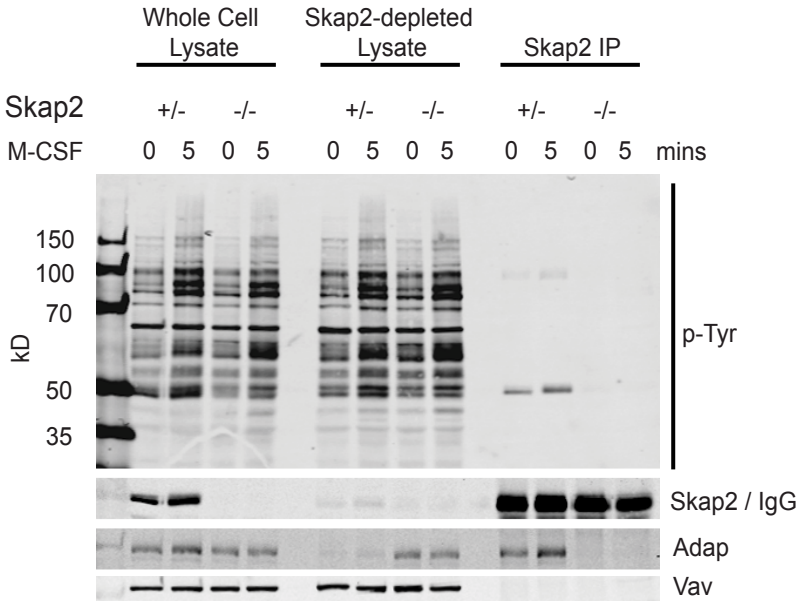


Fig. S1. There are no significant changes in M-CSF-driven tyrosyl phosphorylation conferred by Skap2 deficiency, except for the lack of phosphorylation of Skap2 itself. Adherent *Skap2+/-* and *Skap2-/-* BMMs, with or without 5 minutes of M-CSF treatment, were lysed, and half of each lysate was subjected to Skap2 immunoprecipitation. The original lysate, the Skap2-depleted lysate, and the immunoprecipitate were electrophoresed and immunoblotted for phosphotyrosine (p-Tyr), Skap2, Adap, and Vav as a loading control. Skap2 is effectively immunodepleted, and removing Skap2 also depletes Adap from *Skap2+/-* cells. Note that the IgG heavy chain used for immunoprecipitation migrates at the same molecular weight as Skap2.

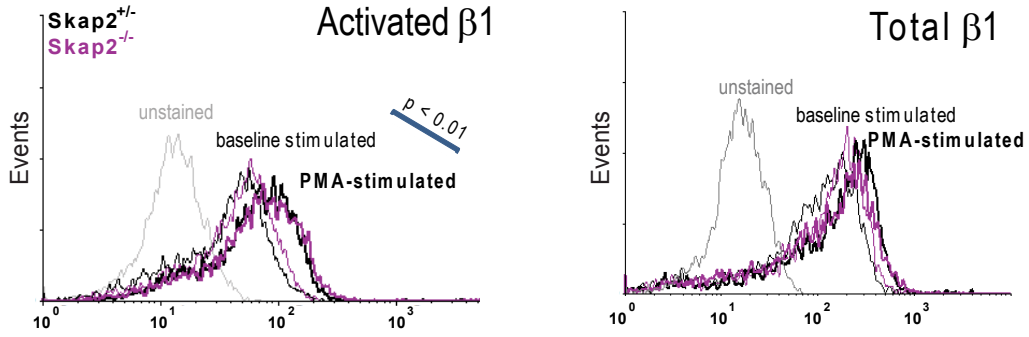


Fig. S2. β1 integrin activation is not affected by Skap2. *Skap2+/-* and *Skap2-/-* BMMs in suspension were incubated for 15 minutes at 37 C with either activation-specific anti-β1 (9EG7) or non-selective anti-β1 antibody in the presence or absence of PMA. The cells were then subjected to FACS analysis for this antibody staining.

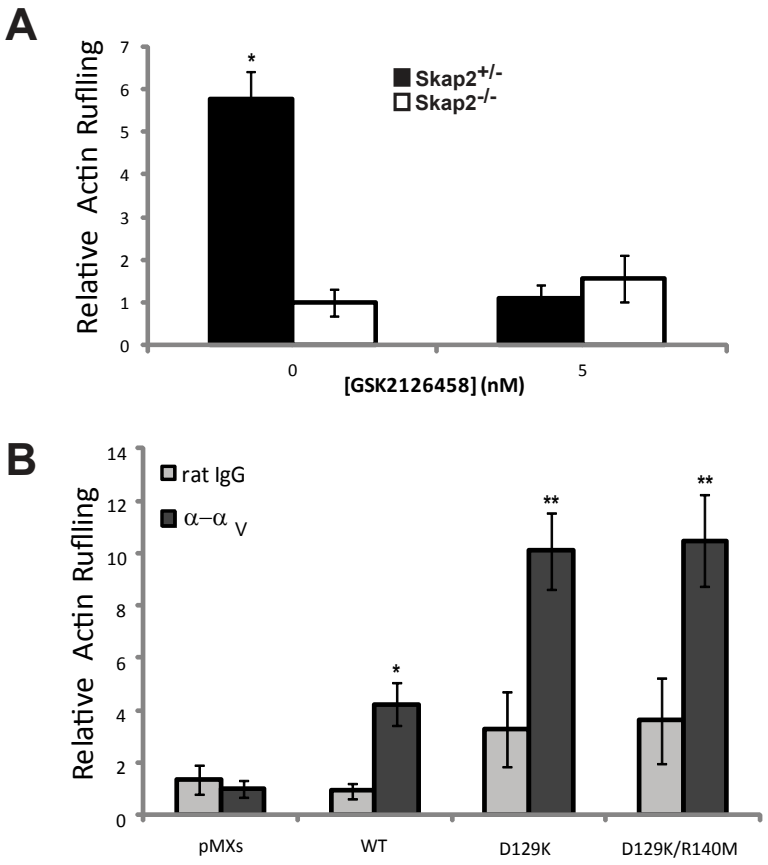


Fig. S3. PI3K inhibition blocks, whereas D129K mutation promotes, integrin-induced actin ruffling. (**A**) Actin ruffling induced by beads coated with anti-αV bound to *Skap2+/-* and *Skap2-/-* BMMs with or without 30 minutes of pre-treatment with the PI3K inhibitor GSK2126458. Data are presented as mean ± S.E.M., n=10 per condition, * $p < 0.05$ compared to all other conditions. (**B**) Actin ruffling induced by beads coated with rat IgG (control) or anti-αV bound to *Skap2-/-* BMMs infected with empty vector (pMXs), WT Skap2 (WT), or Skap2 mutants with a D129K substitution or with combined D129K and R140M substitutions. Data are presented as mean ± S.E.M., n=10-20 per condition, * $p < 0.05$ compared to pMXs, ** $p < 0.05$ compared to WT.

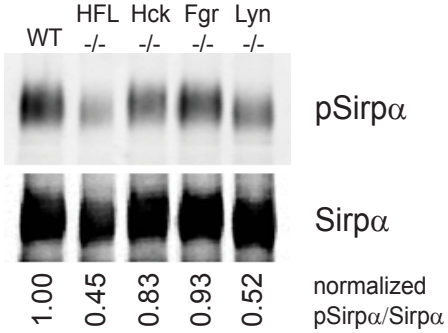
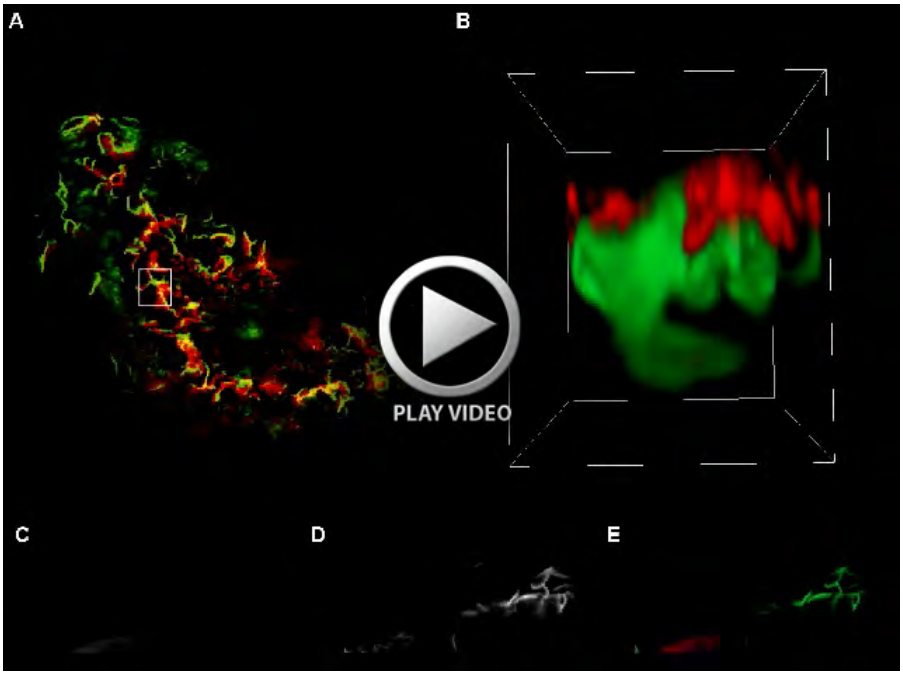
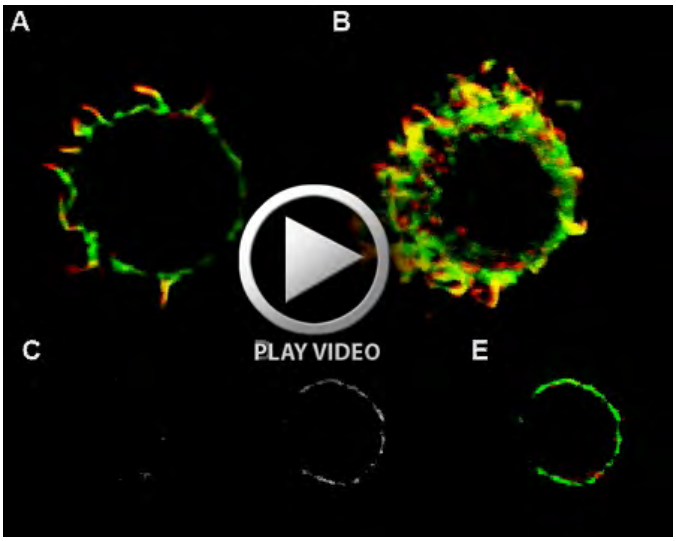


Fig. S4. BMMs from *Hck-/-*, *Fgr-/-*, and *Lyn-/-*, and Hck/Fgr/Lyn triple knockout (*HFL-/-*) mice were lysed after plating on fibrinogen, subjected to immunoprecipitation for Sirpα, and immunoblotted for p-Tyr and Sirpα, with ratiometric band quantification as indicated.



Movie 1. Skap2 localizes to the ends of actin ruffles. (**A**) Fluorescence micrograph of a typical phalloidin- and Skap2-immunostained *Skap2*+/- BMM, demonstrating curvilinear actin ruffles (green) with Skap2 (red) colocalization (yellow). (**B**) Video 3-D reconstruction from the region in the inset of (A) shows that Skap2 is localized at the ends of ruffles, with trails of actin extending away from it. The apical surface of the cell is at the top. (**C-E**) Skap2 antibody does not stain *Skap2*-/- cells, providing evidence of its specificity (**C** – Skap2, **D** – actin, **E** – merge).



Movie 2. Confocal micrographs of representative 10 μm-diameter beads bound to αV integrins. Cells are stained for actin (green) and Skap2 (red). In a *Skap2*+/- BMM, actin ruffles emanate from the integrin-directed bead, and Skap2 is concentrated at their leading edges, as shown at the bead equator (**A**) and as a video 3-D reconstruction of the bead (**B**). *Skap2*-/- cells do not have integrin9 mediated actin ruffling, as shown at the bead equator (**C** – Skap2, **D** – actin, **E** – merge).