

## **Reprogrammed macrophages promote spread** of breast cancer

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Transcriptomic analysis identifies characteristic changes in reactive ECs during metastatic colonization of the lung. a, Immunofluorescence images showing association of lung ECs (CD31) with metastatic breast cancer cells (GFP) in mouse lung at indicated time points post intravenous injection of MDA231-LM2 breast cancer cells. Scale bars, 50  $\mu$ m. Dashed lines indicate margins of metastatic foci. b, Quantification of metastatic nodules from a with intranodular ECs; n = 72 nodules (week 1), n = 76 nodules (week 2) and n = 83 nodules (week 3) from four mice were analyzed for each time point. Data are presented as



means  $\pm$  s.e.m. c, Size of MDA231-LM2-derived metastatic nodules in lung at weeks 1–3. A minimum of 16 nodules were analyzed for each lung; n = 4 mice per group. d, MDA231-LM2 cancer cells (left) and ECs (right) in lung at indicated time points. Data show means  $\pm$  s.d; n = 4 mice per time point. P values were determined by one-way ANOVA with Dunnett's multiple comparison test. e, Experimental setup for EC isolation from mouse lung at different stages of MDA231-LM2-derived metastasis, followed by transcriptomic analysis. f, PC analysis of gene expression profiles from ECs isolated from healthy lung (control) or lung with different stages of metastasis (as in e). g, GSEA of isolated ECs using proliferation- or inflammation-related signatures. Signatures with nominal P

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