fsANP (frameshift ANP) / Mutant ANP (mANP)

fsANP is the familial ANP mutation associated with atrial fibrillation. Mutant ANP (mANP) activates cGMP in vitro and exerts greater and more sustained natriuretic, diuretic, glomerular filtration rate, and renal blood flow enhancing actions than native ANP in vivo

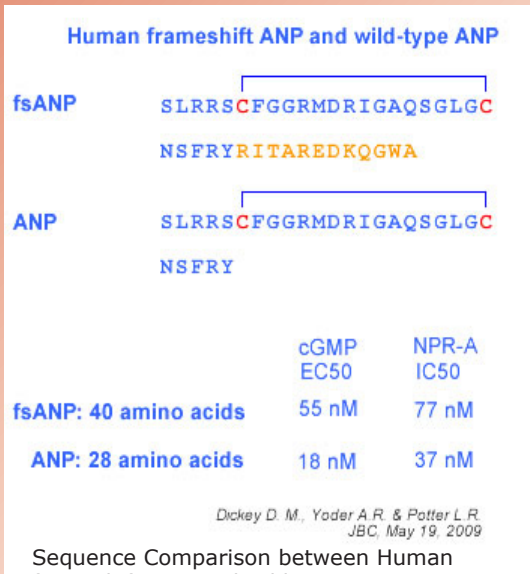
A familial mutation renders atrial natriuretic Peptide resistant to proteolytic degradation

A heterozygous frameshift mutation causing a 12-amino acid extension to the C terminus of atrial natriuretic peptide (ANP) was recently genetically linked to patients with familial atrial fibrillation (Hodgson-Zingman, D. M., Karst, M. L., Zingman, L. V., Heublein, D. M., Darbar, D., Herron, K. J., Ballew, J. D., de Andrade, M., Burnett, J. C., Jr., and Olson, T. M. (2008) N. Engl. J. Med. 359, 158-165). The frameshift product (fsANP), but not wild-type ANP (wtANP), was elevated in the serum of affected patients, but the molecular basis for the elevated peptide concentrations was not determined. Here, we measured the ability of fsANP to interact with natriuretic peptide receptors and to be proteolytically degraded. fsANP and wtANP bound and activated human NPR-A and NPR-C similarly, whereas fsANP had a slightly increased efficacy for human NPR-B. Proteolytic susceptibility was addressed with novel bioassays that measure the time required for kidney membranes or purified neutral endopeptidase to abolish ANP-dependent activation of NPR-A. The half-life of fsANP was markedly greater than that of wtANP in both assays. Additional membrane proteolysis studies indicated that wtANP and fsANP are preferentially degraded by neutral endopeptidase and serine peptidases, respectively. These data indicate that the familial ANP mutation associated with atrial fibrillation has only minor effects on natriuretic peptide receptor interactions but markedly modifies peptide proteolysis.
Dickey et al. J Biol Chem. 2009 Jul 17;284(29):19196-202. Epub 2009 May 19.

A human atrial natriuretic peptide gene mutation reveals a novel peptide with enhanced blood pressure-lowering, renal-enhancing, and aldosterone-suppressing actions

OBJECTIVES: We sought to determine the physiologic actions and potential therapeutic applications of mutant atrial natriuretic peptide (mANP). BACKGROUND: The cardiac hormone atrial natriuretic peptide (ANP) is a 28-amino acid (AA) peptide that consists of a 17-AA ring structure together with a 6-AA N-terminus and a 5-AA C-terminus. In a targeted scan for sequence variants within the human ANP gene, a mutation was identified that results in a 40-AA peptide consisting of native ANP((1-28)) and a C-terminal extension of 12 AA. We have termed this peptide mutant ANP. METHODS: In vitro 3',5'-cyclic guanosine monophosphate (cGMP) activation in response to mANP was studied in cultured human cardiac fibroblasts known to express natriuretic peptide receptor A. The cardiorenal and neurohumoral properties of mANP compared with ANP were assessed in vivo in normal dogs. RESULTS: We observed an incremental in vitro cGMP dose response with increasing concentrations of mANP. In vivo with high-dose mANP (33 pmol/kg/min), we observed significantly greater plasma cGMP activation, diuretic, natriuretic, glomerular filtration rate enhancing, renin-angiotensin-aldosterone system inhibiting, cardiac unloading, and blood pressure lowering properties when compared with native ANP. Low-dose mANP (2 pmol/kg/min) has natriuretic and diuretic properties without altering systemic hemodynamics compared with no natriuretic or diuretic response with low-dose native ANP. CONCLUSIONS: These studies establish that mANP activates cGMP in vitro and exerts greater and more sustained natriuretic, diuretic, glomerular filtration rate, and renal blood flow enhancing actions than native ANP in vivo.
McKie et al. J Am Coll Cardiol. 2009 Sep 8;54(11):1024-32

Catalog Number	Name	Standard Size
005-15	fsANP	100 µg
T-005-15	fsANP - I-125 Labeled	10 µCi
H-005-18	Urodilatin / ANP (95-126) - Antibody for Immunohistochemistry	50 µl
T-005-18	Urodilatin / ANP (95-126) - I-125 Labeled	10 µCi
RK-005-18	Urodilatin / ANP (95-126) - RIA Kit	1 kit
MRK-005-18	Urodilatin / ANP (95-126) - Magnetic Bead RIA kit	1 kit
G-005-18	Urodilatin / ANP (95-126) - Purified IgG Antibody	400 µg
T-G-005-18	Urodilatin / ANP (95-126) - I-125 Labeled Purified IgG	10 µCi
005-18	Urodilatin / ANP (95-126)	200 µg



Sequence Comparison between Human frameshift ANP and wild-type ANP

Phoenix Pharmaceuticals, Inc.
330 Beach Road, Burlingame CA, 94010, USA
Phone: (650) 558-8898 email: info@phoenixpeptide.com
www.phoenixpeptide.com

Phoenix Europe GmbH
Viktoriastrasse 3-5, D-76133 Karlsruhe, Germany
phone: +49-721-1611950 email: germany@phoenixpeptide.com
www.phoenixpeptide.com