

## SEXUAL DYSFUNCTION

## Blue light, not blue pills, for erectile dysfunction

An erectile optogenetic stimulator (EROS) has been used to enable blue-light-induced erection in male rats.

Penile erection relies on the release of nitric oxide, which activates soluble guanylyl cyclase, thus increasing cyclic GMP (cGMP) levels, closing calcium channels and decreasing intracellular calcium, causing relaxation of the corpora cavernosa, increased blood flow, and erection. Although use of a phosphodiesterase type 5 inhibitor (PDE5I) can prevent cGMP degradation, these drugs are not effective in all patients, and an alternative means to cause cGMP accumulation could be a useful option in such patients.

Optogenetics is a technique that enables researchers to specifically engineer target cells to respond to stimulation by light by predictable induction of the chosen genes. In this study, a team lead by Martin Fussenegger from the University of Basel, Switzerland, designed the EROS system, which enables control of the intracellular cGMP pool by blue light.



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Corpora cavernosa of male rats were transfected with the constitutive EROS-encoding expression vector designed to programme a cGMP surge under stimulation by blue light, or with a control vector. 24 h later, transfected rats were placed in metabolic cages illuminated from below with blue light (or white light as a

control), and penile reflexes were observed. EROS-transfected rats in blue-light cages showed penile reflexes within  $55 \pm 22$  s of exposure, ranging from tumescence of the penile tip ( $11 \pm 3$  s), to erection ( $37 \pm 2$  s) and even ejaculation. No erectile responses were observed in either the control-transfected rats, or the EROS rats exposed to white light. Further investigation showed that relaxation of the corpora could be repeatedly triggered by the blue light and that coadministration of sildenafil had a synergistic effect.

PDE5Is exert their effect by preventing cGMP degradation, but cannot produce it *de novo*. By decoupling erectile response from physiological control, the EROS system could find its place in the therapeutic armamentarium for ED.

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