

Figure S1. Related to Figure 1. Characteristics of the IL6 detector cell line. (A) Schematic of transfer vector constructs. The SINp-detector transfer vector contains the self-inactivating promoter (SINp), a packaging signal ( $\Psi$ ), a CMV promoter (CMVp) regulating PM-labelled RCaMP1.07, a CMVp regulating IL6Rchi, a SV40 promoter (SV40p) regulating the fusion protein of thymidine kinase and zeocin resistance gene (TK-zeor) (Invivogen), and the 3' long terminal repeat (LTR). The SINp-source transfer vector contains SINp,  $\Psi$ , CMVp regulating LynCherry, CMVp regulating IL6, SV40p regulating blasticidin resistance gene (blast<sup>r</sup>), and the 3' LTR. The SINp-null transfer vector contains SINp,  $\Psi$ , CMVp regulating LynCerulean, SV40p regulating blast<sup>r</sup>, and the 3' LTR. The SINp-seeking transfer vector contains SINp,  $\Psi$ , CMVp regulating CaRQ, CMVp regulating IL6Rchi, a SV40p regulating TK-zeor, and the 3' LTR. The SINp-fuse transfer vector contains SINp,  $\Psi$ , CMVp regulating CeruNES, CMVp regulating VSVG, a SV40p regulating puromycin resistance gene (puro<sup>r</sup>), and the 3' LTR. (B) Percent response of IL6 detector cells when stimulated with indicated IL6 concentrations. Error bars show standard deviation. (C) Representative Ca<sup>2+</sup> trace of IL6 detector cells when stimulated twice with [IL6]<sub>f</sub> = 10 ng/mL. All experiments were repeated at least 3 times.

A

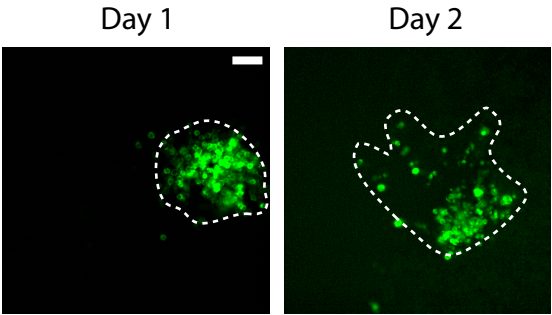
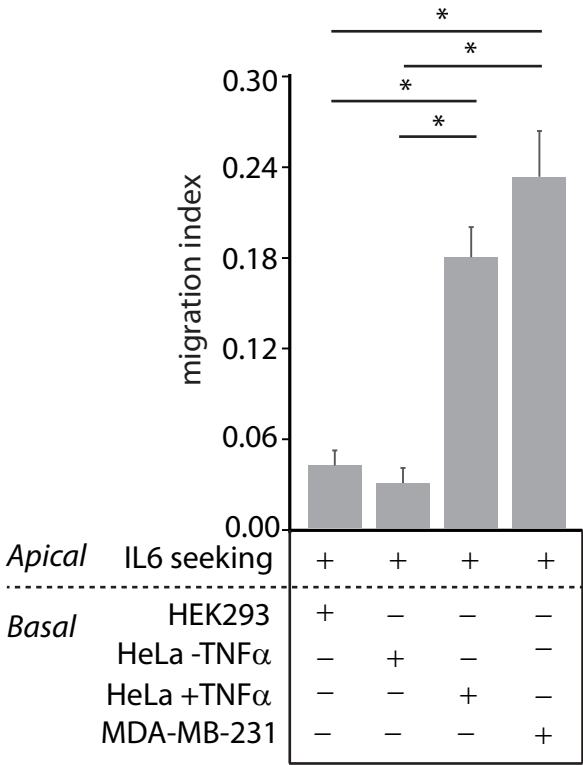
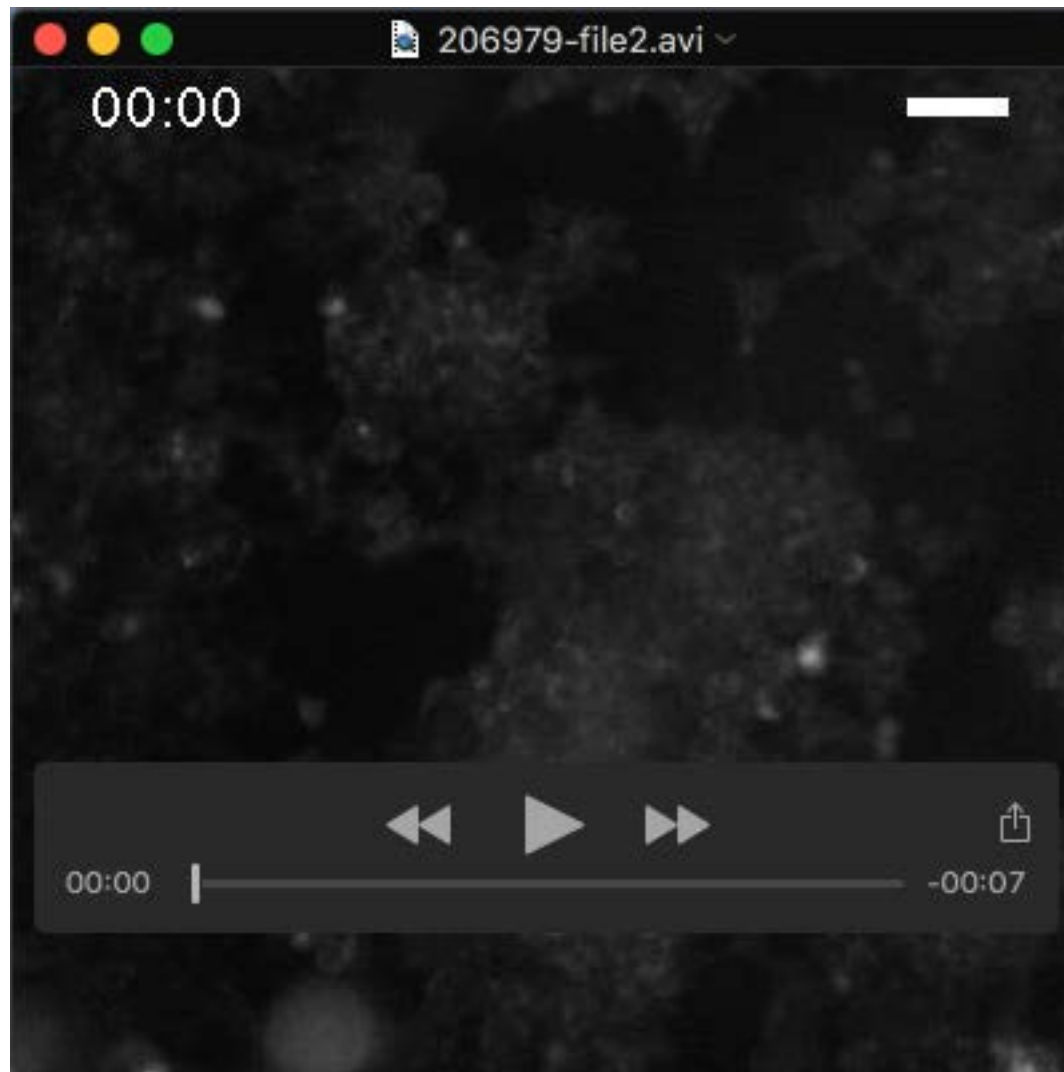


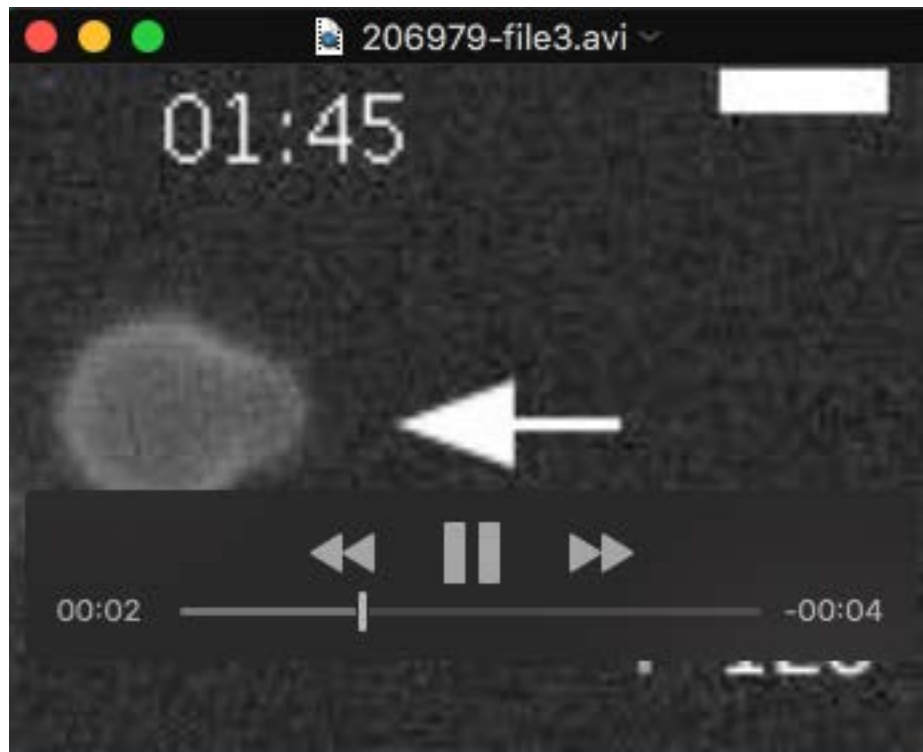
Figure S2. Related to Figure 3. IL6 seeking cells migrate towards senescent cells. (A) Representative images of seeking cell clusters on Day 1 and 2 showing breakage and spread, used to generate the rose plots. The source cluster is in the upper left direction. Images are false colored: YFP, green. Scale bar is 100  $\mu$ m. (B) Transwell experiments showing IL6 seeking cell migration in response to co-culturing with MDA-MB-231 and HeLa cells. Sample groups were compared with one-factor ANOVA followed by a Tukey-Kramer post-hoc test. Starts indicated significance;  $p < 0.05$ . All experiments were repeated at least 3 times.

B





**Video S1.** Related to Figure 1. IL6Rchi responds to extracellular IL6. The IL6 detector cell line expressing IL6Rchi and the  $\text{Ca}^{2+}$  sensor RCaMP1.07 responded to 10 ng/mL bolus addition of IL6 to the media. The detector cells show an oscillation in fluorescence intensity, indicative of a  $\text{Ca}^{2+}$  signal. Scale bar is 100  $\mu\text{m}$ . Experiment was repeated at least 3 times.



**Video S2.** Related to Figure 2. IL6 seeking cells bleb in response to extracellular IL6. Dynamic blebbing of IL6Rchi chimera and CaRQ cells when stimulated with  $[IL6]_f = 10$  ng/ml. Arrow points to a blebbing cell. Scale bar is 40  $\mu$ m. Experiment was repeated at least 3 times.



**Video S3.** Related to Figure 2. IL6 seeking cell migrates towards an IL6 source cell. One-hour time-lapse of an IL6 seeking cell co-cultured with IL6 source cells. Scale bar is 20  $\mu\text{m}$ . Experiment was repeated at least 3 times.