

## **Supplementary Data:**

### **Total oocyte [cAMP]**

Total cAMP concentrations of oocytes were measured by immunoassay in extracts from single oocytes that were either not injected (control), or injected with 3 ng of cRNA coding for PAC $\alpha$ , or with 20 ng cRNA coding for PAC $\beta$ . Oocytes were kept for three days in the dark before measuring [cAMP]<sub>i</sub>; or were, after 3 days in the dark, irradiated for 5 min with blue light before measuring [cAMP]: **Dark:** Control, [cAMP] =  $1.3 \pm 0.6 \mu\text{M}$  (n = 5, range 0.5 – 2  $\mu\text{M}$ ); PAC $\alpha$ , [cAMP] =  $27 \pm 21 \mu\text{M}$  (n = 5, 13 – 64  $\mu\text{M}$ ); PAC $\beta$ , [cAMP] =  $1.3 \pm 0.6 \mu\text{M}$  (n = 5, 0.4 – 1.9  $\mu\text{M}$ ). **5 min blue light:** Control, [cAMP] =  $1.2 \pm 0.7 \mu\text{M}$  (n = 5, 0.4 – 2  $\mu\text{M}$ ); PAC $\alpha$ , [cAMP] =  $280 \pm 180 \mu\text{M}$  (n = 5, 22 – 480  $\mu\text{M}$ ); PAC $\beta$ , [cAMP] =  $1.6 \pm 0.6 \mu\text{M}$  (n = 5, 0.7 – 2.3  $\mu\text{M}$ ). Statistical analysis (student's t-test): At the 0.01 level, the difference of the population means is significant for control and PAC $\alpha$  in the dark; PAC $\alpha$  in the dark and 5 min blue light; the difference of the population means is not significant for control and PAC $\beta$  in the dark; for control in the dark and 5 min blue light; for PAC $\beta$  in the dark and 5 min blue light; and for control and PAC $\beta$  in 5 min blue light.

### **Intensity- and duration-dependence of PAC $\alpha$ -mediated light-induced CFTR activation**

The amplitude of the response increased with the intensity or duration of light stimulation, but the shape of the two curves differed (**Supplementary Fig. 2**). Whereas the dependence on flash duration is nearly linear in a wide range, the dependence on flash intensity (at fixed duration) indicates saturation at high light intensity. However, only a lower limit for light-saturation of PAC $\alpha$  can be deduced from this result, as saturation of one of the subsequent enzymatic steps that lead to CFTR activation is equally probable.

### **Expression of PACs in *Drosophila melanogaster* under the control of the *tubulin*-promoter**

Expressing PAC $\beta$  under the control of the strong and ubiquitous *tubulin*-promoter (*tub-Gal4/UAS-PAC $\beta$* ) did not affect grooming behavior (**Supplementary Fig. 3**). Expression of

PAC $\alpha$  under the control of the *tubulin*-promoter resulted in lethality, even when flies were kept in complete darkness, probably during an early stage of development as a result of increased [cAMP] caused by the basal activity of PAC $\alpha$  (data not shown).