



**Supplementary figure 3.** Morphology of sprouting spheroids in collagen I matrix. *a*, spheroids embedded in collagen I cultured 48 hours. Nuclei are visualized by Hoechst staining. Scale bars equal 100  $\mu\text{m}$ . *b*, representative picture of matrix proteolysis at invasive strands of tumor spheroids detected with dye-quencher (DQ) labeled collagen I. Pictures are overlays of 10 confocal planes. Scale bars equal 100  $\mu\text{m}$ .