Claims

[Claim 1] A method of producing an osteoinductive bone regeneration material comprising a targetable bone morphogenetic protein-2 (tBMP-2)~~formed of a plurality of electrospun biodegradable fibers~~, comprising:
preparing a fibrous scaffold material formed of ~~the~~ a plurality of electrospun biodegradable fibers, ~~wherein the plurality of electrospun biodegradable fibers are 40-320 μm in diameter and 5-20mm in length,~~ wherein
the plurality of electrospun biodegradable fibers entangle with each other to form a cotton-wool like structure having inter-fiber spaces forming a microenvironment for cell growth therein,
the electrospun biodegradable fibers comprise 43-60 vol% β-TCP particles distributed in the electrospun biodegradable fibers such that a portion of the β-TCP particles is partially exposed on a surface of the electrospun biodegradable fibers without being coated by a polymer layer, and
~~immersing the fibrous scaffold in a solution containing BMP-2~~contacting the fibrous scaffold material with tBMP-2 contained in an acetate buffer solution so that the tBMP-2 is bound to the β-TCP particles exposed on the surface of the fibers forming the microenvironment throughout the cotton-wool like structure to produce the osteoinductive bone graft,
wherein an area of binding site for tBMP-2 on β-TCP particles exposed on a surface of the electrospun biodegradable fibers is adjusted by an amount of the β-TCP particles contained in the electrospun biodegradable fibers.

[Claim 2] The method of claim 1, wherein diameters of the plurality of electrospun biodegradable fibers are ~~70-250~~40-320 μm.

[Claim 3] The method of claim 1 or 2, wherein lengths of the plurality of electrospun biodegradable fibers are ~~4-10~~5-20 mm.

[Claim 4] The method of ~~claim 1~~any one of the preceding claims, wherein the plurality of electrospun biodegradable fibers comprise PLGA

[Claim 5] The method of ~~claim 1~~any one of the preceding claims, wherein diameters of the β-TCP particles are 2-5 μm.

[Claim 6] ~~The method of claim 1, wherein the BMP-2 is targetable BMP-2.~~ The method of any one of the above claims, wherein the tBMP-2 comprises a β-TCP binding peptide fused to BMP-2, the β-TCP binding peptide has the amino acid sequence selected from the group consisting of LLADTTHHRPWT (SEQ ID NO: 1), GQVLPTTTPSSP (SEQ ID NO: 2), VPQHPYPVPSHK (SEQ ID NO: 3), HNMAPATLHPLP (SEQ ID NO: 4), QSFASLTNPRVL (SEQ ID NO: 5), HTTPTTTYAAPP (SEQ ID NO: 6), QYGVVSHLTHTP (SEQ ID NO: 7), TMSNPITSLISV (SEQ ID NO: 8), IGRISTHAPLHP (SEQ ID NO: 9), MNDPSPWLRSPR (SEQ ID NO: 10), QSLGSMFQEGHR (SEQ ID NO: 11), KPLFTRYGDVAI (SEQ ID NO: 12), MPFGARILSLPN (SEQ ID NO: 13), QLQLSNSMSSLS (SEQ ID NO: 14), TMNMPAKIFAAM (SEQ ID NO: 15), EPTKEYTTSYHR (SEQ ID NO: 16), DLNELYLRSLRA (SEQ ID NO: 17), DYDSTHGAVFRL (SEQ ID NO: 18), SKHERYPQSPEM (SEQ ID NO: 19), HTHSSDGSLLGN (SEQ ID NO: 20), NYDSMSEPRSHG (SEQ ID NO: 21), and ANPIISVQTAMD (SEQ ID NO: 22). VIGESTHHRPWS (SEQ ID NO: 23), IIGESSHHKPFT (SEQ ID NO: 24), GLGDTTHHRPWG (SEQ ID NO: 25), and ILAESTHHKPWT (SEQ ID NO: 26).

~~[Claim 7]~~ ~~An osteoinductive bone regeneration material produced by the method of claims 1-6.~~

~~[Claim 8]~~ ~~A fibrous scaffold material for osteoinductive bone regeneration material comprising a plurality of electrospun biodegradable fibers,~~
~~wherein the plurality of electrospun biodegradable fibers is 40-320 μm in diameter and 5-20 mm in length,~~
~~wherein the plurality of electrospun biodegradable fibers are entangled with each other to form a cotton-wool like structure having inter-fiber spaces forming a microenvironment for cell growth therein,~~
~~wherein the electrospun biodegradable fibers comprise 45-60 vol% β-TCP particles distributed in the electrospun biodegradable fibers such that a portion of the β-TCP particles is partially exposed on a surface of the electrospun biodegradable fibers without being coated by a polymer layer,~~
~~wherein an area of binding site for BMP-2 on β-TCP particles exposed on a surface of the electrospun biodegradable fibers is adjusted by an amount of the β-TCP particles contained in the electrospun biodegradable fibers.~~

[Claim 9] The fibrous scaffold material of claim 8, wherein diameters of the plurality of electrospun biodegradable fiber are 70-250 μm.

[Claim 10] The fibrous scaffold material of claim 8, wherein lengths of the plurality of electrospun biodegradable fibers are 4-10 μm.

[Claim 11] The fibrous scaffold material of claim 8, wherein the electrospun biodegradable fibers comprise PLGA.

[Claim 12] The fibrous scaffold material of claim 8, wherein diameters of the β-TCP particles are 2-5μm.

[Claim 13] The fibrous scaffold material of claim 8, wherein the β-TCP particles are bound to BMP-2.

[Claim 14] The fibrous scaffold material of claim 13, wherein the BMP-2 is targetable BMP-2.

[Claim 15] The fibrous scaffold material of any one of the previous claims, wherein the BMP-2 comprises any one of SEQ ID NOS: 1-38, or a combination or two more sequences from SEQ ID NOS: 1-38.

[Claim 16] A composition comprising:
a scaffold comprising about 60 wt% to about 80 wt% calcium containing compound, and
a targetable BMP-2 comprising (i) VIGESTHHRPWS (SEQ ID NO: 23), (ii) IIGESSHHKPFT (SEQ ID NO: 24), (iii) GLGDTTHHRPWG (SEQ ID NO: 25), (iv) ILAESTHHKPWT (SEQ ID NO: 26), or (v) a combination of two more of (i)-(iv).

[Claim 17] The composition of claim 16, wherein the targetable BMP-2 comprises VIGESTHHRPWS (SEQ ID NO: 23).

[Claim 18] The composition of claim 16 or claim 17, wherein the targetable BMP-2 comprises IIGESSHHKPFT (SEQ ID NO: 24).

[Claim 19] The composition of any one of claims 16-18, wherein the targetable BMP-2 comprises GLGDTTHHRPWG (SEQ ID NO: 25).

[Claim 20] The composition of any one of claims 16-19, wherein the targetable BMP-2 comprises ILAESTHHKPWT (SEQ ID NO: 26).

[Claim 21] The composition of any one of claims 16-20, wherein the targetable BMP-2 further comprises LLADTTHHRPWT (SEQ ID NO: 1).

[Claim 22] The composition of any one of claims 16-21, wherein the targetable BMP-2 comprises QAKHKQRKRLKSSCKRHPLYVDFSDVGWNDWIVAPPGYHAFYCHGECPFPLADHLNSTNHAIVQTLVNSVNSKIPKACCVPTELSAISMLYLDENEKVVLKNYQDMVVEGCGCR (SEQ ID NO: 32).

[Claim 23] The composition of any one of claims 16-22, wherein the targetable BMP-2 comprises any one of SEQ ID NOS: 33-38.

~~[Claim 24]~~ ~~The composition of any one of claims 16-22, wherein the targetable BMP-2 comprises SEQ ID NO: 33.~~

~~[Claim 25]~~ ~~The composition of any one of claims 16-24, wherein the calcium containing compound comprises calcium phosphate, vaterite, or calcium phosphate and vaterite.~~

~~[Claim 26]~~ ~~The composition of any one of claims 16-24, wherein the calcium containing compound comprises beta-tricalcium phosphate (β-TCP).~~

~~[Claim 27]~~ ~~The composition of claim 26, wherein the β-TCP is present in the scaffold at about 60 wt% to about 80 wt% of the scaffold.~~

~~[Claim 28]~~ ~~The composition of claim 27, wherein the β-TCP is present in the scaffold at about 70 wt%.~~

~~[Claim 29]~~ ~~The composition of claim 26, wherein the β-TCP is present in the scaffold at about 30 wt% to about 50 wt% of the scaffold.~~

~~[Claim 30]~~ ~~The composition of claim 29, wherein the β-TCP is present in the scaffold at about 40 wt%.~~

~~[Claim 31]~~ ~~The composition of any one of claims 16-26 or claims 29-30, wherein the calcium containing compound comprises vaterite.~~

~~[Claim 32]~~ ~~The composition of claim 31, wherein the vaterite is present in the scaffold at about 20 wt% to 40 wt% of the scaffold.~~

~~[Claim 33]~~ ~~The composition of claim 32, wherein the vaterite is present in the scaffold at about 30 wt%.~~

~~[Claim 34]~~ ~~The composition of any one of claims 25 or 31-33, wherein the vaterite comprises silicon-doped vaterite (SiV).~~

~~[Claim 35]~~ ~~The composition of any one of claims 16-34, wherein the scaffold comprises a biodegradable polymer.~~

~~[Claim 36]~~ ~~The composition of any one of claims 16-34, wherein the scaffold comprises poly(lactic-co-glycolic acid) (PLGA).~~

~~[Claim 37]~~ ~~The composition of claim 36, wherein the scaffold comprises about 20 wt% to about 40 wt% PLGA.~~

~~[Claim 38]~~ ~~The composition of claim 37, wherein the scaffold comprises about 30 wt% PLGA.~~

~~[Claim 39]~~ ~~A method of treating a subject in need thereof, comprising administering to the subject a composition of any previous claim.~~

~~[Claim 40]~~ ~~The method of claim 38, wherein the subject has a bone defect.~~