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Supplementary Materials

Association Between Serum Zinc and Calcification Propensity (T_{50}) in Patients With Type 2 Diabetes Mellitus and In Vitro Effect of Exogenous Zinc on T_{50}

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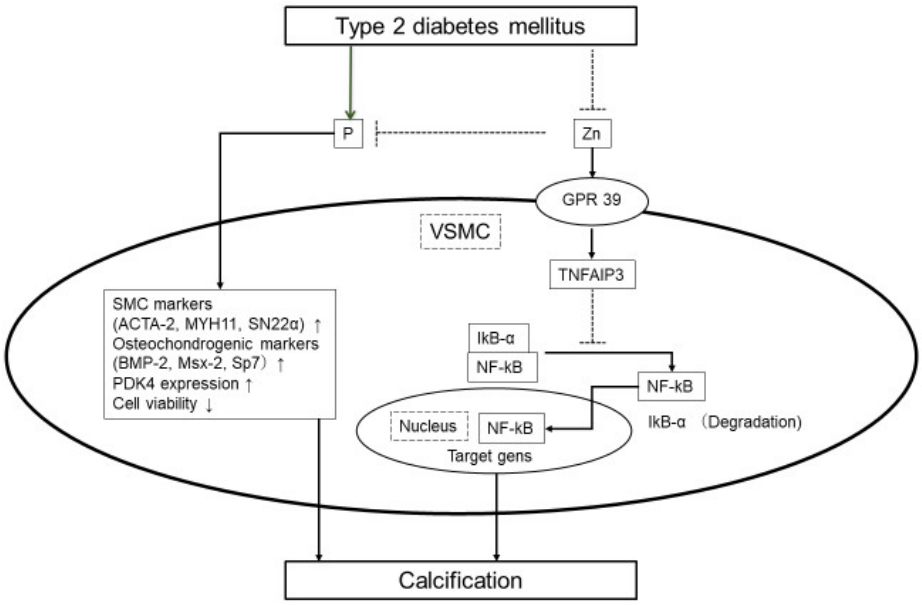
Supplemental Table S1. Clinical characteristics of the pooled serum from healthy volunteers and patients with hemodialysis.

Measurement	Pooled Sample from Healthy Volunteers	Pooled Sample from Hemodialysis Patients
Creatinine (mg/dL)	0.83	9.92
Serum albumin (g/dL)	4.7	3.5
Corrected calcium (mg/dL)	9.6	9.4
Phosphate (mg/dL)	3.2	5.7
Magnesium (mg/dL)	2.4	2.6
Zinc (μg/dL)	105	66



Supplemental Figure S1. Schematic illustration of zinc and calcification.

Type 2 diabetes mellitus induces hypozincemia and hyperphosphatemia. In vascular smooth muscle cells (VSMCs), exposure to elevated phosphate levels induces NF-kB activation. That active NF-kB transcription factor translocates to the nucleus and induces target gene expression to promote osteo/chondrogenic trans-differentiation of VSMCs, leading to calcification. Zinc supplementation may increase zinc finger protein TNF-α-induced protein 3 (TNFAIP3) levels by upregulating zinc-sensing receptor ZnR/GPR39-dependent TNFAIP3 gene expression. Increased TNFAIP3 inhibits NF-kB activation and osteo-/chondrogenic reprograming, resulting in suppression of phosphate-induced VSMC calcification [38].

Zinc also inhibits osteochondrogenic phenotypic switch of VSMCs, reflected by a lower phosphate uptake, thus decreasing the osteochondrogenic gene expressions of Msx-2, BMP-2, and Sp7, as well inducing loss of smooth muscle cell-specific markers. Zinc preserves the phosphorylation state of Runx2 and Ser451, decreases pyruvate dehydrogenase kinase 4 (PDK4) level, and restores cell viability [51].