

## Experience and Development. Towards Smarter Biomaterials

**Nureddin Ashammakhi\***

*Division of Plastic Surgery, Department of Surgery, Oulu University, Oulu, Finland*

**\*Corresponding Author:** Nureddin Ashammakhi, Division of Plastic Surgery, Department of Surgery, Oulu University, Oulu, Finland.

**Received:** April 14, 2017; **Published:** May 11, 2017

Man has worked long to control the surroundings and discovered various materials that can help living and life. Surgeons have used materials (biomaterials) to reconstructive, repair and regenerate tissues.

Biomaterials were first used to replace tissues, e.g. hip prosthesis and “inertness” was greatly valued to avoid inflammation, osteolysis and implant failure [1]. Much work with biomaterials appeared later for reconstructive surgery. Bioactive glass was experimented on in animals and was found to bind to bone without interfering fibrous tissue formation and the term “bonding” was used for the first time. Thus, new concept has started by Larry Hench of Florida in 1960s [2]. Later, biodegradable polymers attracted attention to develop sutures replacing natural materials, and even strong osteosynthesis devices successfully marketed in 1990s. In our research, we have worked on developing bioresorbable implants for bone regeneration [3,4] and osteosynthesis in orthopedics [5], hand [6,7], and cranio-maxillofacial [8] surgery. However, because of accompanying inflammation, osteolysis and fibrous tissue encapsulation that may lead to complications, several strategies were developed to prevent or modify such adverse tissue reactions. These include surface modification, e.g. with anti-biofouling polymer [9], or the use tissue reaction-modifying agents released from implants [10-12]. We have investigated various polymers and agents including anti-inflammatory drugs such as diclofenac sodium (DS) [10], dexamethasone (DX) [11], antios-teolytic such as the bisphosphonate (BS) [12], and antibiotics [13]. These implants are characterised by having early drug release peak and slower prolonged release at later stages. To advance this further, we developed “multicomponent” implant [14] that includes parts processed by using various techniques and have different release patterns. We have also developed an implant having several drugs, i.e. “multidrug” implant [15] that has DS, DX and BS as a model. Naturally, tissue reactions involve a multitude of events, soluble factors and reactions. Thus, there is often a need to use various active agents released from implant in orchestrated manner at various stages. We have employed possibilities offered by nanotechnology and used electrospinning to study various polymers and develop multifunctional biomimetic drug releasing nanofibres [16] that we have also combined them with macro-implants to achieve planned surface patterning and controlled cell attachment. We succeeded in achieving aligned organised attachment of chondrocytes [17]. Aligned fibres have effect on cell communication by paracrine and gap junctional means [18].

Further and more precise control of drug release from smart biomaterials remained an objective when such materials react to need in autonomous or remotely controlled way. Such bioresponsive materials [19] can act in response to chemical stimuli such as pH, NO, enzymes, glucose, etc. or physical such as magnetic field, electricity, ultrasound, temperature, light, etc., or combination of these triggers. Thus, these smart materials offer the possibility to be remotely controlled [20]. One can develop a system based on polymer responsive to pH and to glucose [21].

Implants may contain and release cells such as stem cells, erythrocytes, immune cells, bacteria or viruses may for targeted drug delivery [22]. Salmonella typhimurium (selectively targets tumours) was studied for treating prostate tumour in mice using weekly injections [23]. They can also be programmed to recognize they're in a tumour and release anti-cancer drugs which is too toxic as an injection [24]. As research and development continue, we are going to see more advanced devices in future with more precise control of their function, e.g. with on/off switchable system [25]. We will see more ... better tools for the benefit of the craft and patient.

## Bibliography

1. Ashammakhi N. "Reactions to biomaterials: the good, the bad, and ideas for developing new therapeutic approaches". *Journal of Craniofacial Surgery* 16.2 (2005): 195-196.
2. Hench LL and Paschall HA. "Direct chemical bond of bioactive glass-ceramic materials to bone and muscle". *Journal of Biomedical Materials Research* 7.3 (1973): 25-42.
3. Ashammakhi N., et al. "Absorbable membranes for bone repair: an experimental study on rabbits". *Clinical Materials* 17.3 (1994): 113-118.
4. Kellomäki M., et al. "Bioabsorbable scaffolds for guided bone regeneration and generation". *Biomaterials* 21.24 (2000): 2495-2505.
5. Waris E., et al. "Bioabsorbable fixation devices in trauma and bone surgery: current clinical standing". *Expert Review of Medical Devices* 1.2 (2004): 229-240.
6. Waris E., et al. "Self-reinforced bioabsorbable miniplates for skeletal fixation in complex hand injury: three case reports". *Journal of Hand Surgery* 29.3 (2004): 452-457.
7. Kujala S., et al. "Successful treatment of scaphoid fractures and nonunions using bioabsorbable screws: report of six cases". *Journal of Hand Surgery* 29.1 (2004): 68-73.
8. Ashammakhi N., et al. "Successful use of biosorb osteofixation devices in 165 cranial and maxillofacial cases: a multicenter report". *Journal of Craniofacial Surgery* 15.4 (2004): 692-701.
9. Yesilyurt V., et al. "Facile and Versatile Method to Endow Biomaterial Devices with Zwitterionic Surface Coatings". *Advanced Healthcare Materials* 6.4 (2017).
10. Viitanen P., et al. "Release of diclofenac sodium from polylactide-co-glycolide 80/20 rods". *Journal of Materials Science: Materials in Medicine* 17.12 (2006): 1267-1274.
11. Vapalahti K and Ashammakhi N. "Dexamethasone Loaded PLGA 80/20 Implant". Multiscale and Functionally Graded Materials Conference 2006 (FGM2006), Honolulu, Hawaii (2006).
12. Huolman R, Ashammakhi N. "New multifunctional anti-osteolytic releasing bioabsorbable implant". *Journal of Craniofacial Surgery* 18.2 (2007): 295-301.
13. Veiranto M., et al. "Novel bioabsorbable antibiotic releasing bone fracture fixation implants". *Advances in Experimental Medicine and Biology* 553 (2004): 197-208.
14. Nikkola L., et al. "Temporal control of drug release from biodegradable polymer: multicomponent diclofenac sodium releasing PLGA 80/20 rod". *Journal of Biomedical Materials Research Part B: Applied Biomaterials* 89.2 (2009): 518-526.
15. Nikkola L., et al. "Multilayer implant with triple drug releasing properties". *Journal of Biomedical Nanotechnology* 4.3 (2008): 331-338.
16. Ashammakhi N., et al. "Electrospinning: methods and development of biodegradable nanofibres for drug release". *Journal of Biomedical Nanotechnology* 5.1 (2009): 1-19.
17. Wimpenny I., et al. "Chondrogenic potential of electrospun nanofibres for cartilage tissue engineering". *Journal of Tissue Engineering and Regenerative Medicine* 6.7 (2012): 536-549.

18. Xu Y., *et al.* "Combined chemical and structural signals of biomaterials synergistically activate cell-cell communications for improving tissue regeneration". *Acta Biomaterialia* (2017).
19. Lu Y., *et al.* "Bioresponsive materials". *Nature Reviews Materials* 2 (2016).
20. Li S., *et al.* "Remote controlled drug release from multi-functional Fe<sub>3</sub>O<sub>4</sub>/GO/Chitosan microspheres fabricated by an electrospray method". *Colloids and Surfaces B: Biointerfaces* 151 (2016): 354-362.
21. Wang Y. "Glycopolymers and Glyconanomaterials for Biomedical and Environmental Applications". PhD Thesis Department of Chemical and Materials Engineering, University of Alberta, Canada (2016).
22. Yue Hu., *et al.* "Bioresponsive materials". *Nature Reviews Materials* 2 (2016).
23. Kazmierczak., *et al.* "Salmonella Bacterial Monotherapy Reduces Autochthonous Prostate Tumor Burden in the TRAMP Mouse Model". *PLoS One* 11.8 (2016): e0160926.
24. Regalado A. "Companies Bet on Designer Bacteria as New Way to Treat Disease". *Technology Review* (2016).
25. Wang H., *et al.* "Chitosan-Gated Magnetic-Responsive Nanocarrier for Dual-Modal Optical Imaging, Switchable Drug Release, and Synergistic Therapy". *Advanced Healthcare Materials* 6.6 (2017).

**Volume 6 Issue 4 May 2017**

**© All rights reserved by Nureddin Ashammakhi.**