



# Editorial: Multifunctional Bioactive Nanomaterials for Tissue Regeneration

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## Editorial on the Research Topic

### Multifunctional Bioactive Nanomaterials for Tissue Regeneration

In the biomedical field, human organ repair and regeneration represent a very important and challenging tasks (Christman, 2019). Many promising tissue regenerative strategies involve biomaterials in the form of engineered scaffolds. Conventional biomaterials are usually effective in enhancing tissue regeneration through the addition of cells and growth factors. However, recent studies have shown that biomaterials themselves can induce or support tissue regeneration without needing cells or the addition of growth factors, and these biomaterials are considered “bioactive.” Well-investigated and emerging bioactive biomaterials include bioactive glasses, bioactive ceramics, natural polymers such as proteins and polysaccharides, as well as a series of natural and synthetic biomaterials (and their combinations) with biological functions (anti-bacterial, anti-oxidant, anti-inflammatory, and anti-tumor etc.) (Lei et al., 2019; Li et al., 2019; Ranganathan et al., 2019; Schuhladen et al., 2019; Wang C. et al., 2019; Wang M. et al., 2019; Zhou et al., 2019). Relative to conventional biomaterials, nanoscale bioactive biomaterials applied in regenerative medicine have attracted increasing interest in recent years, due to their special nanoscale biological effects and enhanced capacity for tissue regeneration (Guo et al., 2018; Zhao et al., 2018; Niu et al., 2019; Wu et al., 2019; Xue et al., 2019).

Among bioactive nanomaterials, bioactive glass nanoparticles have shown special advantages including controlled biodegradation, controlled bioactive ion release, controlled multifunctional properties and high bioactivity, which render them highly attractive for both bone and soft tissue regeneration (Zheng and Boccaccini, 2017). Monodispersed bioactive glass nanoparticles with porous structure, for example, have been developed to load drugs and genes for cancer therapy and for enhancing bone formation (Xue et al., 2017; Yu et al., 2017). Through trace elements doping, it is possible to enable the tunable physicochemical and biological properties of bioactive glass nanoparticles such as photoluminescence (Xue et al., 2015), anti-bacterial (Vale et al., 2018), and anti-inflammatory capacity (Kim et al., 2019). Other bioactive nanomaterials including calcium phosphate and polymer nanoparticles have been reviewed by Loo et al. (2010) and (Torres-Giner et al., 2016).

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Although the synthesis and biomedical applications of multifunctional bioactive nanomaterials have received much progress in recent years, challenges still exist, for example: (1) control of intrinsic multifunctional properties for enhanced bioactivity and drug/gene delivery; (2) Control of bioactivity and biodegradation; and (3) understanding molecular mechanism of nanomaterials controlling tissue regeneration. This Research Topic has attracted a series of papers that show the recent advances in the synthesis and biomedical application of bioactive nanomaterials especially bioactive glass nanoparticles, and provide new insights on designing bioactive nanomaterials. In this Research Topic, Zheng et al. reported the synthesis of dispersed mesoporous bioactive glass nanoparticles with high Cu concentration by an ascorbic acid complex precursor. Zhuang et al. reviewed the advance of nanocomposite electrospun fibers in periodontal regeneration. The advances of electrospinning for designing nanomaterials were also reviewed by Wang et al. In addition, Tian et al. and Wang et al. showed the preparation and properties of hollow mesoporous bioglass nanoparticles and micro-nano bioactive composites scaffolds for bone regeneration application. Lim et al. presented a novel multifunctional

nanowire platform for highly isolation and analysis of circulating tumor specific markers.

The editors hope that the Research Topic “Multifunctional Bioactive Nanomaterials for Tissue Regeneration” will contribute to the progress of research and development activities in the field of novel bioactive nanomaterials for regenerative medicine, inspiring future work leading to the expansion of the biomedical applications of such bioactive nanomaterials.

## AUTHOR CONTRIBUTIONS

BL proposed the Research Topic and editorial and in charge of 2 manuscript for review process. AB revised the topic and editorial. XC was in charge of 1 manuscript for review process. All authors listed have made a substantial, direct and intellectual contribution to the work.

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## REFERENCES

- Christman, K. L. (2019). Biomaterials for tissue repair. *Science* 363, 340–341. doi: 10.1126/science.aar2955
- Guo, Y., Xue, Y., Niu, W., Chen, M., Wang, M., Ma, P. X., et al. (2018). Monodispersed bioactive glass nanoparticles enhance the osteogenic differentiation of adipose-derived stem cells through activating TGF- $\beta$ /Smad3 signaling pathway. *Part. Part. Syst. Charact.* 35:1800087. doi: 10.1002/ppsc.201800087
- Kim, T. H., Kang, M. S., Mandakhbayar, N., El-Fiqi, A., and Kim, H. W. (2019). Anti-inflammatory actions of folate-functionalized bioactive ion-releasing nanoparticles imply drug-free nanotherapy of inflamed tissues. *Biomaterials* 207, 23–38. doi: 10.1016/j.biomaterials.2019.03.034
- Lei, B., Guo, B., Rambhia, K. J., and Ma, P. X. (2019). Hybrid polymer biomaterials for bone tissue regeneration. *Front. Med.* 13, 189–201. doi: 10.1007/s11684-018-0664-6
- Li, Y., Li, N., Ge, J., Xue, Y., Niu, W., Chen, M., et al. (2019). Biodegradable thermal imaging-tracked ultralong nanowire-reinforced conductive nanocomposites elastomers with intrinsic efficient antibacterial and anticancer activity for enhanced biomedical application potential. *Biomaterials* 201, 68–76. doi: 10.1016/j.biomaterials.2019.02.013
- Loo, S. C., Moore, T., Banik, B., and Alexis, F. (2010). Biomedical applications of hydroxyapatite nanoparticles. *Curr. Pharm. Biotechnol.* 11, 333–342. doi: 10.2174/138920110791233343
- Niu, W., Guo, Y., Xue, Y., Chen, M., Wang, M., Cheng, W., et al. (2019). Monodisperse branched molybdenum-based bioactive nanoparticles significantly promote osteogenic differentiation of adipose-derived stem cells. *Part. Part. Syst. Charact.* 2019:1900105. doi: 10.1002/ppsc.201900105
- Ranganathan, S., Balagangadharan, K., and Selvamurugan, N. (2019). Chitosan and gelatin-based electrospun fibers for bone tissue engineering. *Int. J. Biol. Macromol.* 133, 354–364. doi: 10.1016/j.ijbiomac.2019.04.115
- Schuhladen, K., Roether, J. A., and Boccaccini, A. R. (2019). Bioactive glasses meet phytotherapeutics: the potential of natural herbal medicines to extend the functionality of bioactive glasses. *Biomaterials* 2019:119288. doi: 10.1016/j.biomaterials.2019.119288
- Torres-Giner, S., Pérez-Masiá, R., and Lagaron, J. M. (2016). A review on electrospun polymer nanostructures as advanced bioactive platforms. *Polym. Eng. Sci.* 56, 500–527. doi: 10.1002/pen.24274
- Vale, A. C., Carvalho, A. L., Barbosa, A. M., Torrado, E., Mano, J. F., and Alves, N. M. (2018). Novel antibacterial and bioactive silicate glass nanoparticles for biomedical applications. *Adv. Eng. Mater.* 20:1700855. doi: 10.1002/adem.201700855
- Wang, C., Wang, M., Xu, T., Zhang, X., Lin, C., Gao, W., et al. (2019). Engineering bioactive self-healing antibacterial exosomes hydrogel for promoting chronic diabetic wound healing and complete skin regeneration. *Theranostics* 9:65. doi: 10.7150/thno.29766
- Wang, M., Guo, Y., Xue, Y., Niu, W., Chen, M., Ma, P. X., et al. (2019). Engineering multifunctional bioactive citric acid-based nanovectors for intrinsic targeted tumor imaging and specific siRNA gene delivery *in vitro/in vivo*. *Biomaterials* 199, 10–21. doi: 10.1016/j.biomaterials.2019.01.045
- Wu, J., Zheng, K., Huang, X., Liu, J., Liu, H., Boccaccini, A. R., et al. (2019). Thermally triggered injectable chitosan/silk fibroin/bioactive glass nanoparticle hydrogels for in-situ bone formation in rat calvarial bone defects. *Acta Biomater.* 91, 60–71. doi: 10.1016/j.actbio.2019.04.023
- Xue, Y., Du, Y., Yan, J., Liu, Z., Ma, P. X., Chen, X., et al. (2015). Monodisperse photoluminescent and highly biocompatible bioactive glass nanoparticles for controlled drug delivery and cell imaging. *J. Mater. Chem. B* 3, 3831–3839. doi: 10.1039/C5TB00204D
- Xue, Y., Guo, Y., Yu, M., Wang, M., Ma, P. X., and Lei, B. (2017). Monodispersed bioactive glass nanoclusters with ultralarge pores and intrinsic exceptionally high miRNA loading for efficiently enhancing bone regeneration. *Adv. Healthc. Mater.* 6:1700630. doi: 10.1002/adhm.201700630
- Xue, Y., Zhang, Z., Niu, W., Chen, M., Wang, M., Guo, Y., et al. (2019). Enhanced physiological stability and long-term toxicity/biodegradation *in vitro/in vivo* of monodispersed glycerolphosphate-functionalized bioactive glass nanoparticles. *Part. Part. Syst. Charact.* 2019:1800507. doi: 10.1002/ppsc.201800507
- Yu, M., Xue, Y., Ma, P. X., Mao, C., and Lei, B. (2017). Intrinsic ultrahigh drug/miRNA loading capacity of biodegradable bioactive glass nanoparticles toward highly efficient pharmaceutical delivery. *ACS Appl. Mater. Interfaces* 9, 8460–8470. doi: 10.1021/acsami.6b13874
- Zhao, F., Lei, B., Li, X., Mo, Y., Wang, R., Chen, D., et al. (2018). Promoting *in vivo* early angiogenesis with sub-micrometer strontium-contained bioactive microspheres through modulating macrophage phenotypes. *Biomaterials* 178, 36–47. doi: 10.1016/j.biomaterials.2018.06.004

- Zheng, K., and Boccaccini, A. R. (2017). Sol-gel processing of bioactive glass nanoparticles: a review. *Adv. Colloid Interface Sci.* 249, 363–373. doi: 10.1016/j.cis.2017.03.008
- Zhou, L., Xi, Y., Xue, Y., Wang, M., Liu, Y., Guo, Y., et al. (2019). Injectable self-healing antibacterial bioactive polypeptide-based hybrid nanosystems for efficiently treating multidrug resistant infection, skin-tumor therapy, and enhancing wound healing. *Adv. Funct. Mater.* 2019:1806883. doi: 10.1002/adfm.201806883

**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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