

CTGF by TGF- $\beta$ 1 was reduced by an ETRA or ETRB antagonist, and a dual ETRA/ETRB antagonist had an additive inhibitory effect. In conclusion, TGF- $\beta$ 1 produced ET-1 through Smad3 phosphorylation and a dual ETRA/ETRB antagonist decreased COL1A1 and CTGF mRNA levels in fibroblasts. Inhibition of ET-1 signaling may exert anti-fibrotic effects in SSC fibroblasts.

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### Effect of feeding behavior on circadian regulation of endothelin expression in mouse colon epithelia

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The function, regulation and gene expression of the endothelin (ET) system in intestine are not well understood. We investigated the dependence on feeding schedule and biological clock of the regulation of ET-1 gene expression in mouse colon. Mice were fed freely, fasted for 48 h, and re-fed after fasting. Gene expression was analyzed by real-time RT-PCR. ET-1 gene expression was highest in colon compared with other tissues examined in fasted mice. Fasting increased the amplitude, while maintaining the rhythmicity, of ET-1 gene expression in epithelial colonic tissue. Re-feeding, however, decreased gene expression and suppressed rhythmic oscillation, even though the rhythmicity of Per-1 and Per-2 gene expression remained unchanged. Furthermore, the decrease in ET-1 gene expression induced by re-feeding was blocked by pre-treatment with hexamethonium and atropine. The daily change in ET-1 gene expression and peptide production in colon epithelia, which depends on feeding schedule via autonomic nervous system, is synchronized with peripheral circadian oscillators under conditions of free feeding and fasting but not re-feeding. ET-1 plays important physiological roles, which is dependent on feeding behavior.

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### cDNA cloning and sequence analysis of preproendothelin from barfin flounder (*Verasper moseri*)

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The presence of endothelin (ET)-like immunoreactivity and the cardiovascular effects of mammalian ET-1 in fish have been reported. To identify ET-related peptides in fish, we screened the cDNA library of the barfin flounder (*Verasper moseri*) intestine by means of rapid amplification of cDNA ends, and we cloned cDNAs encoding an ET-related peptide. The ET-related sequence of 21 amino acids is similar to the trout ET-1 peptide recently purified from kidney specimens of *Oncorhynchus mykiss*. The deduced amino acid sequence

of pre- proET-1 (PPET-1) comprises 244 amino acids, including a putative signal sequence and mature ET-1, as well as big ET-1 and ET-1-like sequences. This precursor, the first reported PPET-1 sequence, has low homology with the sequences of human, mouse, frog (*Xenopus laevis*), and zebrafish (*Danio rerio*) PPET-1.

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### Shark endothelin: cDNA cloning, sequence and evolutionary analysis

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Endothelin (ET)-related receptors homologous to mammalian receptors have been cloned from fish, indicating that ET-related ligands may be present in lower species. Here we cloned cDNAs encoding preproendothelin (PPET) from the Shark intestinal cDNA library. Shark ET cDNAs encode 200 amino acids, including a 20-amino-acid putative signal sequence, as well as mature ET, big ET, and ET-like sequences. These sequences together with other published PPET sequences were used to analyze the phylogenetic relationship among all ET family genes.

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### Molecular cloning and sequence analysis of preproendothelin from medaka, *Oryzias latipes*

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The presence of endothelin (ET)-like immunoreactivity and the cardiovascular effects of mammalian ET-1 in fish have been reported. To identify ET-related peptides in fish, we screened the cDNA library of the medaka (*Oryzias latipes*) intestine by means of rapid amplification of cDNA ends, and we cloned cDNAs encoding an ET-related peptide. The medaka ET-related sequence of 21 amino acids is similar to the trout ET-1 peptide recently purified from kidney specimens of *Oncorhynchus mykiss*. The deduced amino acid sequence of pre-proET-1 (PPET-1) comprises 200 amino acids, including a putative signal sequence and mature ET-1, as well as big ET-1 and ET-1-like sequences. This precursor, the first reported PPET-1 sequence, has low homology with the sequences of human, mouse, frog (*Xenopus laevis*), and zebrafish (*Danio rerio*) PPET-1.

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