the serine kinase receptor for TGF-β (TβRI). This response will be considered in the context of responses to endothelin-1 and the options for therapeutically targeting endothelin-1 broadened to include downstream signalling otherwise associated with TGF-β receptor activation.


Structure of the precursor of salmon, Oncorhynchus keta, endothelins and phylogenetic analysis
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Endothelin (ET)-related receptors homologous to mammalian receptors have been present in fish, indicating that ET-related ligands may be present in this species. Here we cloned cDNAs encoding preproendothelins (PPETs) from the intestinal cDNAlibrary. Salmon ETs cDNAs encode 200 amino acids, including a 20-amino-acid putative signal sequence, as well as mature ETs, big ETs, and ET-like sequences. This sequences together with other published PPET sequences were used to analyze the phylogenetic relationship among all ET family genes.


Decreased MYPT-1 phosphorylation at Thr696 and Cdc42 protein expression are associated with decreased contractile responses to ET-1 in corpora cavernosa and internal pudendal artery from Goto-Kakizaki diabetic rats
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Endothelin-1 (ET-1) plays a crucial role in the development of erectile dysfunction (ED). The Goto-Kakizaki (GK) rat is a non-obese type 2 diabetes mellitus model, which displays ED and increased ET-1 plasma levels. The present study tested the hypothesis that GK rats display increased corpora cavernosa (CC) and internal pudendal artery (IPA) contractions to ET-1 as a contributing mechanism for ED. GK rats demonstrated impaired erectile function represented by decreased cGMP/EP responses after cavernous nerve stimulation. In GK rats contractile responses to ET-1 were decreased in both CC tissue [Control: 960.0 ± 10 vs GK: 186.00 ± 16.00; Emax, mN/mg of tissue] and in IPA [Control: 25.00 ± 1.75 vs GK: 14.83 ± 1.66; Emax, mN]. Gene expression of prepro-ET-1 [Control: 1.00 vs GK: 0.25 ± 0.04] and ETB receptors [Control: 1.00 vs GK: 0.58 ± 0.09], but not ETA receptors was decreased in CC from GK rats. In GK rats, CC protein expression of ETA receptor [Control: 1.00 vs GK: 4.18 ± 0.58], and phosphorylation of ERK 1/2 [Control: 1.00 vs GK: 1.31 ± 0.09] were increased, whereas ETB receptor expression [Control: 1.00 vs GK: 0.75 ± 0.08], Cdc42 protein expression [Control: 1.00 vs GK: 0.40 ± 0.08] and phosphorylation of MYPT-1 [Control: 1.00 vs GK: 0.36 ± 0.15] were decreased. In conclusion, GK rats display ED and exhibit decreased cavernosal and IPA reactivity to ET-1. Whereas decreased phosphorylation of MYPT-1 and Cdc42 protein expression may account for decreased ET-1 responses, it indicates that ED in GK rats is not associated with augmented CC and IPA reactivity to ET-1.


Generation of Edn2-iCre transgenic mice
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Endothelin-2 (ET-2) is a potent vasoconstrictive peptide. Though similar to ET-1, recent studies suggest that ET-2 may act through distinct pathways, necessitating deeper study. ET-2 may play a role in heart failure, inflammation, macular degeneration, and cancer metastasis. It is transiently expressed and tightly regulated in the periovulatory ovary, where it may aid ovulation by inducing constriction of the follicular wall. Here, we present a transgenic mouse line that expresses iCre (codon-improved Cre recombinase) under the regulation of the promoter of the endothelin-2 (edn2) gene, which was developed as a novel model for characterizing the expression of ET-2 and for conditional deletion of genes in cells where ET-2 is expressed. A vector was generated containing iCre, a polyadenylation signal sequence, and an frt-neomycin-resistance-frt cassette. Two homologous regions of the edn2 gene flanking the ATG start codon were isolated from a BAC (bacterial artificial chromosome) clone and inserted upstream and downstream of the iCre-pa-FNF cassette. Homologous recombination was used to re-insert the cassette into the BAC plasmid. Following purification, the plasmid was inserted into fertilized eggs of C57BL/6 mice through pronucleus injection, and resulting eggs were implanted into pseudopregnant mice. Five Edn2-iCre transgene-containing lines of mice were established, and one line was bred with ROSA26 reporter. Offspring were used to localize iCre-expressing cells through X-gal staining. Characterization of the staining pattern revealed that iCre was expressed in granulosa cells of ovulatory follicles, cardiomyocytes, the pituitary, and the liver. We expect this novel mouse model to be a useful tool for future studies on the role of ET-2.


The calcitonin gene-related peptide (CGRP) plays beneficial roles in myocardial ischemia elicited by endothelin-1
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Purpose: In addition to the adrenergic and cholinergic nerves, the cardiovascular tissues are also innervated by several peptidergic neurons that mediate nonadrenergic noncholinergic (NANC) functions. Among such neuropeptides, CGRP is released from capsaicin-sensitive sensory neurons in peripheral organs. CGRP is known as