Editorial

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Multifunctional implantable biomaterials: integration of controlled release and sensing systems with biomaterials

Editorial

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The history of using materials inside the human body to replace or augment the damaged tissue or organs goes back to hundred years ago, such as using metals for fixation or replacement of the broken bones. The first generation of the materials used inside the human body were inert biomaterials which only physically filled the place of the damaged tissues. In the last several decades, more advanced engineered materials have been developed that show improved performance in terms of biological and mechanical properties; the emergence of bioactive and resorbable biomaterials could improve the quality of the patients' life and increase the life-time of the implants. However, since the world population is getting older, and the old population has a higher risk of tissue failure, continuing research to develop smart biomaterials with higher biocompatibility and longer life-time is still in high demand.

Combining a delivery and controlled release system with the implantable biomaterials has demonstrated highly effective results in manipulating the biomaterial-tissue interface events during implantation and enhancing the biocompatibility of them. Biodegradable polymeric carriers (e.g., polyglycolic acid (PGA) and poly anhydrides) or porous bioceramics such as silica-based mesoporous materials have been utilized in the form of matrices or reservoirs to carry and deliver the drugs, proteins or other biologically active agents.[1–3] For instance, drug-eluting vascular stents interfere with the biological events in in-stent restenosis (e.g., smooth muscle cells activation and migration at the site of the injury) via releasing anti-inflammatory agents and contribute majorly to reduce the in-stent restenosis rate which is the main limitation of vascular stents in long-term. The drugs are either directly bonded to the metallic stent or placed in a polymeric matrix coated on the stent.[4] The other example is the integration of controlled release antibiotics systems with orthopedic implants to reduce the infection rate. Infection of orthopedic implants is still the current challenge for surgeons; therefore, polymeric carriers of antibiotic are coated on the orthopedic implants to release antibiotic agents.[5] In another example, silk based-hydrogels were utilized as biomaterials that can deliver and release cytokines in order to regulate immune response of biomaterial-host tissue microenvironment.[6] However, there still remains multiple challenges for controlled releasing systems in terms of biocompatibility, target specificity and controlling the releasing rate to have a sustained and stable release in the long-term duration.

In addition to the emergence of integrated controlled release systems with implantable biomaterials, the advancement of micro and nanofabrication techniques and wireless technology, has opened the window for developing miniaturized microelectronics devices to continuously monitoring the performance of biomaterials in real time *in vivo* such as monitoring the blood flow velocity and pressure for cardiovascular implants, and real-time measurement of pressure for intraocular and brain implants. Lieber et al.[7] developed a novel structure containing nanowire nanoelectronic scaffold from silicon nanowire field-effect transistor (FET) combined with biomaterials which enables to monitor the local electrical potential of biomaterials in cardiac and neural tissue applications.[7] Many systems such as the polydimethylsiloxane (PDMS)-based strain gauge with piezo-resistive readout and wireless components have been studied as an implantable biosensor for real-time monitoring of bone remodeling process.[8] In spite of the limited number of success in monitoring parameters related to biomaterials performance *in vivo*, there still exist numerous challenges for developing implantable sensor systems that can monitor physiological conditions such that just a limited number of implantable sensors have shown the capability of real-time monitoring of molecular detection or physical parameters such as blood oxygen concentration, glucose or pressure measurement.[9,10]

A sensor system implanted *in vivo* needs to operate at the warm and humid environment of the body and under the presence of enzymes, cells and proteins. Immunological response during implantation might form a fibrosis capsule around the sensor and cause sensor failure. The other challenges include lack of selectivity in the complex biological environment, sterilization of the sensor and the need for more biocompatible materials and developing more effective methods to prevent biofouling occurrence (i.e., the accumulation of proteins and other biological matters on a biosensor surface).[11,12] The advancement in micro and nanotechnology, materials science, engineering and biotechnology provides outstanding capabilities to fabricate smart biomaterials that in addition to replace the function of the damaged tissue, enable them to regulate the surrounding biological microenvironment via releasing biologically active molecules such as proteins, cytokines and drugs and continuously monitor their performance through integration with biosensors. The combination

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of the controlled release systems and biosensors to the conventional biomaterials can develop more efficient and highly durable implants that can address their current limitations, but there are numerous challenges to develop implantable *in vivo* real-time biosensors, and effective integration of them with the biomaterials. Integration of controlled release and sensing systems with biomaterials might build a future generation of biomaterials.

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Conflict of interest

The author declares no conflict of interest.

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