FIGS. 9a and 9b show the results of administering a bisphosphonate-conjugated imaging agent to detect osteogenic activity, after administering sitagliptin to eNOS-/-•mice.

FIG. 10a shows the results of VK staining of the whole body (upper raw) and aortic valve (lower raw) of eNOS-/- mice after administration of sitagliptin to the eNOS-/-•mice; and FIG. 10b graphically shows a VK positive area.

FIG. 11 shows that osteoblast differentiation of human valvular interstitial cells (hVICs) is inhibited by treatment with DPP-4.

BEST MODE FOR CARRYING OUT THE INVENTION

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains. Generally, the nomenclature used herein and the experiment methods, which will be described below, are those well known and commonly employed in the art.

The present disclosure is directed to a composition for prevention and treatment of valvular calcification, which includes a DPP-4 (Dipeptidyl peptidase-4) inhibitor, and to a method for treatment of valvular calcification using the composition for prevention and treatment of valvular calcification.

In the present disclosure, the DPP-4 (Dipeptidyl peptidase-4) is also designated as a cluster of differentiation 26 (CD26), and is known as a protein involved in immunomodulation, apoptosis, signal transduction, and the like.

In the composition of the present disclosure, the DPP-4 inhibitor may be either an inhibitor for inhibiting the expression of a DPP-4 nucleotide sequence or an inhibitor for

similar to those of VSMCs, and are capable of differentiating into osteoblasts.

Using human VICs, the role of DPP-4 in osteoblast differentiation was analyzed.

Human VICs were isolated from aortic valve leaflets according to a conventional cell isolation method, and VIC cells at passage 2 to 10 were used. The VIC cells were incubated with DPP-4 (R & D), sitagliptin or DETA-NONOate (Enzo Life Sciences).

As a result, as shown in FIG. 11, DPP-4 treatment increased the osteogenic ability of VICs, and this phenomenon was eliminated by sitagliptin treatment.

To examine the relation of DPP-4 with disease activity, plasma DPP-4 levels in CAVD patients were analyzed. Patients with rheumatic aortic valve diseases and patients administered with a DPP-4 inhibitor were excluded from the analysis.

As a result, the DPP-4 level in the CAVD patients was higher than that in normal persons (Table 1).

Table 1: Clinical characteristics of aortic valve disease patients

	Avpathology (-) (n=111)	AV pathology +) (n=48)	*p* value
Age, y [a]	60±41	78±15	<0.001
Male, n[b]	69 (62)	20 (42)	0.017

Body surface area, m^2	1.7±0.4	1.54±0.35	<0.001
Systolic blood pressure, mmHg	118±38	123±45	0.079
Diastolic blood pressure, mmHg	71±32	66±33	0.023
Hypertension, n	53 (48)	37 (77)	0.001
Diabetes, n	23 (21)	12 (25)	0.550
Dyslipidemia, n	53 (48)	25 (52)	0.616
Renal insufficiency, n	3 (3)	8 (17)	0.001
Coronary artery disease, n	56 (50)	19 (40)	0.208
Previous stroke, n	15 (14)	9 (19)	0.410
Hemoglobin, g/dL	13.6±4.5	11.8±6.7	<0.001
Creatinine, mg/dL	0.95±6.26	1.48±7.76	0.006
Cholesterol, mg/dL	165±155	158±77	0.316
Aortic Vmax (peak velocity), m/s	1.4±1.1	4.6±2.1	<0.001

The DPP-4 level was 34% higher in CAVD patients with calcification than in patients with no calcification, and DPP-4 having the ability to degrade activated protein also increased in the CAVD patients. This suggests that the DPP-4 circulation level is related to the severity of CAVD patients (Table 2).

Table 21: Clinical characteristics of CAVD patients determined by CT calcium score

	Group I	Group II	*p*