Designer Channels to Combat Painful Bladder Syndrome

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Interstitial cystitis (IC), often referred to as painful bladder syndrome, is a debilitating urinary bladder disease. It causes intense pelvic pain and urgency to urinate due to inflammation-induced hypersensitivity of bladder afferents. Treatment options for IC are limited and ineffective. We recently developed a new IC therapy using ion channels as drugs. We designed non-native chloride channels that can either passively respond to inflammatory tissue changes in the bladder or be activated by metabolites of certain foods to reset the sensitivity of bladder afferents, thereby alleviating IC symptoms.In animal experiments, which were approved by the IACUC at University of Pittsburgh, plasmidsexpressing the designerchannelswere encapsulated in liposomes and instilled into the urinary bladder of Sprague Dawley rats using a transurethral catheter.One to two weeks later, we induced bladder inflammation by intraperitoneal injection of cyclophosphamide (CYP, 150mg/kg) and measured bladder activity using metabolic cages and bladder cystometry. Expression of the designer channels was confirmedin the bladder smooth muscle, urothelium, and dorsal root ganglia by RT-PCR. Transfected animals before bladder inflammation showed a voiding frequency similar to that of control animals, suggesting that the designer channels are functionally silent under normal physiological conditions. After CYP-induced inflammation, rats transfected with the designer channels showed resistance to the excitatory effects of CYP. Metabolic cage and cytometryexperiments showed that after activation of the designer channels, the transfected animals showed a decreased CYP-induced bladder activity and peak micturition pressure as compared to the un-transfected animals with CYP-induced bladder inflammation. These results point to a new direction for the development of more effective treatmentsfor painful bladder disorders.