated aligned cardiac tissues by bioprinting anisotropic organ building blocks (aOBBs) (hiPSC-CMs). These aOBBs are elongated microtissues composed of cellular aligned human induced pluripotent stem cell-derived cardiomyocytes hiPSC-CMs that can be modularly assembled into a printable bioink. This discovery opens up new avenues for generating aligned, vascularized cardiac tissues for therapeutic use.

Another exciting biofabrication strategy from Harvard by the group of Yu Shrike Zhang features a vertical 3D cryo-bioprinting technique allowing to engineer anisotropic tissues as well as interface tissues like muscle-tendon [32]. For tissue repair applications, Jason Burdick and colleagues (University of Pennsylvania, Philadelphia, USA) have observed that using rod-shaped, rather than spherical, particles in the preparation of granular hydrogels endows these injectable and porous biomaterials superior functional properties in the process of integration with the host tissue when compared to solid hydrogels [33]. This is also underlining the high potential of microgel-based systems where we expect further exciting developments in the field.

Author Manuscript

Author Manuscript

In addition, two remarkable studies from Radboud University (Nijmegen, Netherlands) have brought tissue engineering science a huge step closer to nature. The first one by Paul H. J. Kouwer et al. demonstrates nanocomposites constructed from a synthetic fibrous hydrogel based on polyisocyanide (PIC) with a responsive cross-linker. Here, the hydrogel is transformed from a static extracellular matrix mimic to a highly dynamic and biocompatible material, allowing the scientists to spatially and temporally manipulate the mechanical properties of a material while maintaining responsiveness towards a variety of cues [34]. The second study by Manzar Abbas and Evan Spruijt et al. demonstrates the construction of coacervates photocells from tyrosine-rich peptide conjugates which can be used as artificial cells capable of communication in tissue engineering as well as potential vehicles for drug delivery [35].

One of the most exciting breakthroughs in regenerative medicine was the development of liver-like metabolic biofactories from bioprinted organoids, and hydrogels from the group of Riccardo Levato (Utrecht University, The Netherlands). They use the recently developed volumetric bioprinting method for the fabrication of organoids, which capture the key functions of the human liver and undergo hepatocytic differentiation with albumin synthesis, liver-specific enzyme activity and have remarkably acquired a native-like cell polarization [36]. Another excellent research comes from Sichuan university where a collaboration of Hang Zhao, Xianglong Han and Qianming Chen et al. have developed an injectable, high-strength and anti-inflammatory hydrogel constructed by the self-assembly of a monomeric nucleoside molecular gelator (2-amino-2′ -fluoro-2′ -deoxyadenosine (2-FA)) for bone healing applications. Omics analysis has revealed that the antibacterial activity was attributed to the "secondary messenger storm" effect, which downgraded the carbon–nitrogen balance of bacteria [37]. In addition, David Mooney's group from Harvard demonstrated an unprecedentedly tough tissue adhesive, made of alginate–polyacrylamide (pAAm) with a chitosan bridge for strong adhesion to not only skin and tendon but also heart tissue [38]. Moreover, collaborators from the labs of Young Keun Kim and Heemin Kang from Korea University and Ramasamy Paulmurugan from Stanford University (Palo Alto, United States) have successfully engineered in situ localized assemblies of gold nanoparticles arrays on nanomagnetite templates, which are used to tune liganded gold nanoparticle (GNP) size and spacing and hereby manipulate macrophage-adhesion-assisted pro-regenerative polarization [39]. To top this off, Zhou Li et al. from the Chinese Academy of Science (Beijing, China) have demonstrated a self-healing, stretchable, conductive and versatile hydrogel and used it to generate an artificial nerve fiber made from polyvinyl alcohol (PVA) and polyethyleneimine (PEI) by mimicking the myelinated axon's structure and functions of signal transmission. The nerve was then implanted into a synchronous

bionic robotic hand system where it showed a real-time high fidelity and high throughput information interaction, both under deformation and cryogenic temperatures [40].

In the medical devices field, Jennifer Rupp et al. from MIT have developed the smallest to date ceramic glucose fuel cell which can be easily integrated into bioelectronics. These micro-glucose fuel cells hold the potential to power the next generation of highly miniaturized implantable medical devices [41]. Furthermore, the group of Can Dincer (Freiburg, Germany) demonstrated a versatile biosensor for therapeutic drug monitoring for potential application in personalized therapy. The microfluidic biosensor is comprised of multiple dry film photoresist layers stacked onto a platinum-patterned polyimide substrate, on which the microchannels and electrodes are realized. This ensures a rapid, low-cost, sample-independent drug monitoring in both blood and non-invasive samples like urine, saliva and exhaled breath condensate [42].

Several promising strategies in the area of cancer therapeutics were developed in 2022. Chaoyong Liu and Haihua Xiao et al. from the Chinese academy of science (Beijing, China) developed a biodegradable pseudo-semiconducting polymer for bioimaging, photodynamic immunotherapy and photoactivated chemotherapy of cancer. This new polymer is degraded by intracellular glutathione ultimately resolving the poor degradability problem of semiconducting polymers which could improve their clinical applicability [43]. In addition, the lab of Dan Peer from Tel Aviv University (Israel) gives chemo-immunotherapy a much needed nanotherapeutic boost by using RNAi-loaded lipid nanoparticles. Specifically, siRNA against HO1 was entrapped in lipid nanoparticles (ionizable lipid nanotherapeutic boost (iLNTB)) and their surface was modified anti-PD-L1 antibody. This novel tumor myeloid cell- and cancer cell-dual targeted HO1-inhibiting lipid nanotherapeutic boost (T-iLNTB) sensitizes cancer cells to "standard-of-care" chemotherapeutics by increasing immunogenic cell death, and directly reprograms tumor myeloid cells with distinguished phenotype. Furthermore, tumor myeloid cell reprogramming by T-iLNTB induces CD8+ cytotoxic T cell recruitment, which drives "Cold-to-Hot" transition and correlates with improved responsiveness to immune checkpoint inhibitors in combination therapy [44].

5. *Biomaterials* (Kam W. Leong, PhD, Editor-in-Chief)

Biomaterials covers the wide range of physical, chemical, and biological sciences that enable the design of biomaterials to impact biomedical investigations and applications. The papers published in 2022 reflect such diversity in scientific content. I will focus only on the

Author Manuscript

research instead of review articles as the former is more indicative of the emerging excitement in the field.

Papers related to immunotherapy continue to increase in the journal, and together with cancer therapy, these two topics represent 52% of the papers published in 2022. Papers related to tissue engineering and regenerative medicine capture 28%. The journal continues to publish a healthy number of papers related to implant design and performance (~20).

I will first highlight four articles published in 2022 that have over 6,000 downloads by extracting from their abstracts.

1) Wang, et al., "Flexible patch with printable and antibacterial conductive hydrogel electrodes for accelerated wound healing" [45]. This article, written by a large collaboration led by Wujin Sun and Ali Khademhosseini (at University of California, Los Angeles, Virginia Tech, Blacksburg, and Terasaki Institute for Biomedical Innovation, among others, all USA) describes a flexible electrical patch made with conductive hydrogel comprising silver nanowires and methacrylated alginate as electrodes to improve wound management. Named ePatch, this hydrogel promotes re-epithelization, enhances angiogenesis, mediates immune response, and prevents infection development in the wound microenvironment.
2) Ripoll et al., "An imidazole modified lipid confers enhanced mRNA-LNP stability and strong immunization properties in mice and non-human primates" [46]. The study performed at Sanofi (Marcy l'Etoile, France) addresses some of the limitations of the current mRNA/LNP vaccine technology that has made an impact in fighting infectious diseases such as the Covid-19 crisis. The authors describe the use of a novel imidazole-modified lipid, DOG-IM4, in combination with standard helper lipids to improve the thermostability of mRNA/LNP. They demonstrate that the DOG-IM4 LNPs confer strong immunization properties to influenza HA mRNA in mice and macaques and remarkable stability to the encapsulated mRNA when stored in PBS at 4ºC.
3) Tu et al., "Promoting the healing of infected diabetic wound by an anti-bacterial and nano-enzyme-containing hydrogel with inflammation-suppressing, ROS-scavenging, oxygen and nitric oxide-generating properties" [47]. This work by the group of Feng Xu (Zhejiang University School of Medicine, Hangzhou, China) describes the design of a multifunctional hydrogel synthesized by crosslinking hydrophilic poly(PEGMA-co-GMA-co-AAm) (PPGA) polymers with hyperbranched poly-L-lysine (HBPL)-modified MnO_2 nanozymes, which is further loaded with pravastatin sodium. The hydrogel can scavenge different types of ROS, generate O_2, kill a broad spectrum of bacteria, and

Author Manuscript

protect cells against oxidative stress. The HBPL-crosslinked hydrogels can kill up to 94.1%-99.5% of methicillin-resistant *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* even at 10^9 CFU/mL.

4) Daniell et al., "Debulking different Corona (SARS-CoV-2 delta, omicron, OC43) and Influenza (H1N1, H3N2) virus strains by plant viral trap proteins in chewing gums to decrease infection and transmission" [48]. This interesting study performed at University of Pennsylvania, Philadelphia, USA, advances the concept of using chewing gum to deliver proteins to debulk oral viruses and decrease infection/transmission. It describes the delivery of viral trap proteins (CTB-ACE2, FRIL) expressed in plant cells by chewing gum. The gum powder can reduce the virus load below the detection level of spike protein in the RAPID assay in 17 of the 20 delta or omicron nasopharyngeal samples. Chewing simulator studies reveal that the CTB-ACE2 release is dose-dependent and sustained for 20 min of chewing. A Phase I/II placebo-controlled, double-blinded clinical trial (IND 154897) is in progress to evaluate the viral load in saliva before or after chewing CTB-ACE2/placebo gum.

CRISPR-based gene editing technology is one of the most exciting scientific breakthroughs in the past decade. In addition to advancing our understanding of diseases, it opens up new venues for tackling genetic disorders. More than half a dozen papers describe the development of carriers for the delivery of gene editing elements or their applications *in vivo*. The group of Prashant Mali (University of California San Diego, La Jolla, USA) describes the integration of large-scale CRISPR screens with tissue-engineered models for screening therapeutically relevant cancer vulnerabilities [49]. Lu et al. report the use of a nonviral CRISPR-Cas9 gene editing nanoplatform to activate the cGAS-STING pathway combined with immune checkpoint blockade within the immunosuppressive tumor microenvironment to induce a strong immune response, in a study led by Bangshun He, Xin Han and Yujun Song (Nanjing University, China) [50]. Yu-Kyoung Oh and Jongpil Kim et al. (Seoul National University and Dongguk University, Seoul, Republic of Korea) present the development of magnetoplexes targeting the miR34a gene that can improve cardiac function in a mouse model of myocardial infarction [51]. A collaboration between the groups of Marina E Emborg and Shaoqin Gong (University of Wisconsin–Madison, USA) uses biodegradable PEGylated nanocapsules that can deliver preassembled Cas9-sgRNA ribonucleoproteins (RNPs) to the brain by intracerebral injection for robust genome editing of the neurons [52]. Dong-Wook Kim and Jong-Hoon Kim et al (Korea University, Seoul, Republic of Korea) describe the engineering of CRISPR/Cas9-edited

Author Manuscript

hiPSCs from Hemophilia A (HA) patients and their implantation into HA mice to restore the plasma FVIII activity and manage bleeding episodes [53]. Finally, the labs of Yong Ma, Jinao Duan and Ming Zhao (Nanjing University of Chinese Medicine, China) created a photothermal nanoplatform including CRISPR-Cas9 ribonucleoprotein that can improve tissue penetration, reduce thermal damage to normal tissues, and induce thermo-tolerance by heat shock proteins [54].

Addressing the recent COVID pandemic, researchers have published a cluster of papers ranging from virus detection, generation of ex vivo models, mitigation of viral inflammation, and therapy [55-59]. Several papers also describe innovative vaccine designs that should help fight future pandemics.[56, 60-64].

This is only a glimpse of the many interesting papers innovating in biomaterials science and engineering. The field of biomaterials continues to grow and contribute to society. We strive to provide a platform for biomaterials researchers to publish their best work in the journal and look forward to exciting breakthroughs in the coming year.

6. *Journal of Biomedical Materials Research Part A* (JBMR A; J. Kent Leach, PhD, Editor-in-Chief)

Biomaterials are continually modified to control their mechanical properties for use in tissue engineering [65], utilized for local release of bioactive moieties [66], employed as model systems to study the immune system [67], or designed to impede colonization by dangerous bacteria[68]. Over the last year, advances in biomaterials have been widespread with significant progress in innovative methods to deliver bioactive moieties and regulate how biomaterials interact with the immune system.

The most downloaded article in JBMR A in 2022 described an exciting advance in the design of lipid nanoparticles (LNPs) for mRNA delivery. The effective packaging and delivery of mRNA has benefited millions of lives around the world, with the most prominent examples being the Pfizer/BioNTech and Moderna COVID-19 mRNA vaccines. Importantly, the translation efficiency of mRNA is impaired by the inflammatory response that has been traced to the cholesterol within common formulations, and such inflammatory responses may even provoke immune-associated adverse effects.[69] To address this challenge, the group of Michael J. Mitchell (University of Pennsylvania, Philadelphia, Pennsylvania, USA) partially substituted dexamethasone for cholesterol within the LNPs, which has a similar structure and is a potent anti-inflammatory agent.[70] The resulting LNPs were morphologically similar and highly efficient in entrapping the mRNA payload as the standard LNPs. Moreover,

Author Manuscript

dexamethasone-substituted LNPs achieved comparable gene expression in HepG2 liver cells in culture as the standard cholesterol-containing nanoparticles. When delivered intravenously, mice treated with the dexamethasone-substituted nanoparticles exhibited nearly 40% reduction in TNF-α levels in the serum and a 1.5-fold increase in gene delivery to the liver. Thus, dexamethasone substitution within LNPs could be a potentially promising strategy to reduce inflammation-related adverse effects of LNPs while enhancing protein expression of mRNA therapeutics.

Cationic polymers such as poly(L-lysine) and polyethylenimine are widely studied to deliver genes due to their low immunogenicity and low cost, yet challenges remain with cytotoxicity and targeting the vehicle to the desired site.[71] Single-walled carbon nanotubes (SWNTs) have been examined as delivery vehicles for bioactive molecules. Unlike most polymers, SWNTs may be heated, which allows their potential application in photothermal and photoacoustic therapy. Amylose is a natural polysaccharide, typically consisting of 200–20,000 glucose units that form a helix. Building on prior work that covalently linked poly(L-lysine) to the amylose helix for gene delivery, Haijun Deng, Liming Zhang, Baoxiong Zhuang (Southern Medical University, Guangzhou, China) et al. modified SWNTs with amylose derivatives containing poly(L-lysine) dendrons in an effort to establish bioactive, water-soluble SWNTs for clinical use.[72] Unlike unmodified SWNTs that have poor water solubility, the amylose-modified SWNTs remained stable in water for at least 48 hours. The authors confirmed the photothermal effect of the SWNTs following irradiation, with increases in temperature achievable by increasing the SWNT dosage. When used to treat a tumor of colorectal origin injected into the flank of mice, the authors reported smaller tumor volumes when treated with amylose-modified SWNTs delivering plasmid DNA encoding for TNF-a, which is known to slow tumor growth, compared to the amylose polymer alone. When irradiation was applied, tumor volume sharply reduced by 50% in two days in the amylose-modified SWNT treated mice. Collectively, these findings demonstrate the promise of modifying SWNTs to improve water solubility and apply photothermal therapy for improved clinical utility in combating cancer.

Biomaterials play a critical role in combating or reducing infection by serving as delivery vehicles for antibiotics and restricting the ability of microbes to effectively colonize the implant surface. Infection is a key challenge in tissue transplantation or the use of implants that can undermine the effectiveness of the treatment. In corneal transplantation, bacterial infection can cause corneal scarring and delayed or impaired healing. Silk fibroin is under broad examination for use as a corneal implant material due to its transparency, tunability, and biodegradability.

Author Manuscript

Author Manuscript

To address the potential challenge of infection with corneal implantation, the team of Anita K. Ghag (University of Birmingham, UK) created a methacrylated silk (SilkMA), which was loaded with gentamicin and rapidly crosslinked with ultraviolet light.[73] The mechanical properties of the construct were readily tunable by modulating the polymer concentration and matched those or the native cornea. Gentamicin-loaded SilkMA effectively inhibited the growth of both *Staphylococcus aureus* and *Pseudomonas aeruginosa* on agar plates. These results establish the promise of a photocrosslinkable, transparent silk material that can release bioactive quantities of antibiotics to locally combat infection with potential use as a corneal replacement.

Infections associated with biomedical implants are the most common cause of healthcare-related infections. Biofilms provide a protective niche for bacteria, making it difficult to treat infections with antibiotics alone. Moreover, the rise of antibiotic or multidrug-resistant bacteria is evident around the world, motivating the importance for developing new strategies to prevent biofilms on materials and reduce the occurrence of implant-associated infections. Bacterial cells may sense and respond to 3D surface topography, leading to different levels of adhesion on surfaces. Over the last decade, we have seen exciting advances in impeding biofilm development by controlling the surface characteristics of biomaterials, but there have been limited reports of how various parameters may synergistically impede bacterial interaction. Li-Chong Xu, and Christopher A. Siedlecki (The Pennsylvania State University, Hershey, USA) designed a series of submicron pillar patterns with different pillar size, spacing, height, and shape and fabricated these patterns on polyurethane biomaterial surfaces to observe how these morphological characteristics would influence staphylococci adhesion and biofilm formation [74]. Compared to round, smooth surfaces, decreasing the size of the top fractional surface by addition of pillars increased substrate hydrophobicity due to air trapped in spaces between pillars and significantly reduced bacterial adhesion. When comparing pillars with the same surface area but different shape, no difference in bacterial adhesion was noted, thereby establishing that pillar shape is not a key parameter. The authors noted that biofilm development was markedly reduced in patterned substrates, and surface contact area was the dominant factor in affecting bacterial adhesion. This rigorous study provides important insight into biomaterial design to minimize bacterial adhesion and biofilm development.

JBMR A published many outstanding papers in 2022 that considered the application of biomaterials in other areas besides those highlighted. Furthermore, the Journal is proud to showcase the winners of the Society For Biomaterials annual awards including the Founders Award, Mid-Career Award, Young Investigators Award, and Student Awards for Outstanding

Research. The Journal provides a vehicle for publishing high-quality literature in the field of biomaterials science.

7. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* (JBMR B; Jeremy Gilbert, PhD, Editor-in-Chief)

In conjunction with my Editor-in-Chief colleagues in the biomaterials field, this part of the "Year in Review" article is intended to highlight the year's publishing efforts in *Journal of Biomedical Materials Research Part B: Applied Biomaterials* (JBMR B). JBMR B's mission, as outlined in its scope and aims, relates to "the common focus of biomaterials applied to the human body and covers all disciplines where medical devices are used. Papers are published on biomaterials related to medical device development and manufacture, degradation in the body, nano- and biomimetic-biomaterials interactions, mechanics of biomaterials, implant retrieval and analysis, tissue-biomaterial surface interactions, wound healing, infection, drug delivery, standards and regulation of devices, animal and pre-clinical studies of biomaterials and medical devices, and tissue-biopolymer-material combination products."

There is a wide range of topics covered in JBMR B's 2022 publications. They span the range of physiological systems (e.g., dental, orthopedic, spinal, cardiovascular, vision, hearing, throat, bladder), broad biomaterial topics areas (drug delivery, bioceramics, metal alloys, biodegradable biomaterials, tissue-engineered scaffolds, surfaces of biomaterials, decellularized extracellular matrix materials, regenerative biomaterials, collagen, etc.) and biomaterials processing, performance and degradation (e.g., 3D printing, electrospinning, composites, corrosion, mechanical properties, blood-interactions, infection, etc.). Regenerative biomaterials and tissue engineering topics were similarly represented.

The top two most downloaded articles for 2022 were open-access review articles: M. Azam Ali et al. (University of Otago, Dunedin, New Zealand), "A review of current advancements for wound healing: Biomaterial applications and medical devices" [75] and Van der Borre et al. (Vrije Universiteit Brussel, Belgium), "How surface coatings on titanium implants affect keratinized tissue: A systematic review" [76]. The two top-most downloaded research articles were: De Meurechy et al. (Vrije Universiteit Brussel, Belgium), "Surface wear in a custom manufactured temporomandibular joint prosthesis" [77], and Schulten et al. (RWTH Aachen University, Germany), "A polyurethane-based surgical adhesive for sealing blood vessel anastomoses – A feasibility study in pigs" [78]. The top two cited papers are: 1. An article by the group of Nasim Annabi (University of California - Los Angeles, USA.), "Engineering a highly elastic bioadhesive for sealing soft and dynamic tissues" [79] and Yusril Yusuf et al.

Author Manuscript

(Universitas Gadjah Mada, Yogyakarta, Indonesia), "In-vitro bioactivity of 3D microstructure hydroxyapatite/collagen based – egg white as an antibacterial agent" [80].

In reflecting on JBMR B's 2022 papers there are some broad themes that stand out that are worth mentioning. These include metallic biomaterials studies, wear and corrosion of biomaterials and 3D printing of biomaterials.

For JBMR B, one such focus area was the study of metals in the body with over 20 papers published on the topic. This includes the study of new alloys for degradable metal applications (e.g., Fe-based, Zn-based, Cu-based, etc.), investigations into the degradation of metals in orthopedics, cardiovascular [81] and dentistry in vivo and in vitro (e.g., CoCrMo, Ti alloys and stainless steels), metals used for antibacterial applications, the use of metallic (Au) nanoparticles for therapeutic and drug delivery applications, and the use of 3D printing of metals. Biodegradable metals and their processes and interactions of degradation were a prominent focus in this past year, including in 3D printed Fe-based scaffolds [82] and alloys [83], zinc alloys [84], magnesium alloys [85, 86] and others.

Wear, corrosion and biomaterials: Studies of the interplay of degradation products in orthopedic alloys and the body were also a focus. Ongoing concerns related to CoCrMo alloys and the corrosion and wear products were evaluated [87-89] including fretting corrosion of modular taper junctions [90], the effects of chromium degradation products [90], mixed metal degradation products [89] and crevice corrosion of orthopedic alloys [87].

3D Printing: 3D printing of soft biomaterials, biomaterial-cell-drug combinations and 3D printing of hard biomaterials have all seen increased attention in the past year. These works have investigated the range of 3D printing from electron-beam printing of titanium-based spinal cages [91] to 3D printing of Hydroxyapatite and/or polymeric hydrogel biomaterials. Three-dimensional printing of gelatin-based hydrogels [92, 93] for bone and cartilage applications was reported as were printed PEEK hip stems [94] and hydroxyapatite-based biomaterials [95].

Many other topics were covered in JBMR B in the past year and no review can possibly cover all that was accomplished. I encourage you to review the work published in 2022 in JBMR B. Many exciting directions are presented in the work published in the journal. JBMR B had a highly successful year with a diversity of topics coming from a wide range of researchers throughout the world.

Conflict of Interest

None of the authors have a conflict of interest to disclose

Author Manuscript

Author Manuscript

References Cited

[1] Esmaeili H, Patino-Guerrero A, Hasany M, et al. Electroconductive biomaterials for cardiac tissue engineering. Acta Biomater. 2022;139:118-140. doi:10.1016/j.actbio.2021.08.031

[2] Morsink M, Severino P, Luna-Ceron E, Hussain MA, Sobahi N, Shin SR. Effects of electrically conductive nano-biomaterials on regulating cardiomyocyte behavior for cardiac repair and regeneration. Acta Biomater. 2022;139:141-156. doi:10.1016/j.actbio.2021.11.022

[3] Li Y, Wei L, Lan L, et al. Conductive biomaterials for cardiac repair: A review. Acta Biomater. 2022;139:157-178. doi:10.1016/j.actbio.2021.04.018

[4] Basara G, Saeidi-Javash M, Ren X, et al. Electrically conductive 3D printed Ti3C2Tx MXene-PEG composite constructs for cardiac tissue engineering. Acta Biomater. 2022;139:179-189. doi:10.1016/j.actbio.2020.12.033

[5] Zhao G, Feng Y, Xue L, et al. Anisotropic conductive reduced graphene oxide/silk matrices promote post-infarction myocardial function by restoring electrical integrity. Acta Biomater. 2022;139:190-203. doi:10.1016/j.actbio.2021.03.073

[6] Manousiouthakis E, Park J, Hardy JG, Lee JY, Schmidt CE. Towards the translation of electroconductive organic materials for regeneration of neural tissues. Acta Biomater. 2022;139:22-42. doi:10.1016/j.actbio.2021.07.065

[7] Kiyotake EA, Martin MD, Detamore MS. Regenerative rehabilitation with conductive biomaterials for spinal cord injury. Acta Biomater. 2022;139:43-64. doi:10.1016/j.actbio.2020.12.021

[8] Guo R, Xiao M, Zhao W, et al. 2D Ti3C2TxMXene couples electrical stimulation to promote proliferation and neural differentiation of neural stem cells. Acta Biomater. 2022;139:105-117. doi:10.1016/j.actbio.2020.12.035

[9] Wu S, Qi Y, Shi W, Kuss M, Chen S, Duan B. Electrospun conductive nanofiber yarns for accelerating mesenchymal stem cells differentiation and maturation into Schwann cell-like cells under a combination of electrical stimulation and chemical induction. Acta Biomater. 2022;139:91-104. doi:10.1016/j.actbio.2020.11.042

[10] Yuan B, Aziz MRF, Li S, Wu J, Li D, Li RK. An electro-spun tri-component polymer biomaterial with optoelectronic properties for neuronal differentiation. Acta Biomater. 2022;139:82-90. doi:10.1016/j.actbio.2021.05.036

[11] Khaw JS, Xue R, Cassidy NJ, Cartmell SH. Electrical stimulation of titanium to promote stem cell orientation, elongation and osteogenesis. Acta Biomater. 2022;139:204-217. doi:10.1016/j.actbio.2021.08.010

Author Manuscript

[12] Oldroyd P, Malliaras GG. Achieving long-term stability of thin-film electrodes for neurostimulation. Acta Biomater. 2022;139:65-81. doi:10.1016/j.actbio.2021.05.004

[13] Nie B, Liu S, Qu Q, Zhang Y, Zhao M, Liu J. Bio-inspired flexible electronics for smart E-skin. Acta Biomater. 2022;139:280-295. doi:10.1016/j.actbio.2021.06.018

[14] Zhou X, Rajeev A, Subramanian A, et al. Self-healing, stretchable, and highly adhesive hydrogels for epidermal patch electrodes [published correction appears in Acta Biomater. 2022 Jun;145:436]. Acta Biomater. 2022;139:296-306. doi:10.1016/j.actbio.2021.07.069

[15] Heck J, Goding J, Portillo Lara R, Green R. The influence of physicochemical properties on the processibility of conducting polymers: A bioelectronics perspective. Acta Biomater. 2022;139:259-279. doi:10.1016/j.actbio.2021.05.052

[16] Anseth, K. S., Xia, Y., A Tribute to Professor Nicholas Peppas. Adv. Healthcare Mater. 2022, 11, 2200412. https://doi.org/10.1002/adhm.202200412

[17] Xia, Y. (2022), A Tribute to Professor Buddy Ratner. Adv. Healthcare Mater., 11: 2200701. https://doi.org/10.1002/adhm.202200701

[18] Davoodi, E., Montazerian, H., Zhianmanesh, M., Abbasgholizadeh, R., Haghniaz, R., Baidya, A., Pourmohammadali, H., Annabi, N., Weiss, P. S., Toyserkani, E., Khademhosseini, A., Template-Enabled Biofabrication of Thick 3D Tissues with Patterned Perfusable Macrochannels. Adv. Healthcare Mater. 2022, 11, 2102123. https://doi.org/10.1002/adhm.202102123

[19] Klubthawee, N., Bovone, G., Marco-Dufort, B., Guzzi, E. A., Aunpad, R., Tibbitt, M. W., Biopolymer Nano-Network for Antimicrobial Peptide Protection and Local Delivery. Adv. Healthcare Mater. 2022, 11, 2101426. https://doi.org/10.1002/adhm.202101426

[20] Sheffey, V. V., Siew, E. B., Tanner, E. E. L., Eniola-Adefeso, O., PLGA's Plight and the Role of Stealth Surface Modification Strategies in Its Use for Intravenous Particulate Drug Delivery. Adv. Healthcare Mater. 2022, 11, 2101536. https://doi.org/10.1002/adhm.202101536

[21] Ouyang, L., Wojciechowski, J. P., Tang, J., Guo, Y., Stevens, M. M., Tunable Microgel-Templated Porogel (MTP) Bioink for 3D Bioprinting Applications. Adv. Healthcare Mater. 2022, 11, 2200027. https://doi.org/10.1002/adhm.202200027

[22] Kittel, Y., Kuehne, A. J. C., De, L., Translating Therapeutic Microgels into Clinical Applications. Adv. Healthcare Mater. 2022, 11, 2101989. https://doi.org/10.1002/adhm.202101989

[23] Nguyen, J., Fuhrmann, G., Extracellular Vesicles — A Versatile Biomaterial. Adv. Healthcare Mater. 2022, 11, 2200192. https://doi.org/10.1002/adhm.202200192

Author Manuscript

[24] van der, L., Gandek, T. B., Nagelkerke, A., Liposomes and Extracellular Vesicles as Drug Delivery Systems: A Comparison of Composition, Pharmacokinetics, and Functionalization. Adv. Healthcare Mater. 2022, 11, 2100639. https://doi.org/10.1002/adhm.202100639

[25] Evers, M. J. W., van de, S. I., de, E. M., de, O. G., Gitz-François, J. J. J., Seinen, C. S., Sluijter, J. P. G., Schiffelers, R. M., Vader, P., Functional siRNA Delivery by Extracellular Vesicle–Liposome Hybrid Nanoparticles. Adv. Healthcare Mater. 2022, 11, 2101202. https://doi.org/10.1002/adhm.202101202

[26] Al, D., Juthani, N., Doyle, P. S., Quantitative and Multiplex Detection of Extracellular Vesicle-Derived MicroRNA via Rolling Circle Amplification within Encoded Hydrogel Microparticles. Adv. Healthcare Mater. 2022, 11, 2102332. https://doi.org/10.1002/adhm.202102332

[27] Yu, R., Li, M., Li, Z., Pan, G., Liang, Y., Guo, B., Supramolecular Thermo-Contracting Adhesive Hydrogel with Self-Removability Simultaneously Enhancing Noninvasive Wound Closure and MRSA-Infected Wound Healing. Adv. Healthcare Mater. 2022, 11, 2102749. https://doi.org/10.1002/adhm.202102749

[28] Ding, Q., Sun, T., Su, W., Jing, X., Ye, B., Su, Y., Zeng, L., Qu, Y., Yang, X., Wu, Y., Luo, Z., Guo, X., Bioinspired Multifunctional Black Phosphorus Hydrogel with Antibacterial and Antioxidant Properties: A Stepwise Countermeasure for Diabetic Skin Wound Healing. Adv. Healthcare Mater. 2022, 11, 2102791. https://doi.org/10.1002/adhm.202102791

[29] Hwang, J., Jeon, S., Kim, B., Kim, J., Jin, C., Yeon, A., Yi, B.-J., Yoon, C.-H., Park, H.-J., Pané, S., Nelson, B. J., Choi, H., An Electromagnetically Controllable Microrobotic Interventional System for Targeted, Real-Time Cardiovascular Intervention. Adv. Healthcare Mater. 2022, 11, 2102529. https://doi.org/10.1002/adhm.202102529

[30] Kosuri, S., Borca, C. H., Mugnier, H., Tamasi, M., Patel, R. A., Perez, I., Kumar, S., Finkel, Z., Schloss, R., Cai, L., Yarmush, M. L., Webb, M. A., Gormley, A. J., Machine-Assisted Discovery of Chondroitinase ABC Complexes toward Sustained Neural Regeneration. Adv. Healthcare Mater. 2022, 11, 2102101. https://doi.org/10.1002/adhm.202102101

[31] John H. Ahrens, Sebastien G. M. Uzel, Mark Skylar-Scott, Mariana M. Mata, Aric Lu, Katharina T. Kroll, Jennifer A. Lewis, “Programming Cellular Alignment in Engineered Cardiac Tissue via Bioprinting Anisotropic Organ Building Blocks”, Adv. Mater. 34 (26), 2022.

[32] Zeyu Luo, Guosheng Tang, Hossein Ravanbakhsh, Wanlu Li, Mian Wang, Xiao Kuang, Carlos Ezio Garciamendez-Mijares, Liming Lian, Sili Yi, Junlong Liao, Maobin Xie, Jie Guo,

Author Manuscript

Zongke Zhou, Yu Shrike Zhang, "Vertical Extrusion Cryo(bio)printing for Anisotropic Tissue Manufacturing", Adv. Mater. 34(12), 2022.

[33] Taimoor H. Qazi, Jingyu Wu, Victoria G. Muir, Shoshana Weintraub, Sarah E. Gullbrand, Daeyeon Lee, David Issadore, Jason A. Burdick, "Anisotropic Rod-Shaped Particles Influence Injectable Granular Hydrogel Properties and Cell Invasion", Adv. Mater. 34(12), 2022.

[34] Wen Chen, Jyoti Kumari, Hongbo Yuan, Fan Yang, Paul H. J. Kouwer, "Toward Tissue-Like Material Properties: Inducing In Situ Adaptive Behavior in Fibrous Hydrogels", Adv. Mater. 34(37) 2022.

[35] Manzar Abbas, Jack O. Law, Sushma N. Grellscheid, Wilhelm T. S. Huck, Evan Spruijt,"Peptide-Based Coacervate-Core Vesicles with Semipermeable Membranes", Adv. Mater. 34(34), 2022.

[36] Paulina Nuñez Bernal, Manon Bouwmeester, Jorge Madrid-Wolff, Marc Falandt, Sammy Florczak, Nuria Ginés Rodriguez, Yang Li, Gabriel Größbacher, Roos-Anne Samsom, Monique van Wolferen, Luc J. W. van der Laan, Paul Delrot, Damien Loterie, Jos Malda, Christophe Moser, Bart Spee, Riccardo Levato, "Volumetric Bioprinting of Organoids and Optically Tuned Hydrogels to Build Liver-Like Metabolic Biofactories", Adv. Mater. 34(15), 2022.

[37] Zheng Wang, Yanan Zhang, Yijia Yin, Jiang Liu, Peiran Li, Yuxi Zhao, Ding Bai, Hang Zhao, Xianglong Han, Qianming Chen, "High-Strength and Injectable Supramolecular Hydrogel Self-Assembled by Monomeric Nucleoside for Tooth-Extraction Wound Healing", Adv. Mater. 34(13), 2022.

[38] Juan A. Cintron-Cruz, Benjamin R. Freedman, Matthew Lee, Christopher Johnson, Hamza Ijaz, David J. Mooney, "Rapid Ultratough Topological Tissue Adhesives", Adv. Mater. 34(35), 2022.

[39] Yuri Kim, Thomas Myeongseok Koo, Ramar Thangam, Myeong Soo Kim, Woo Young Jang, Nayeon Kang, Sunhong Min, Seong Yeol Kim, Letao Yang, Hyunsik Hong, Hee Joon Jung, Eui Kwan Koh, Kapil D. Patel, Sungkyu Lee, Hong En Fu, Yoo Sang Jeon, Bum Chul Park, Soo Young Kim, Steve Park, Junmin Lee, Luo Gu, Dong-Hyun Kim, Tae-Hyung Kim, Ki-Bum Lee, Woong Kyo Jeong, Ramasamy Paulmurugan, Young Keun Kim, Heemin Kang, "Submolecular Ligand Size and Spacing for Cell Adhesion", Adv. Mater. 34(27), 2022.

[40] Chan Wang, Ying Liu, Xuecheng Qu, Bojing Shi, Qiang Zheng, Xubo Lin, Shengyu Chao, Changyong Wang, Jin Zhou, Yu Sun, Gengsheng Mao, Zhou Li, "Ultra-Stretchable and

Author Manuscript

Fast Self-Healing Ionic Hydrogel in Cryogenic Environments for Artificial Nerve Fiber", Adv. Mater. 34(16), 2022.

[41] Philipp Simons, Steven A. Schenk, Marco A. Gysel, Lorenz F. Olbrich, Jennifer L. M. Rupp, "A Ceramic-Electrolyte Glucose Fuel Cell for Implantable Electronics", Adv. Mater. 34(24), 2022.

[42] H. Ceren Ates, Hasti Mohsenin, Christin Wenzel, Regina T. Glatz, Hanna J. Wagner, Richard Bruch, Nico Hoefflin, Sashko Spassov, Lea Streicher, Sara Lozano-Zahonero, Bernd Flamm, Rainer Trittler, Martin J. Hug, Maja Köhn, Johannes Schmidt, Stefan Schumann, Gerald A. Urban, Wilfried Weber, Can Dincer, "Biosensor-Enabled Multiplexed On-Site Therapeutic Drug Monitoring of Antibiotics", Adv. Mater. 34(2), 2022.

[43] Dongsheng Tang, Yingjie Yu, Jinbo Zhang, Xiying Dong, Chaoyong Liu, Haihua Xiao, "Self-Sacrificially Degradable Pseudo-Semiconducting Polymer Nanoparticles that Integrate NIR-II Fluorescence Bioimaging, Photodynamic Immunotherapy, and Photo-Activated Chemotherapy", Adv. Mater. 34(34).

[44] Seok-Beom Yong, Srinivas Ramishetti, Meir Goldsmith, Yael Diesendruck, Inbal Hazan-Halevy, Sushmita Chatterjee, Gonna Somu Naidu, Assaf Ezra, Dan Peer, "Dual-Targeted Lipid Nanotherapeutic Boost for Chemo-Immunotherapy of Cancer", Adv. Mater. 34(13), 2022.

[45] C. Wang, X. Jiang, H. J. Kim, S. Zhang, X. Zhou, Y. Chen, H. Ling, Y. Xue, Z. Chen, M. Qu, L. Ren, J. Zhu, A. Libanori, Y. Zhu, H. Kang, S. Ahadian, M. R. Dokmeci, P. Servati, X. He, Z. Gu, W. Sun and A. Khademhosseini, Biomaterials, 2022, 285, 121479.

[46] M. Ripoll, M. C. Bernard, C. Vaure, E. Bazin, S. Commandeur, V. Perkov, K. Lemdani, M. C. Nicolai, P. Bonifassi, A. Kichler, B. Frisch and J. Haensler, Biomaterials, 2022, 286, 121570.

[47] C. Tu, H. Lu, T. Zhou, W. Zhang, L. Deng, W. Cao, Z. Yang, Z. Wang, X. Wu, J. Ding, F. Xu and C. Gao, Biomaterials, 2022, 286, 121597.

[48] H. Daniell, S. K. Nair, H. Guan, Y. Guo, R. J. Kulchar, M. D. T. Torres, M. Shahed-Al-Mahmud, G. Wakade, Y. M. Liu, A. D. Marques, J. Graham-Wooten, W. Zhou, P. Wang, S. K. Molugu, W. R. de Araujo, C. de la Fuente-Nunez, C. Ma, W. R. Short, P. Tebas, K. B. Margulies, F. D. Bushman, F. K. Mante, R. P. Ricciardi, R. G. Collman and M. S. Wolff, Biomaterials, 2022, 288, 121671.

[49] M. Hu, X. Y. Lei, J. D. Larson, M. McAlonis, K. Ford, D. McDonald, K. Mach, J. M. Rusert, R. J. Wechsler-Reya and P. Mali, Biomaterials, 2022, 280, 121276.

Author Manuscript

[50] Q. Lu, R. Chen, S. Du, C. Chen, Y. Pan, X. Luan, J. Yang, F. Zeng, B. He, X. Han and Y. Song, Biomaterials, 2022, 291, 121871.

[51] H. Park, D. Kim, B. Cho, J. Byun, Y. S. Kim, Y. Ahn, J. Hur, Y.-K. Oh, J. Kim, In vivo therapeutic genome editing via CRISPR/Cas9 magnetoplexes for myocardial infarction, Biomaterials, 2022, 281, 121327.

[52] J. M. Metzger, Y. Wang, S. S. Neuman, K. J. Snow, S. A. Murray, C. M. Lutz, V. Bondarenko, J. Felton, K. Gimse, R. Xie, D. Li, Y. Zhao, M. T. Flowers, H. A. Simmons, S. Roy, K. Saha, J. E. Levine, M. E. Emborg and S. Gong, Biomaterials, 2023, 293, 121959.

[53] J. S. Son, C. Y. Park, G. Lee, J. Y. Park, H. J. Kim, G. Kim, K. Y. Chi, D. H. Woo, C. Han, S. K. Kim, H. J. Park, D. W. Kim and J. H. Kim, Biomaterials, 2022, 283, 121429.

[54] W. Tao, X. Cheng, D. Sun, Y. Guo, N. Wang, J. Ruan, Y. Hu, M. Zhao, T. Zhao, H. Feng, L. Fan, C. Lu, Y. Ma, J. Duan and M. Zhao, Biomaterials, 2022, 287, 121621.

[55] L. Bian, Z. Li, A. He, B. Wu, H. Yang, Y. Wu, F. Hu, G. Lin and D. Zhang, Biomaterials, 2022, 288, 121694.

[56] H. K. Kim, H. Kim, M. K. Lee, W. H. Choi, Y. Jang, J. S. Shin, J. Y. Park, D. H. Bae, S. I. Hyun, K. H. Kim, H. W. Han, B. Lim, G. Choi, M. Kim, Y. Chang Lim and J. Yoo, Biomaterials, 2022, 283, 121460.

[57] I. Naqvi, N. Giroux, L. Olson, S. A. Morrison, T. Llanga, T. O. Akinade, Y. Zhu, Y. Zhong, S. Bose, S. Arvai, K. Abramson, L. Chen, L. Que, B. Kraft, X. Shen, J. Lee, K. W. Leong, S. K. Nair and B. Sullenger, Biomaterials, 2022, 283, 121393.

[58] S. Sun, E. Li, G. Zhao, J. Tang, Q. Zuo, L. Cai, C. Xu, C. Sui, Y. Ou, C. Liu, H. Li, Y. Ding, C. Li, D. Lu, W. Zhang, P. Luo, P. Cheng, Y. Gao, C. Tu, B. Pitard, J. Rosenecker, B. Wang, Y. Liu, Q. Zou and S. Guan, Biomaterials, 2023, 292, 121907.

[59] T. Wu, S. A. Rabi, W. A. Michaud, D. Becerra, S. E. Gilpin, M. Mino-Kenudson and H. C. Ott, Biomaterials, 2022, 285, 121509.

[60] J. H. Han, Y. Y. Lee, H. E. Shin, J. Han, J. M. Kang, C. P. James Wang, J. H. Park, S. N. Kim, J. H. Yoon, H. K. Kwon, D. H. Park, T. E. Park, Y. B. Choy, D. H. Kim, T. H. Kim, J. Min, I. H. Kim, C. G. Park, D. K. Han and W. Park, Biomaterials, 2022, 289, 121762.

[61] A. J. Najibi, T. Y. Shih and D. J. Mooney, Biomaterials, 2022, 281, 121329.

[62] V. Sunil, A. Mozhi, W. Zhan, J. H. Teoh, P. B. Ghode, N. V. Thakor and C. H. Wang, Biomaterials, 2022, 290, 121843.

[63] Y. Tahara, R. Mizuno, T. Nishimura, S. A. Mukai, R. Wakabayashi, N. Kamiya, K. Akiyoshi and M. Goto, Biomaterials, 2022, 282, 121385.

Author Manuscript

[64] W. Zhou, X. Chen, Y. Zhou, S. Shi, C. Liang, X. Yu, H. Chen, Q. Guo, Y. Zhang, P. Liu, C. Li, Y. Chu, Y. Luo, Y. Wang, Z. Zhou, Z. Zhao, Q. Chen, T. Sun and C. Jiang, Biomaterials, 2022, 280, 121306.

[65] V. Vassallo, A. Tsianaka, N. Alessio, J. Grubel, M. Cammarota, G.E.M. Tovar, A. Southan, C. Schiraldi, Evaluation of novel biomaterials for cartilage regeneration based on gelatin methacryloyl interpenetrated with extractive chondroitin sulfate or unsulfated biotechnological chondroitin, J Biomed Mater Res A 110(6) (2022) 1210-1223.

[66] L.J. Born, S.T. McLoughlin, D. Dutta, B. Mahadik, X. Jia, J.P. Fisher, S.M. Jay, Sustained released of bioactive mesenchymal stromal cell-derived extracellular vesicles from 3D-printed gelatin methacrylate hydrogels, J Biomed Mater Res A 110(6) (2022) 1190-1198.

[67] P.L. Graney, Z. Zhong, S. Post, I. Brito, A. Singh, Engineering early memory B-cell-like phenotype in hydrogel-based immune organoids, J Biomed Mater Res A 110(8) (2022) 1435-1447.

[68] V.K. Manivasagam, G. Perumal, H.S. Arora, K.C. Popat, Enhanced antibacterial properties on superhydrophobic micro-nano structured titanium surface, J Biomed Mater Res A 110(7) (2022) 1314-1328.

[69] S.C. Semple, T.O. Harasym, K.A. Clow, S.M. Ansell, S.K. Klimuk, M.J. Hope, Immunogenicity and rapid blood clearance of liposomes containing polyethylene glycol-lipid conjugates and nucleic Acid, J Pharmacol Exp Ther 312(3) (2005) 1020-6.

[70] H. Zhang, X. Han, M.G. Alameh, S.J. Shepherd, M.S. Padilla, L. Xue, K. Butowska, D. Weissman, M.J. Mitchell, Rational design of anti-inflammatory lipid nanoparticles for mRNA delivery, J Biomed Mater Res A 110(5) (2022) 1101-1108.

[71] A.I.S. van den Berg, C.O. Yun, R.M. Schiffelers, W.E. Hennink, Polymeric delivery systems for nucleic acid therapeutics: Approaching the clinic, J Control Release 331 (2021) 121-141.

[72] Z. Chen, J. Zhuang, J. Pang, Z. Liu, P. Zhang, H. Deng, L. Zhang, B. Zhuang, Application of a cationic amylose derivative loaded with single-walled carbon nanotubes for gene delivery therapy and photothermal therapy of colorectal cancer, J Biomed Mater Res A 110(5) (2022) 1052-1061.

[73] I.A. Barroso, K. Man, T.J. Hall, T.E. Robinson, S.E.T. Louth, S.C. Cox, A.K. Ghag, Photocurable antimicrobial silk-based hydrogels for corneal repair, J Biomed Mater Res A 110(7) (2022) 1401-1415.

[74] L.C. Xu, C.A. Siedlecki, Submicron topography design for controlling staphylococcal bacterial adhesion and biofilm formation, J Biomed Mater Res A 110(6) (2022) 1238-1250.

Author Manuscript

[75] Deng X, Gould M, Ali MA, "A review of current advancements for wound healing: Biomaterials applications and medical devices", J Biomed Mat Res – Part B, Vol 10 (11) p 2542-2573.

[76] Van den Borre CE, Zigterman BGR, Mommaerts MY, Braem A, J Biomed Mat Res – Part B Vol 110 (7), p 1713-1723.

[77] De Meurechy N, Atkan MK, Boeckmans B, Huys S, Verwilghen DR, Braem A, Mommaerts MY, "Surface wear in a custom manufactured temporomandibular joint prosthesis", J Biomed Mat Res – Part B, Vol 110 (6) p 1425-1438.

[78] Schulten L, Spillner J, Kanzler S, Teubner A, Jockenhoevel S, Apel C, "A polyurethane-based surgical adhesive for sealing blood vessel anastomoses – A feasibility study in pigs", J Biomed Mat Res – Part B, Vol 110 (8), p 1922-1933.

[79] Ghovvati M, Baghdasarian S Baidya A, Dhal J, Annabi N, "Engineering a highly elastic bioadhesive for sealing soft and dynamic tissues", J Biomed Mat Res – Part B, Vol 110 (7), p 1511-1522.

[80] Patty DJ, Nugraheni AD, Ana ID, Yusuf Y, "In vitro bioactivity of 3D microstructure hydroxyapatite/collagen based-egg white as an antibacterial agent", J Biomed Mat Res – Part B, Vol 110 (6), p 1412-1424.

[81] Mani G, Porter D, Collins S, Ornberg A, Shulfer R, "Surface finishing of nitinol for implantable medical devices: A review", J Biomed Mat Res – Part B, Vol 110 (12), p 2763-2778.

[82] Mishra DK, Pandey PM, "Corrosion behavior and degradation mechanism of micro-extruded 3D printed ordered pore topological Fe scaffolds", J Biomed Mat Res – Part B, Vol 110 (6), p 1439-1459.

[83] Yang T, Hao S, Wang P, Qin Y, You G, Shi Y, Yang B, Zhang A, Guo L, Jiang T, " Material properties of degradable alloy Fe-30Mn-0.6N and its effects on ferroptosis in synoviocytes", J Biomed Mat Res – Part B, Vol (110 (1), p 127-139.

[84] Zeng Y, Guan Z, Linsley C, Pan S, Liu J, Wu BM, Li X, "Experimental study on novel biodegradable Zn-Fe-Si alloys", J Biomed Mat Res – Part B, Vol 110 (10, p 2266 – 2275.

[85] Yu PH, Yang W, Wu H, Sun L, Xiu X, Xiu C, Zhang X, Zhang W, "Magnsium promotes osteogenesis via increasing OPN expression and actvating CaM/CaMKIV/CREB1 pathway", J Biomed Mat Res – Part B, Vol 110 (7), p 1594-1603.

[86] Sontgen S Leilig L, Kabir K, Weber A, Reimann S, Welle K, Bourauel C, "Mechanical and numerical investigations of biodegradable magnesium alloy screws for fracture treatment", J Biomed Mat Res – Part B, Vol 110 (1), p 7-15.

Author Manuscript

[87] Herbster M, Rosemann P, Michael O, Harnisch K, Ecke M, Heyn A, Lohmann CH, Bertrand J, Halle T, "Microstructure-dependent crevice corrosion damage of implant materials (CoCr28Mo6, TiAL6V4 and REX 734 under severe inflammatory conditions", J Biomed Mat Res – Part B, Vol 110 (7), p 1687 – 1704.

[88] Wolf S, Johannessen AC, Ellison P, Furnes O, Hallan G, Roog K, Skarstein K, Hol PJ, "Inflammatory tissue reactions around aseptically loose cemented hip prostheses: A retrieval study of the Spectron EF stem with Reflection All-Poly acetabular cup", J Biomed Mat Res – Part B, Vol 110 (7), p 1624 – 1636.

[89] Stratton-Powell AA, Williams S, Tipper JL, Redmond AC, Brockett CL, "Mixed material wear particle isolation from periprosthetic tissue surrounding total joint replacements", J Biomed Mat Res – Part B, Vol 110 (10), p 2276 – 2289.

[90] Pechancova R, Gallo J, Baron D Milde D, Antal P, Slobodova Z, Lemr K, Pluhacek T, "Detailed instight into chriomium species released from failed CoCrMo inplants: Ex vivo periprosthetic tissues study", J Biomed Mat Res – Part B, Vol 110(2), p271-283.

[91] Distefano F, Epasto G, Guglielmina E, Amata A, Mineo R, "Subsidence of a partially porous titanium lumbar cage produced by electron beam melting technology", J Biomed Mat Res – Part B, Vol 110 (3), p 590 – 598.

[92] Shopperly LK, Spinnen J, Kruger JP, Endres M, Sittinger M, Lam T, Kloke L, Dehne T, "Blends of gelatin and hyaluronic acid stratified by stereolithographic bioprinting approximate cartilaginous matrix gradients", J Biomed Mat Res – Part B, Vol 110 (10), p 2310 – 2322.

[93] Celikkin N, Mastrogiacomo S, Dou W, Heerschap A, Oosterwijk E, Walboomers XF, Swieszkowski W, "In vitro and in vivo assessment of a 3D printable gelatin methacrylate hydrogel for bone regeneration applications", J Biomed Mat Res – Part B, Vol 110 (9), p 2133 – 2145.

[94] Wu C, Zeng B, Deng J, Shen D, Wang X, Tan L, Liu X, Qiu G, "Custom design and biomechanical clinical trials of 3D-printed polyether ether ketone femonral shaft prosthesis", J Biomed Mat Res – Part B, Vol 110 (9), p 2006 – 2014.

[95] Avanzi IR, Parisi JR, Souza A, Crus MA, Martignago CCS, Ribeiro DA, Braga ARC, Renno AC, "3D-Printed hydroxyapatite scaffolds for bone tissue engineering: A systematic review in experimental animal studies", J Biomed Mat Res – Part B, Vol 110 (1), p 203-219