



(b)



Fig. S1 Evaluation of the specificity of VEGF-D immunohistochemical analysis. (a) VEGF-D expressing HEK293 cells (293-VEGF-D) were generated by electroporation with the human VEGF-D expression vector. VEGF-D expression was confirmed by Quantikine Human VEGF-D ELISA kit (n = 3 for each cell line). (b) Specificity of immunohistochemical analysis for VEGF-D was evaluated by staining comparison with HEK293 and 293-VEGF-D. FFPE slides were stained with anti-VEGF-D antibody by a Ventana automated immunostainner.



Fig. S2 Comparison of profile between SK-N-DZ and SK-N-DZ-luc cells. (a) SK-N-DZ-luc was generated by infection of lentivirus with luciferase expression region. Luciferase activity was confirmed by Bright-Glo luciferase assay system (n = 3 for each cell line). (b) Comparison of secreted VEGF-D level between SK-N-DZ and SK-N-DZ-luc cells was analyzed by Quantikine Human VEGF-D ELISA kit (n = 3 for each cell line). (c) Comparison of *in vitro* proliferation ability between SK-N-DZ and SK-N-DZ-luc cells was quantified by Cell Count Kit (n = 3 for each cell line). All values are expressed as the mean ± SD.

Fig. S3 (a)



Isotype control Anti-VEGFR2



Fig. S3 Expression of VEGFR-2 and VEGFR-3 in SK-N-DZ-luc cells. (a) VEGFR-2 and (b) VEGFR-3expression on cell surface were analyzed by FACS with anti-VEGFR-2 and VEGFR-3 antibody (R&D systems). HMVEC-Lly was used as a positive control cell.

Fig. S4



Fig. S4 Plot of photons and SK-N-DZ-luc number in each mouse shown in Fig. 5c. (a) The amount of photons in each mouse shown in Fig. 5c was plotted. (b) The number of SK-N-DZ-luc cells in each mouse shown in Fig. 5c was plotted. This cell number was calculated based on the result in Fig. S2a showing the relationship between the number of SK-N-DZ-luc and photons. All statistical tests were performed using the Wilcoxon test.

Anti-mCD31



scale; 100µm

Fig. S5 Immunohistochemical analysis of mCD31 in SK-N-DZ-luc xenograft. The presence of blood vessels in the primary tumors of SK-N-DZ was analyzed by mCD31 immunostaining. FFPE slides were stained with an anti-mouse CD31 antibody (BD Biosciences) using a Ventana automated immunostainer.

Fig. S6



Fig. S6 Expression of VEGF-A in SK-N-DZ-luc cells. Secreted VEGF-A level in SK-N-DZ-luc cells was analyzed by Quantikine Human VEGF-A ELISA kit (R&D systems). Assay was performed by n = 3. All values are expressed as the mean \pm SD.