Optogenetic control of heart muscle *in vitro* and *in vivo*

Optogenetics is an emerging field combining optical and genetic techniques to probe neural circuits within intact mammals and other animals, at the high speeds (millisecond-timescale) needed to understand brain information processing.

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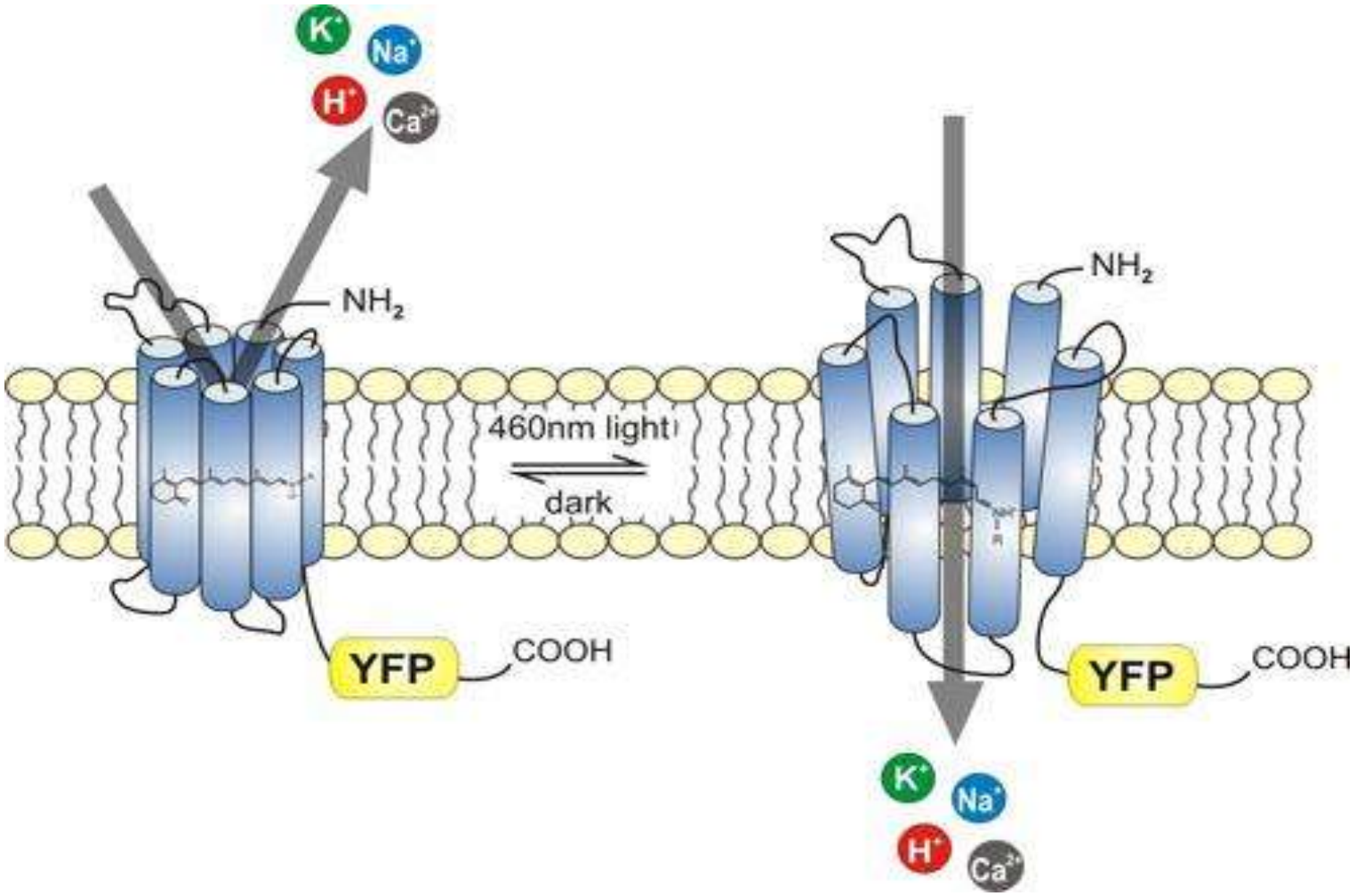
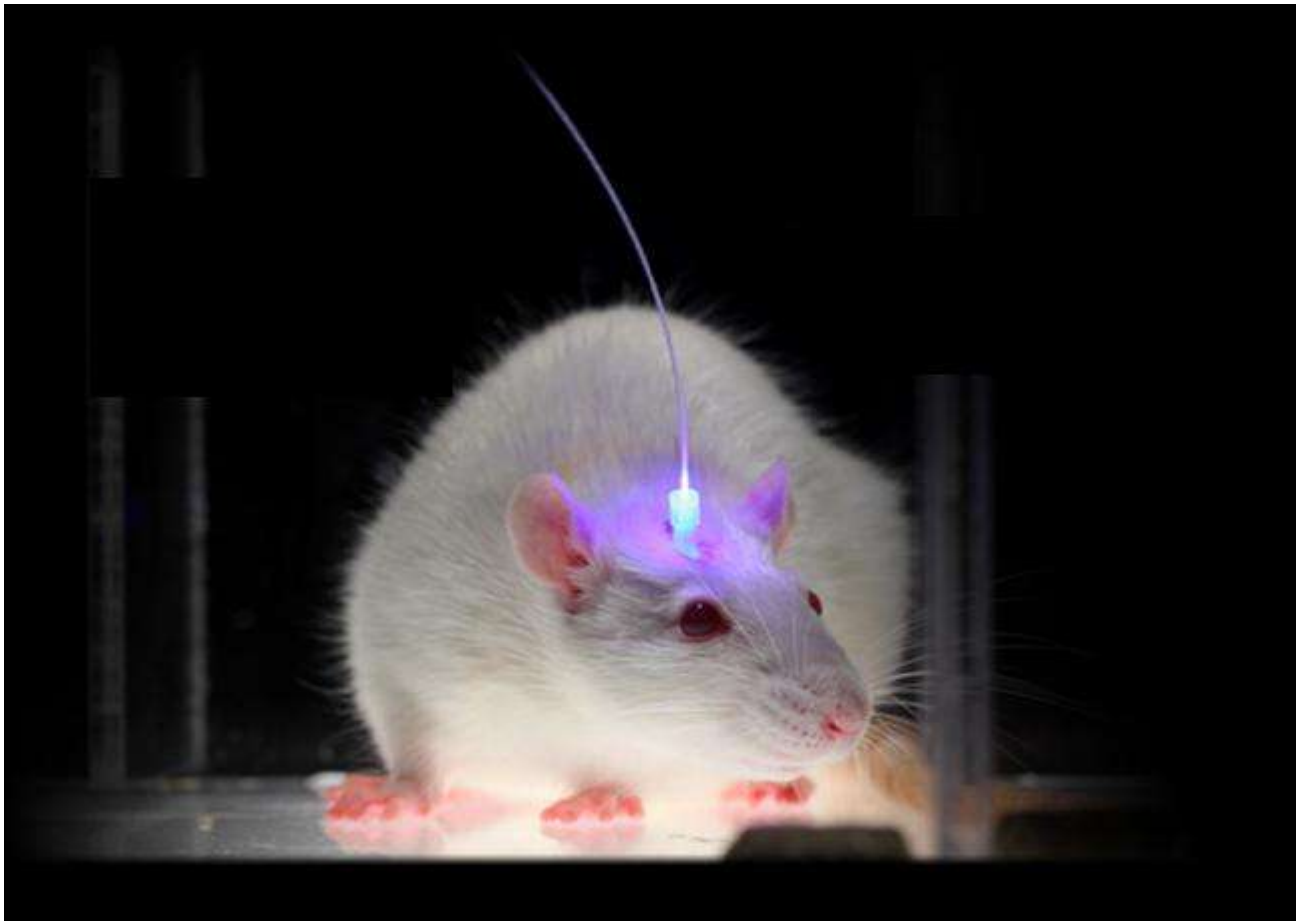
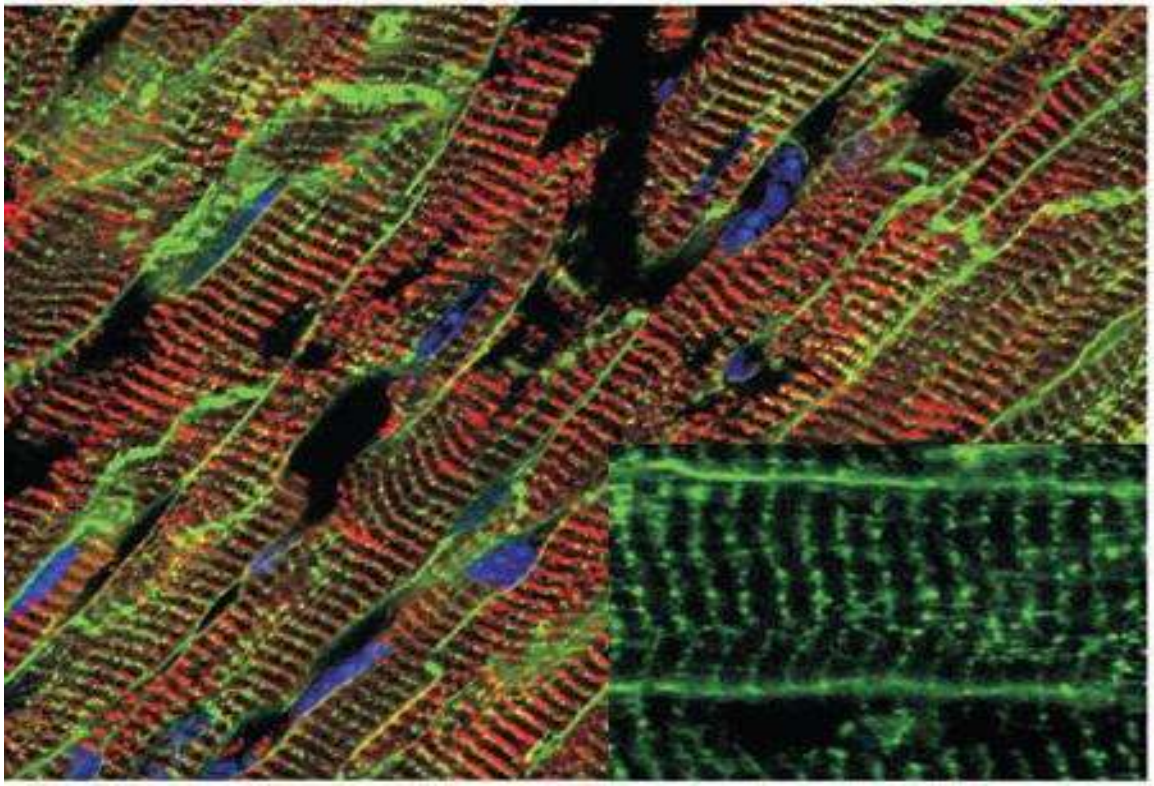


Schematic representation of the light activation of ChR2

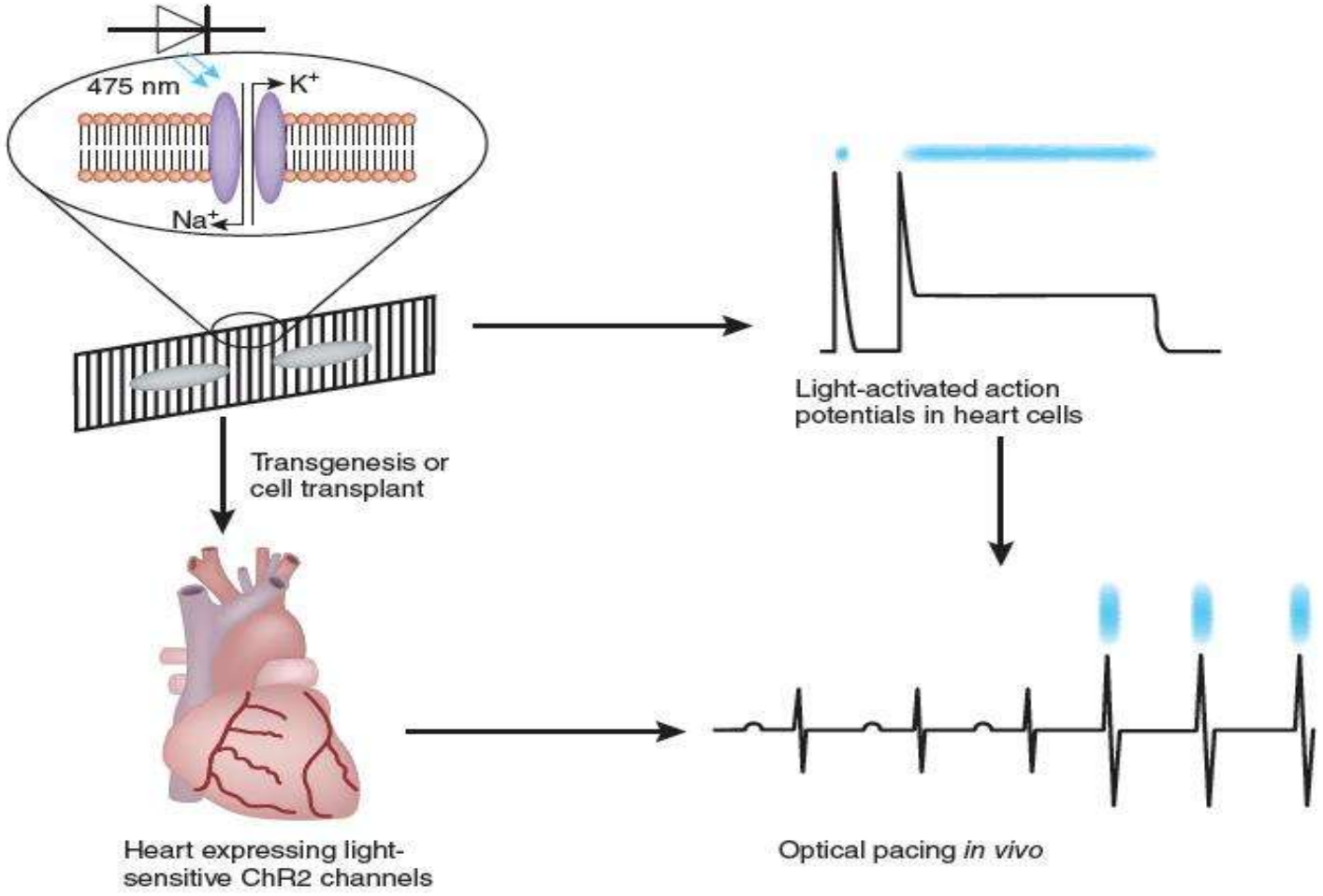
Chlamydomonas reinhardtii is a single celled green alga about 10 micrometres in diameter that swims with two flagella. They have an "eyespot" that senses light.



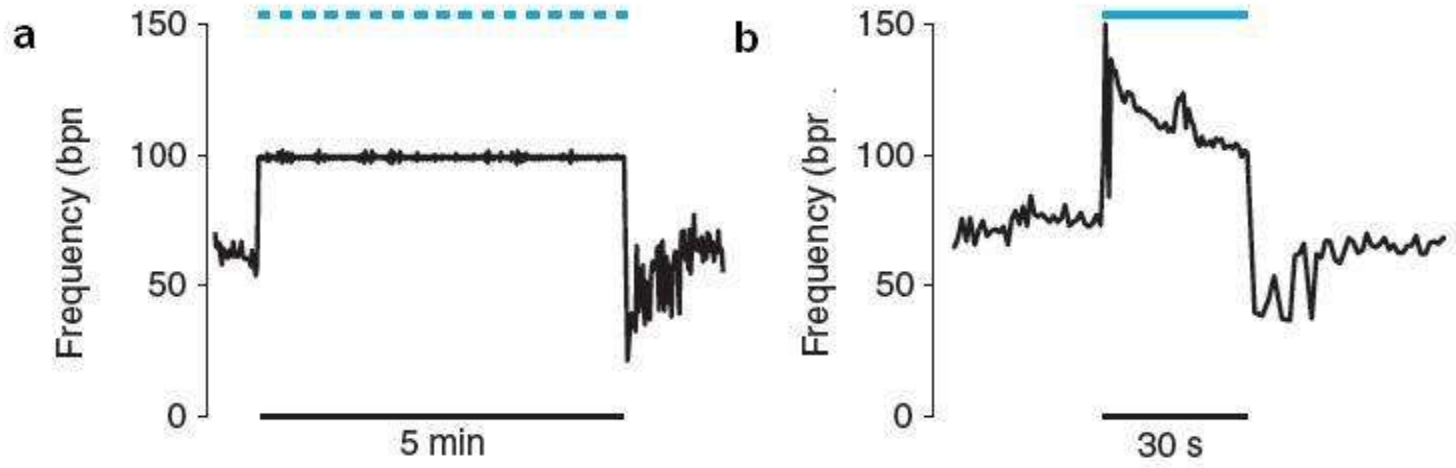
Ready for behavioral testing. Stimulation can be applied by triggering the waveform generator.



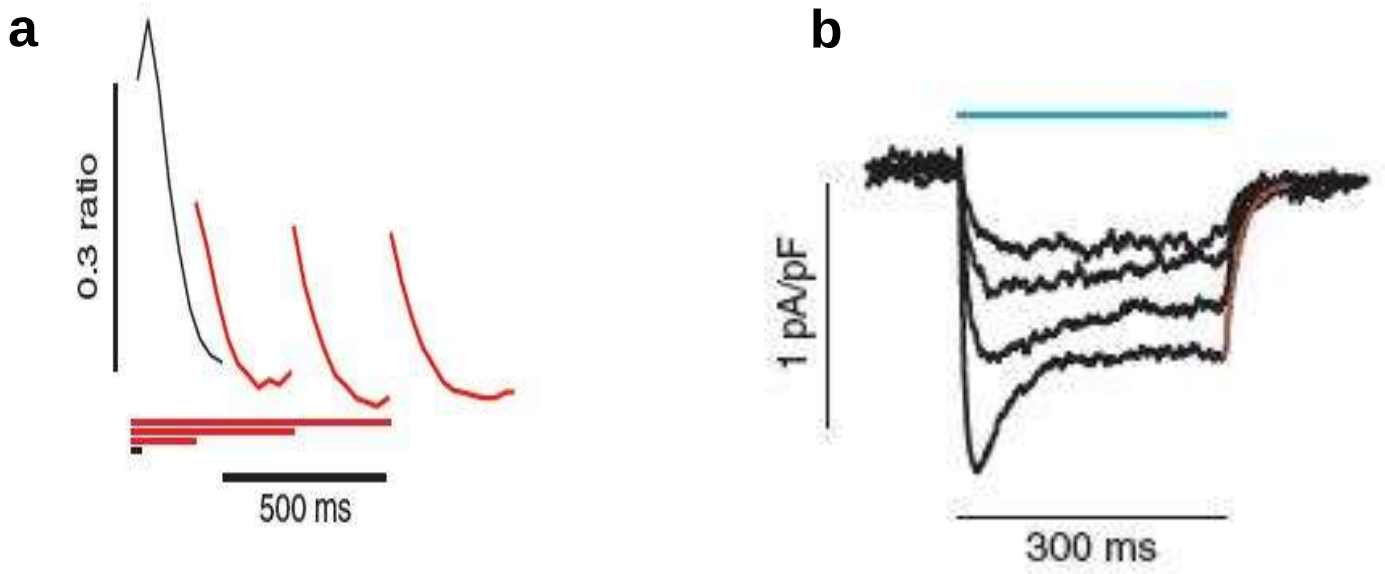
Fluorescence image of the native membrane-bound ChR2-EYFP signal (green) overlaid with α-actinin immunostaining (red) in cardiomyocytes of the ventricle and colocalization with the t-tubulus system (inset). Nuclei are shown in blue. Scale bars, 20 μm.



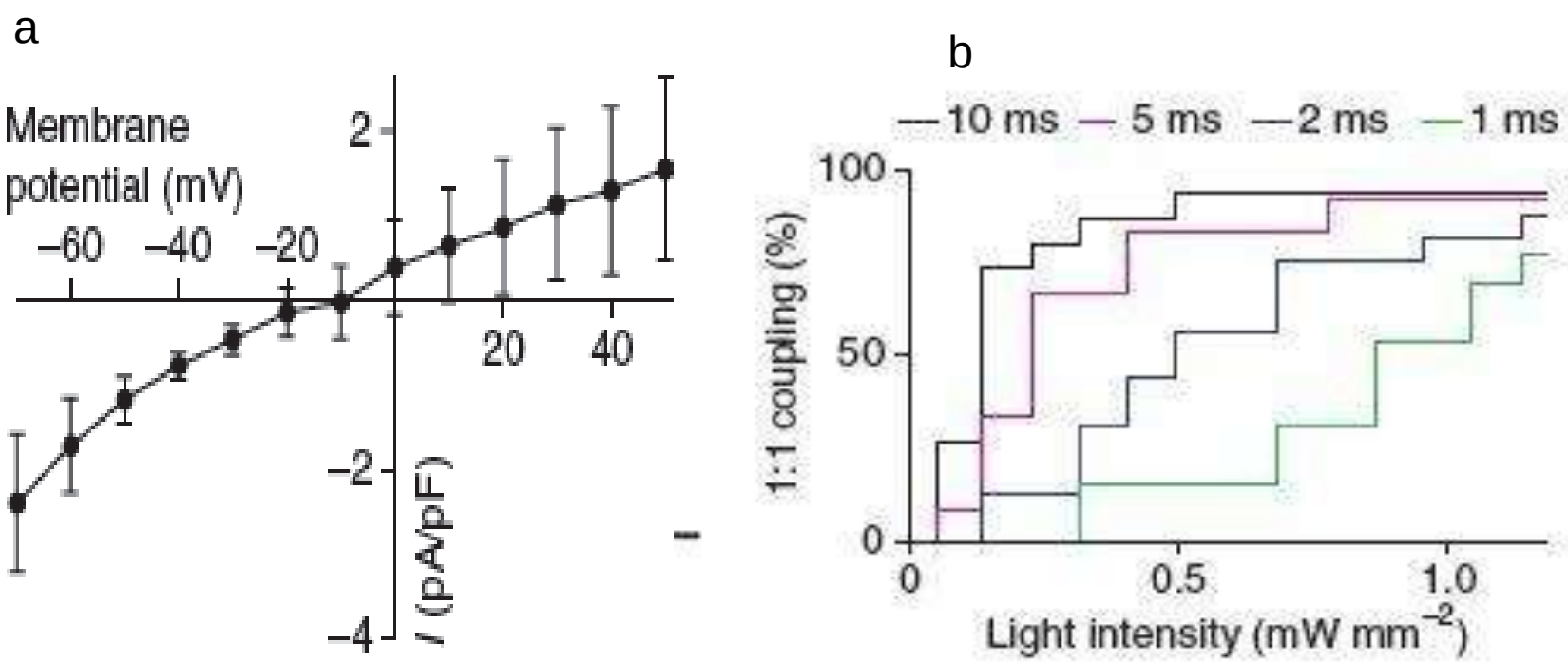
Optogenetic control of heart muscle. Transfer of the gene encoding ChR2 renders heart
muscle cells sensitive to blue light emitted by an LED. The electrical transduction of the optical signal
can be used to control heart muscle membrane potential *in vitro* and *in vivo*.



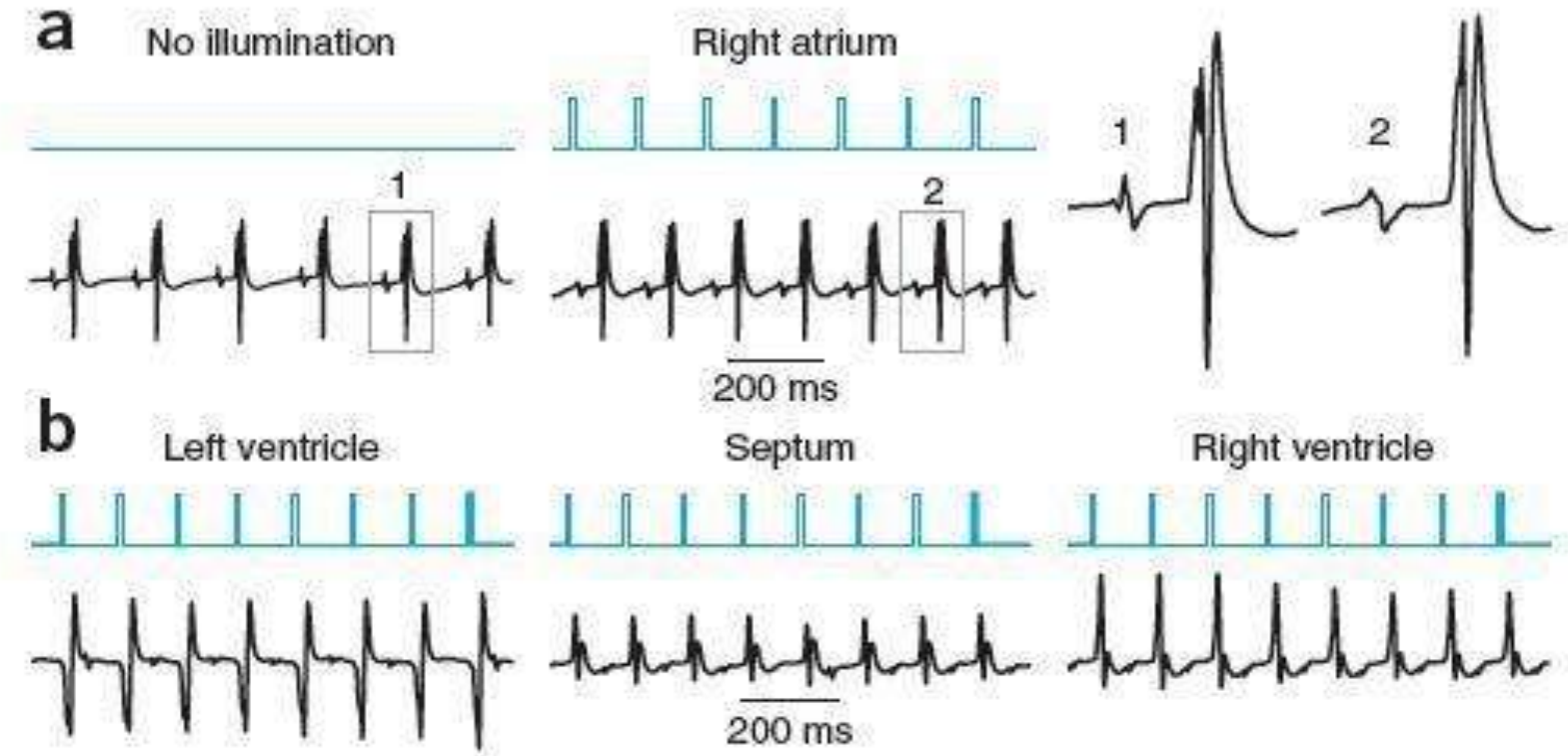
Frequency analysis of spontaneously beating embryoid bodies upon pulsed light stimulation at 100 beats per minute (bpm) (blue dashed line; 20 ms, 0.6 mW mm−2; a) and continuous light stimulation (blue bar; 30 s, 0.6 mW mm−2; b)



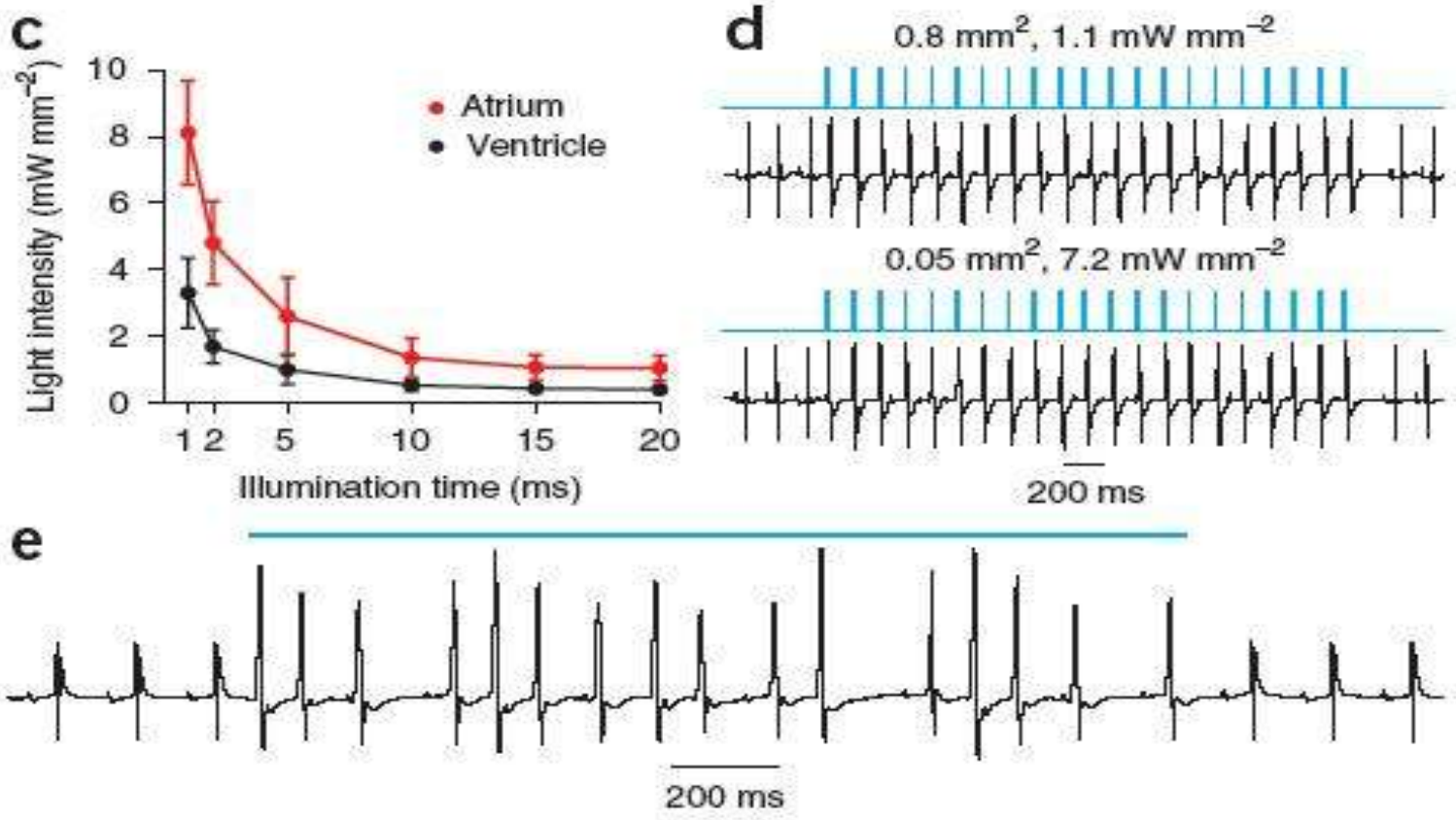
a) Cytosolic Ca2+ imaging traces directly after termination of ChR2 stimulation (47 mW mm−2) for 20 ms (black), 200 ms, 500 ms or 800 ms (red) (durations are indicated by bars below the traces).
b) Inward currents evoked at a holding potential of −40 mV by light stimulation at 0.09, 0.18, 0.45 and 1.75 mW mm−2 (from top to bottom). Monoexponential fit to measure the time constant of decay is shown in red. pA, picoampere; pF, picofarad.



a) Current (*I*) and voltage (membrane potenial) relationship of light-induced steady-state currents. Error bars, s.d. (*n* = 7 cells).
b) Stimulation-response diagram with percentages of cardiomyocytes showing a 1:1 light pulse to action potential coupling depending on the light intensity and duration of light pulses (data for a minimum of 13 cells were used to generate each data point).



Light-induced stimulation of ChR2-expressing hearts *in vivo*. (**a,b**) Pulsed light stimulation (illumination area, 38 mm2; 10 ms, 2.8 mW mm−2, blue) of the right atrium (**a**) or three indicated ventricular areas (**b**) and parallel recordings of the electrocardiogram (black).



(**c**) Strength-duration curve for threshold of 1:1 coupling in atria (*n* = 5) and ventricles (*n* = 4) at 450 beats per min (illumination area, 2.0 mm2). (**d**) Electrocardiogram recording (black traces) during pulsed (20 ms) light stimulations of the left ventricle in an area of 0.8 mm2 (1.1 mW mm−2, top) or 0.05 mm2 (7.2 mW mm−2, bottom). (**e**) Continuous light stimulation (blue bar, 3.9 mW mm−2) of a left ventricular area (0.2 mm2) and recording of the electrocardiogram (black).

Thank you for the attention!!!