## Supplementary Table 1.

Tumor incidence	week 2	week 3	week 4
Collagen	1/10*	2/10	2/10
Vossicle	2/20	4/20	4/20
Mineralized-collagen	0/10	2/10	2/10

LNCaP<sup>luc</sup> cells were implanted s.c. in 4-week-old male nude mice at 250,000 cells/implant in collagen, mineralized-collagen or vossicle scaffolds as described in Materials and Methods. *In vivo* bioluminescent imaging was carried out weekly, after tumor implantation, at the University of Michigan Small Animal Imaging Resource facility, to detect tumorigenesis. \*1 out of a total of 10. There was no difference in incidence among groups.

## Supplementary Fig. 1.



Vossicle, collagen matrices and mineralized-collagen were implanted with 500,000 C4-2b cells s.c. in the backs of 4-week-old athymic mice. ZA or vehicle was administered twice per week for 4-weeks as described in Materials and Methods. Tumor size in vossicles, but not in collagen matrices treated with ZA, was significantly decreased. (n=5, \*p<0.05)

## Supplementary Fig. 2.



ACE-1<sup>luc</sup> cells were seeded at 10,000/well in 12-well plates and cultured in RPMI 1640 media contain 1% FBS and 0.5mM or 2.5mM CaCl<sub>2</sub>. On the indicated days, the luciferase activity of cell lysates, as a reflection of cell number, was determined with the dual luciferase reporter assay system (Promega, Madison, WI) and a Monolight 2010 luminometer (BD-Pharmingen, San Diego, California). Higher luciferase activity of cells cultured with 2.5mM CaCl<sub>2</sub> was found on day 3 and 6. (p<0.05)

## Supplementary Fig. 3.



Mice implanted with 100,000 ACE-1 cells s.c were treated with OPG-Fc at 10mg/kg, 3 times/week for 3 weeks. A trend of reduced total calcium levels in bone marrow aspirates treated with OPG-Fc was found. (n=5, p=0.07)