ARTICLE

Electronic Supplementary Material for

Mixed-Valence Vanadium-Doped Mesoporous Bioactive Glass for the Treatment of Tumor-related Bone Defects

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Supplementary Note 1 | Cytotoxicity of V-doped MBG *in vitro*

Firstly, given the potential toxicity of high concentrations of vanadium species, the cytotoxic effects of single tetravalent or pentavalent vanadium at different concentrations on normal cells (including L929 and BMSCs) were identified using CCK-8 assay. **Figure S4A and S4B** summarized the cytotoxic effects of varying concentrations of sodium metavanadate (Na_3VO_4) and vanadium tetrafluoride (VF_4) on L929 and BMSCs, respectively. The results indicated that both V(V) and V(IV) exhibited no significant cytotoxicity at concentrations ≤ 5.0 μg/mL in both L929 and BMSCs, and put up the most pronounced proliferative promotion around 2.5 μg/mL in BMSCs.

Moreover, the potential cytotoxic effects of the released species from V(IV/V)-MBG on normal cells were evaluated with a series of V(IV/V)-MBG extracts diluted in different proportions. The results, as shown in **Figure S4C and S4D**, indicated that the cell survival rate of L929 and BMSCs remained above 80% when the solid-liquid ratio of V(IV/V)-MBG-LA or V(IV/V)-MBG-ASA extracts was greater than 1/25. This suggested that V(IV/V)-MBG did not exhibit cytotoxic effects on these cells at these solid-liquid ratios. Notably, it was observed that BMSCs exhibited a proliferative effect at a dilution of 1/25 of the extract.

Supplementary Note 2 | *In vivo* degradation of porous scaffolds in rats

The degradation performance of scaffolds after implantation was analyzed based on H&E staining, where the PLGA scaffolds were visualized as white region, as shown in **Figure 11**. During implantation, all groups presented degradation trend, where those incorporating MBG and V-MBG degraded faster. Correspondingly, the regenerated tissues grew into the degraded regions during scaffolds degradation, even with the tumor growth in P0 and P1 groups. Thus, the developed composites exhibited good biocompability and adaptability during tissue regeneration.

Figure S1. X-ray Photoelectron Spectroscopy (XPS) spectra of V(V)-MBG

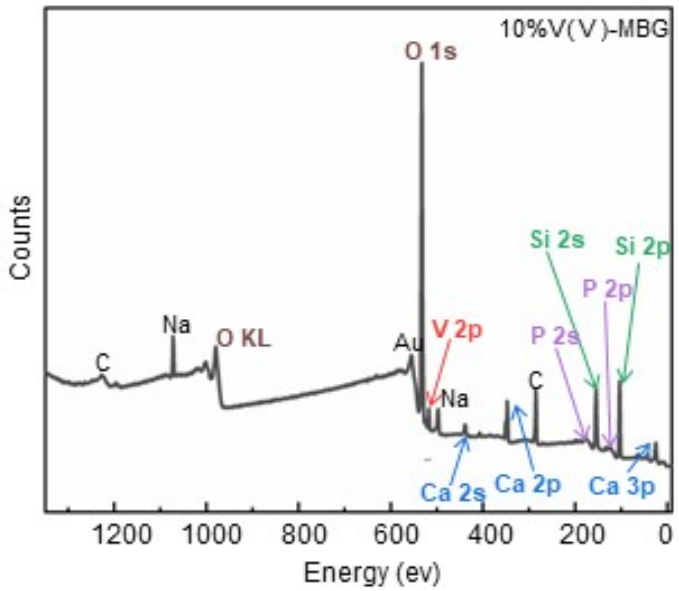

Figure S2. Comparison of the changes in the V 2p spectrum with the addition of different amounts of reducing agent. (**A**)(**B**)(**C**) XPS spectrum of the V2p region in 10%V(IV/V)-MBG-(10%,20%,40%) LA; (**D**)(**E**)(**F**) XPS spectrum of the V2p region in 10%V(IV/V)-MBG-(5%,10%,40%) ASA.

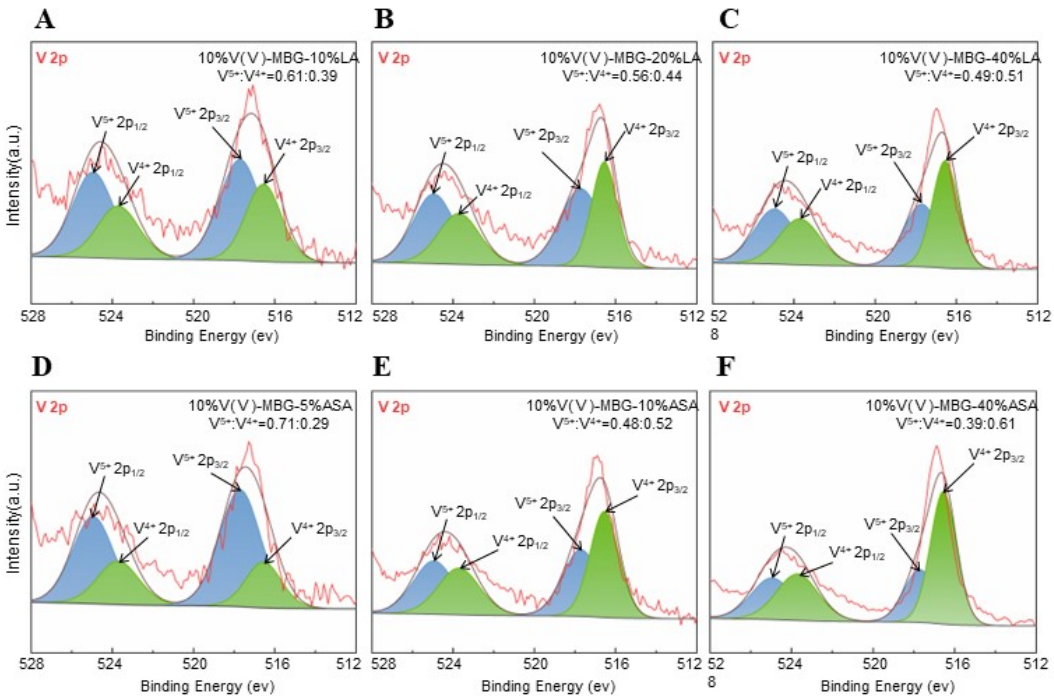

Figure S3. V is distributed in a uniform manner in the silicon-oxygen network structure of MBG. Elemental distribution maps of 1%V(V)-MBG(i), 1%V(IV/V)-MBG-LA(ii), and 1%V(IV/V)-MBG-ASA(iii), respectively.

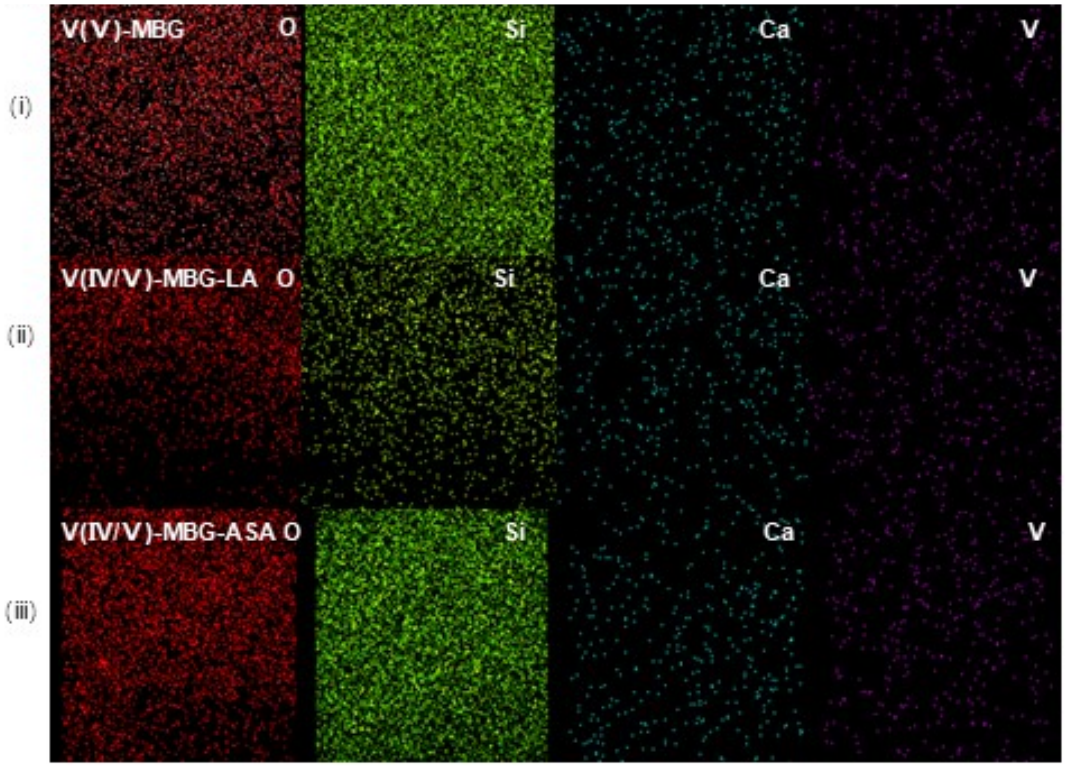

Figure S4. Changes in pH values of SBF after soaking mesoporous 1%V(Ⅴ)-MBG, 1%V(Ⅳ/Ⅴ)-MBG-LA and 1%V(Ⅳ/Ⅴ)-MBG-ASA samples at various time points.

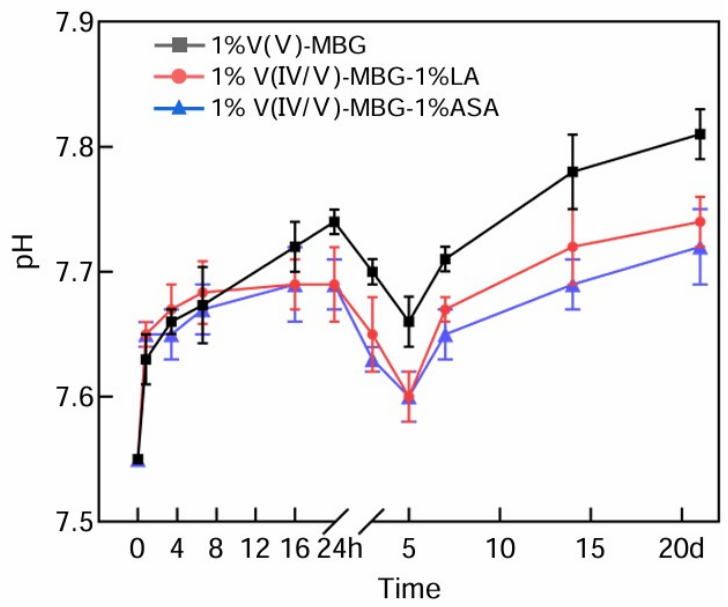

Figure S5. Morphology of the second-generation cultured BMSCs. The cells exhibited a colony-like distribution, growing uniformly with a primarily elongated spindle-shaped morphology.

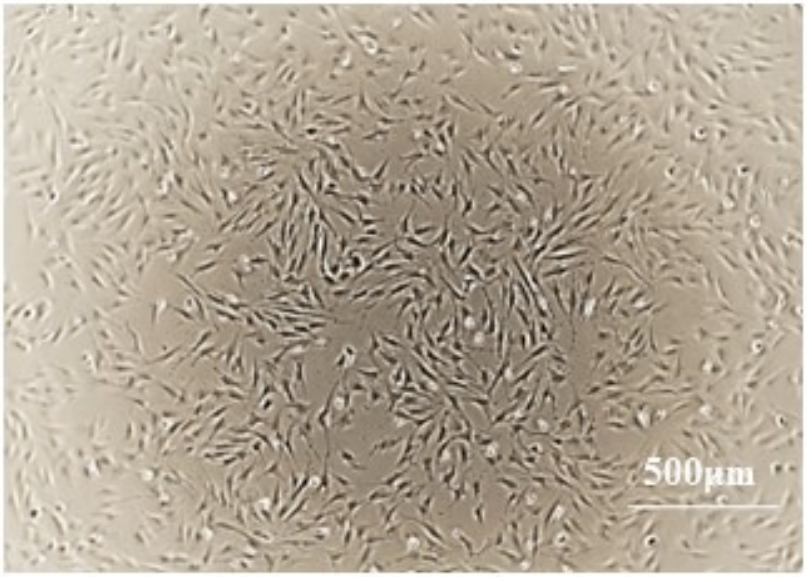

Figure S6 Cytotoxic effect: toxic: effects of tetravalent and pentavalent vanadium species on different normal cells: (**A**) L929; (**B**) BMSCs; toxic effects of different solid-liquid ratios of V(IV/V)-MBG extracts on different normal cells: (**C**) L929; (**D**) BMSCs.

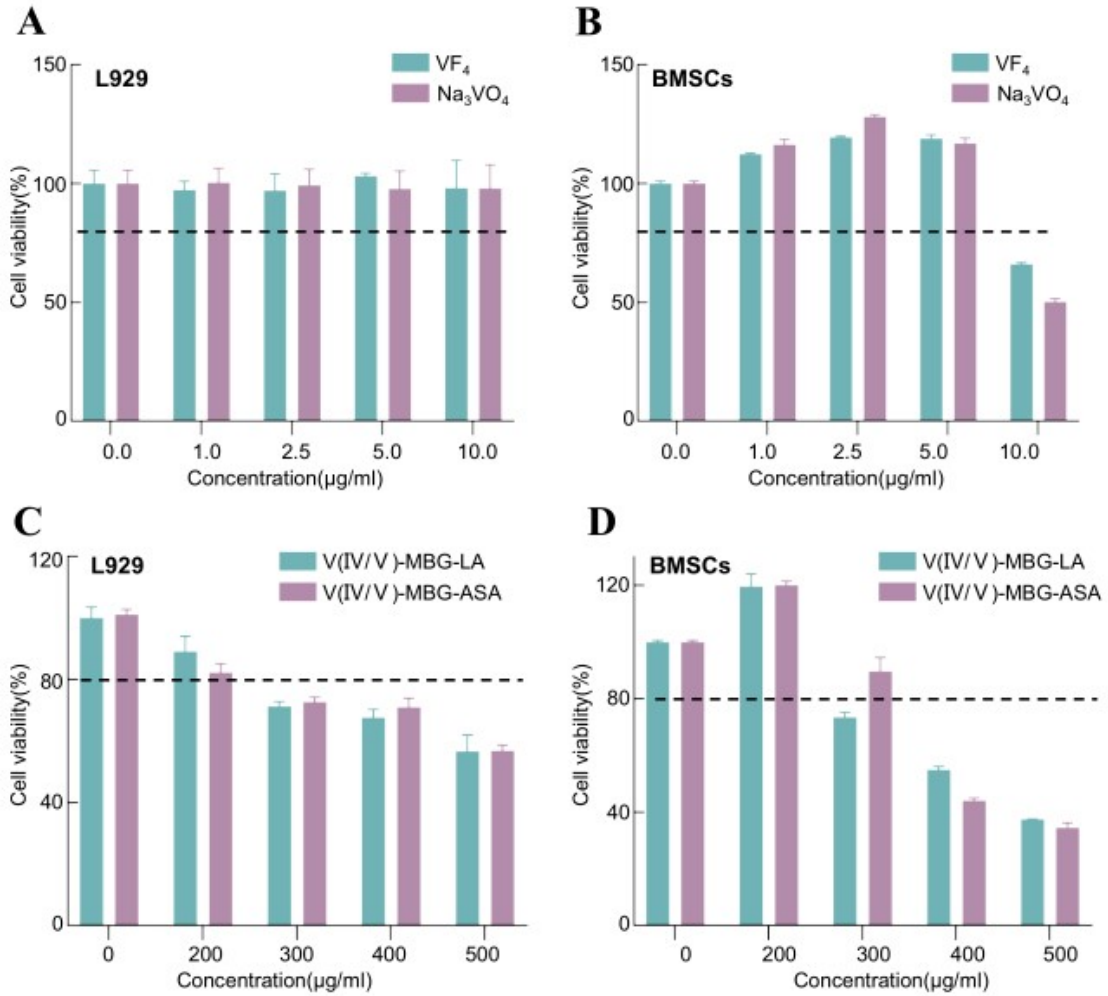

Figure S7. MB oxidative degradation by hydroxyl radical generated at different pH in V(Ⅴ)- MBG group. These results suggested that the presence of V(Ⅴ) alone was insufficient to effectively induce the generation of hydroxyl radical.

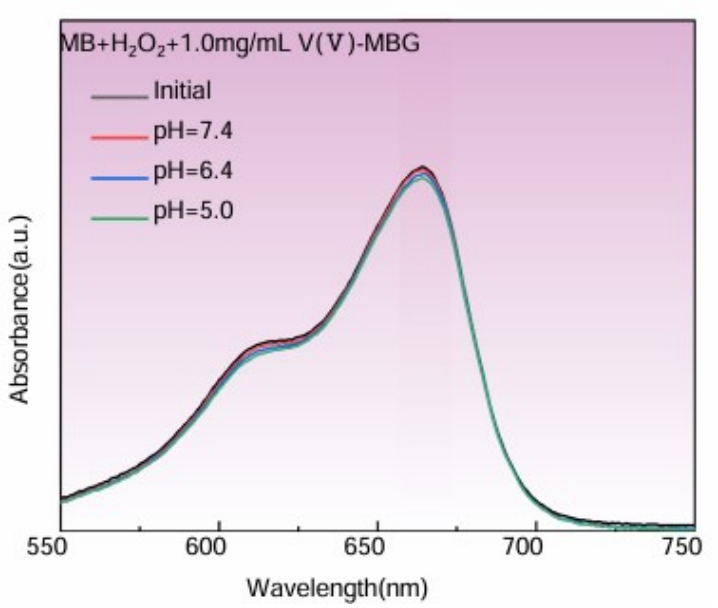

Figure S8. The MDA content in UMR-106 cells after 24 hours of incubation with V(IV/V)-MBG extracts.

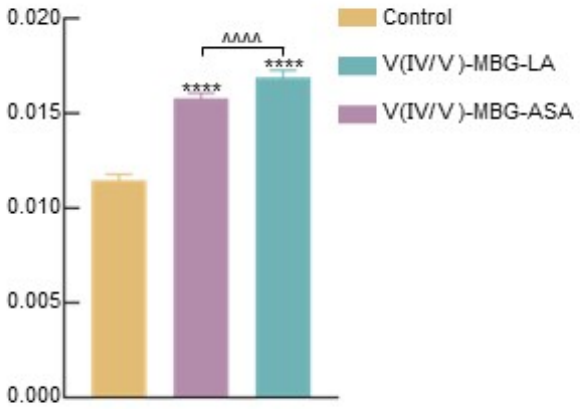

Figure S9. Quantitative counting of tartrate-resistant acid phosphatase (TRAP). There were more TRAP-positive cells in the C0 , P1 and P2 groups, while the number of TRAP-positive cells with mature morphology was lower in the P3 and P4 groups.

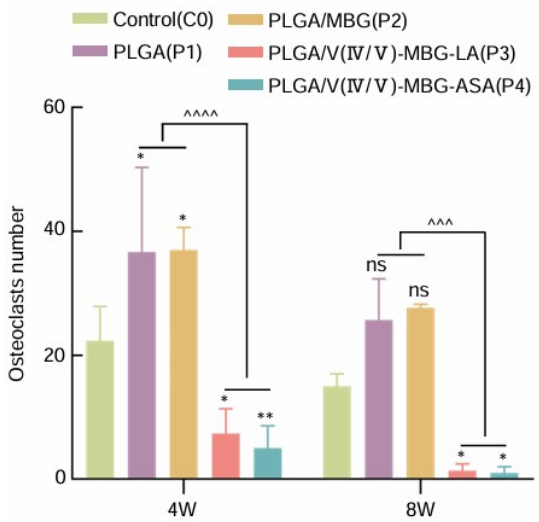

Figure S10. The toxicity of scaffolds with vanadium ion was first examined in the organs of heart, liver, spleen, lung and kidney (Fig. S11A(i-v)) for C0 group, Fig. S11B(i-v) for P1 group, Fig. S11C(i-v) for P2 group, Fig. S11D(i-v) for P3 group, Fig. S11E(i-v) for P4 group). There are no apparent differences in H&E staining images among each group, indicating toxicity of scaffolds with V ions is negligible.