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The Interplay between Hemostasis and Immune Response in Biomaterial Development for Osteogenesis

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Treatment of large bone defects, especially bone non-union remains a clinical challenge. The gold standard bone substitute is still the autologous bone graft and is difficult to be replaced by synthetic biomaterials, suggesting that strategies should be made to improve the material for functional bone regeneration. Recent studies have revealed that hematoma, the first tissue structure formed at the bone injury site, plays an indispensable role in bone healing. Hematoma consists of fibrin clot, infiltrated immune cells, and tissue progenitor cells, which not only bridge the bone defect, but also provide a microenvironment for the interplay between hemostasis and immune systems. Previous studies have found that an ideal fibrin structure with proper fiber thickness and density could benefit progenitor cell infiltration and differentiation, and biomaterial implantation could affect bone healing by altering fibrin structure. Meanwhile, immunoregulation plays an indispensable role in bone healing, especially, materials inducing a shift from inflammatory to anti-inflammatory phenotypes in immune cells showed enhanced osteoinductivity. The balance between coagulation—inflammation and anti-coagulation—anti-inflammation plays a determinant role in not only fibrin structure but also the fibrinolysis process, during which the inflammation could be gradually "quenched" and thereby generating an ideal microenvironment for the following bone regeneration. Therefore, it is essential to develop biomaterial targeting the hemostasis-immune interplay.

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