**Fig. S1. Transfection of exogenous PLCB4 is not necessary for EDN1 to stimulate a DAG reporter response.** Cells were transfected with GFP-C1, EDNRA, and empty vector (pcDNA3.1) and imaged before (0 seconds; t=0) and after addition of EDN1. Cytoplasm to membrane translocation of GFP-C1 was observed within the first imaging frame following EDN1 addition (30 seconds; t=30).
Fig. S2. Types of targeting observed in Plcb4 CRISPR blastocysts. After electroporation, 64 blastocysts were collected and genomic DNA submitted for Sanger sequencing. The bars represent the type of editing that was detected.
Movie 1. Rotating µCT images of E18.5 control (left) and Plcb4<sup>Ki/Ki</sup> (right) embryos.

Movie 2. Rotating µCT images of the digitally-dissected basisphenoid/pterygoid complex from E18.5 control (top) and Plcb4<sup>Ki/Ki</sup> (bottom) embryos.