Editorial

Prospect of mesenchymal stem cells in bone tissue engineering

A fracture with substantial bone defect is a challenging problem in orthopedic surgery. Before the stem cell era, attempts to fill the defects may use autologous bone grafting to avoid rejection problems. However, for large defects the bone graft available may not be sufficient. Moreover, using bone graft may cause donor site morbidity. Therefore, bone graft substitutes in the form of either demineralized allograft bone matrix or calcium-based materials are highly necessary.[1]

In this issue, Kholinne et al. showed that mesenchymal stem cells can survive on a calcium-based material, i.e. hydroxyapatite calcium sulphate in vitro. Therefore, the material may be used as a scaffold in bone tissue engineering,[2] either in vivo or ex-vivo. However, the production of mesenchymal stem cells to be used in bone tissue engineering needs to fulfill some quality control requirements that meet the good manufacturing practices. The protocols to culture and expand the mesenchymal stem cells need to be standardized and tested in different laboratories to ensure that the results are reproducible, and all steps should use xeno-free materials.[3]

In the article by Kholine et al., the mesenchymal stem cells were cultured in a medium containing low glucose Dulbeco's modified Eagle's medium (DMEM) without explicitly mentioning the use of fetal bovine serum (FBS) supplementation.[1] However, they possibly used FBS containing medium, as was used in their group's previous study.[4] Mesenchymal stem cells that are cultured in FBS containing medium are not suitable to be used in patients, as FBS contains xeno-proteins that will be internalized by the cultured cells. Internalized xeno-proteins will remain on the cells, though the cells have been washed and the culture medium has been replaced by xeno-free medium. The xeno-protein containing cells will pose rejection problems, when they are used in patients. Moreover, FBS may transmit zoonosis such as the mad cow disease.[5, 6]

Commercial media that contain various growth factors to replace FBS are available, but the cost is much more higher compared to conventional media supplemented by FBS. Therefore, translation of bone tissue engineering using mesenchymal stem cells to bedside needs cheaper FBS substitute. Various FBS substitutes have been tested, such as human AB serum and platelet rich human AB plasma.[6-8]

Platelets contain various growth factors, such as platelet derived growth factor (PDGF), transforming growth factor β1 (TGF-β1), basic fibroblast growth factor (bFGF), insulin growth factor (IGF) and epidermal growth factor (EGF), which are important for the growth of mesenchymal stem cells in culture.[6] The growth factors can be released using various methods, i.e. repeated abrupt freezing and thawing,[6,8] and activation either by thrombin,[6-8] or thrombin receptor activated peptide (TRAP).[8] A study compared the various methods to release the growth factors from platelets, and showed that thombin activated method as the best.[8] Further, human AB serum and thrombin activated platelet rich plasma showed good result for adipose tissue derived mesenchymal stem cells,[8] while thrombin activated platelet rich human AB plasma is the best for bone marrow derived stem cells.[7]

In conclusion, mesenchymal stem cells are very promising for bone tissue engineering, but to get a safe and effective method, there is still a long way to go.

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