Synthesis and biological activity of peptides equivalent to the IP22 repeat motif found in proteins from Dictyostelium and Mimivirus

Original Research Article

Pages 1799-1805

Andrew Catalano, Wei Luo, Yali Wang, Danton H. O’Day

Research highlights

Synthesis of variants a prototypical IP22 repeat: I/LPxxhxxhxhxxxhxxxhxxxx (where L = leucine, I = isoleucine, h = any hydrophobic amino acid, x = any amino acid). The IP22 peptides all dose-dependently enhanced random cell motility and cAMP-mediated chemotaxis in Dictyostelium. IP22-3 (IPKSLRSLFLGKGYNQPLEF) was most effective peaking in activity around 50 μM. FITC-conjugated IP22 peptides did not penetrate cells indicating they work via cell surface interactions. Treatment of IP22-3-stimulated cells with 50 μM LY294002, 20 μM quinacrine or both suggests that IP22-3 requires both phosphoinositol 3-kinase and phospholipase A2 signaling.

Potent and rapid bactericidal action of alyteserin-1c and its [E4K] analog against multidrug-resistant strains of Acinetobacter baumannii

Original Research Article

Pages 1806-1810

J. Michael Conlon, Eman Ahmed, Tibor Pal, Agnes Sonnevend

Research highlights

Alyteserin-1c is active against multidrug resistant strains of Acinetobacter baumannii (MDRAB). The analog [E4K]alyteserin-1c shows increased potency relative to the natural peptide and is non-toxic. [E4K]alyteserin-1c is
bactericidal producing rapid cell death. Palmitoylated analogs of [E4K]alyesterin-1c are strongly hemolytic.

4 Interaction of cationic antimicrobial peptides with phospholipid vesicles and their antibacterial activity  
Original Research Article  
Pages 1811-1820  
Hung-Ta Chou, Hsiao-Wei Wen, Tsun-Yung Kuo, Chai-Ching Lin, Wei-Jung Chen

Research highlights

► Cationic AMPs adopt amphipathic α-helical conformation in the presence of negatively charged vesicles (DOPC/DOPG = 1:3). ► Cationic AMPs effectively induce calcein-leakage when interacted with DOPC/DOPG-entrapped vesicles. ► Cationic AMPs show preferences for bacteria-mimicking anionic membranes. ► Cationic AMPs exert their cytolytic activity by folding into an amphipathic helix upon selectively binding and insertion into the target membrane, leading to breakdown of the membrane structure, thus causing leakage of cell contents, resulting finally in cell death. ► Elucidating the mechanism of the membranolytic activity of cationic AMPs may facilitate the development of more effective antimicrobial agents.

5 Antioxidant and free radical-scavenging activity of the extracellular death factor in Escherichia coli  
Original Research Article  
Pages 1821-1825  
Yanfeng Gao, Kun Chen, Bin Zhang, Xiang Li, Lu Chen, Yuanjun Li, Xiangjiao Jia, Yongxing Lei, Zhongyi Yan, Liangliang Kong, Nan Wang, Wei Liu, Yuanming Qi

Research highlights

► The antioxidant and free radical-scavenging activities of EDF were firstly studied. ► EDF could prevent proteins, lipids and DNA from being damaged by hydroxyl radicals. ► EDF might have dual effects during the programmed cell death process of Escherichia coli.

6 Mammalian cell toxicity and candidacidal mechanism of Arg- or Lys-containing Trp-rich model antimicrobial peptides and their d-enantiomeric peptides  
Original Research Article  
Pages 1826-1831  
Yong Hai Nan, Sung Haeng Lee, Hak Jun Kim, Song Yub Shin

Research highlights

► Arg-containing peptides (R₆L₂W₃ and R₆L₂W₃-D) were more toxic to human erythrocytes and mammalian cells as
compared to Lys-containing peptides (K₆L₂W₃ and K₆L₂W₃-D). Arg-containing peptides are slightly more hydrophobic than Lys-containing peptides. A little difference in the hydrophobicity of peptides affect their hemolytic activity and mammalian cell toxicity. Lys-containing peptides penetrated the cell wall and cell membrane and accumulated inside the cells, whereas Arg-containing peptides did not penetrate but associated with the membranes. The ultimate target site of action of Arg-containing peptides and Lys-containing peptides may be the membrane and the cytoplasm of Candida albicans, respectively.

A novel analog of antimicrobial peptide Polybia-MPI, with thioamide bond substitution, exhibits increased therapeutic efficacy against cancer and diminished toxicity in mice

Research highlights

- The stability of MPI-1 in serum, a novel analog of MPI with thioamide bond substitution, was significantly elevated.
- MPI-1 exhibited significantly lower mortality to mice than MPI.
- MPI-1 could remarkably suppress the growth of sarcoma xenograft tumors more efficiently than MPI.

A correlation of endocrine and anticancer effects of some antagonists of GHRH

Research highlights

- Human glioblastoma cell lines strongly express pGHRH-Rs.
- The anticancer activity of GHRH antagonists in glioblastomas reflects their endocrine potency.
- In glioblastoma cells GHRH antagonists cause upregulation of pGHRH-R gene expression.
- GHRH antagonists downregulate gene expression of SV1 of GHRH-R in glioblastoma cells.

Role of central NO-cGMP pathway in vasopressin and oxytocin gene expression during sepsis
Research highlights

- There is a differential hormone gene expression in the SON and PVN during sepsis.
- NO-cGMP pathway affects AVP and OXY gene expression in the hypothalamus.
- AVP and OXY gene expression may be also regulated independently of NO-cGMP pathway.

10 Lipopolysaccharide (LPS) detoxification of analogue peptides derived from limulus anti-LPS factor
Original Research Article
Pages 1853-1859
Jiadong Ren, Hongfu Gao, Min Tang, Jinsong Gu, Peiyuan Xia, Guangxia Xiao

Research highlights

- Lipopolysaccharide (LPS) plays a critical role in the pathogenesis of sepsis.
- A peptide (CLP19) derived from limulus anti-LPS factor (LALF) antagonized LPS significantly both in vitro and in vivo, but it displayed unnegligible hemolytic effect on human red blood cells.
- By amino acid substitution, two new peptides (CLP19-1 and CLP19-2) were obtained from CLP19 and their bioactivities were evaluated.
- CLP19-1 exhibited equivalent LPS-detoxifying activity and much lower hemolysis compared with CLP19, while CLP19-2 showed little anti-LPS and cytotoxicity activities.
- The changes in activities were probably attributable to the decrease of peptide hydrophobicity affected by substituting the hydrophobic residues by hydrophilic ones.

11 Calcitonin gene-related peptide regulates the growth of epidermal stem cells in vitro
Original Research Article
Pages 1860-1865
Jie Dong, Yanling He, Xiuying Zhang, Lei Wang, Tongzhu Sun, Meng Zhang, Yongqi Liang, Man Qi

Research highlights

- Epidermal stem cells grow well and keep high proliferative ability in vitro for a period of time with preservation of stem cell characteristics.
- CGRP (10^{-8} M) can stimulate epidermal stem cells detach from their niche, break quiescence and undergo division.
- The expression of β-catenin and c-myc genes are deregulated in CGRP (10^{-8} M) stimulating process, which can be compromised by CGRP8-37 peptide, an antagonist of CGRP receptor.

12 Development of retro-inverso peptides as anti-aggregation drugs for β-amyloid in Alzheimer's disease
Original Research Article
Pages 1866-1872
Research highlights

► Oligomeric forms of the peptide, β-amyloid, are known to damage neurons and to inhibit synaptic plasticity, leading to the cognitive decline in Alzheimer's disease. ► Synthetic peptides containing a retroinversion of residues 16–22 of β-amyloid have been synthesized. ► The retroinverted peptides were found to be more potent than native 16–22 peptides in preventing soluble oligomer and fibril formation from β-amyloid 40 and β-amyloid 42. ► The retroinverted peptides have higher efficacy at blocking the neurotoxicity of β-amyloid in human neuroblastoma cell cultures. ► As the retroinverted peptides prevent formation of both β-amyloid oligomers and fibrils, oligomers and fibrils are likely to be on the same biosynthetic pathway.

13 Identification of a novel muscle targeting peptide in mdx mice  
Yiqi Seow, Haifang Yin, Matthew J.A. Wood

Research highlights

► In vivo phage display in mdx mice identifies a muscle-binding motif. ► Muscle-binding peptide improved binding to C2C12 myoblasts. ► Peptide demonstrates affinity for the heart and quadriceps in vivo.

14 Effects of central neuropeptide S in the mouse formalin test  
Ya-Li Peng, Jian-Nan Zhang, Min Chang, Wei Li, Ren-Wen Han, Rui Wang

Research highlights

► Neuropeptide S (NPS) reduced both first-phase and second-phase nociceptive behaviors in the mouse formalin test, a model of inflammatory pain. ► NPS-induced antinociception was mediated via NPS receptor (NPSR), but not opioid receptors. ► NPS-elicited antinociceptive effect may be associated with the activation of the midbrain periaqueductal gray (PAG).

15 Activation of peritoneal macrophages during the evolution of type 1 diabetes (insulitis) in streptozotocin-treated mice  

Macrophages from diabetic mice (STZ treatment) release NO following stimulation with lipopolysaccharide and desArg9Bradykinin. A selective bradykinin B₁ receptor antagonist, R-954, blocks the release of NO which suggests the involvement of bradykinin B₁ receptors in this process. The release of NO from macrophages of STZ-treated mice precedes the development of hyperglycemia.

Research highlights

Melanocortin-4 receptor activation promotes insulin-stimulated mTOR signaling

Melanocortin receptor 4 agonist NDP-MSH potentiates insulin-stimulated mTOR phosphorylation in GT1-1 cells. cAMP pathway inhibitor Rp-cAMP and MAP kinase pathway inhibitor PD98059 are not involved in NDP-MSH actions on insulin-stimulated mTOR phosphorylation. AMP-activated protein kinase agonist AICAR attenuates the effect of NDP-MSH on insulin-stimulated mTOR phosphorylation.

Graphical abstract
Research highlights

 ► A novel ASIP/MSH hybrid pharmacophore has been designed. ► A direct on-resin peptide lactam cyclodimerization is reported. ► Cyclodimeric ASIP/MSH hybrid peptides displayed nM range hMC1R agonist activities.

CNP/GC-B system: A new regulator of adipogenesis

Original Research Article
Pages 1906-1911
Takeshi Katafuchi, David L. Garbers, Joseph P. Albanesi

Research highlights

 ► C-type natriuretic peptide (CNP) enhances adipogenesis in 3T3-L1 cells through a guanylyl cyclase-B/cGMP-dependent pathway. ► CNP mRNA level is transiently enhanced in early adipogenesis of 3T3-L1 cells. ► Lipolysis in adipocytes derived from 3T3-L1 cells is not enhanced upon stimulation with natriuretic peptides.

Peripheral leptin and ghrelin receptors are regulated in a tissue-specific manner in activity-based anorexia

Original Research Article
Pages 1912-1919
Maria Pardo, Arturo Roca-Rivada, Omar Al-Massadi, Luisa M. Seoane, Jesús P. Camiña, Felipe F. Casanueva

Research highlights

Under prolonged negative energy balance conditions: ► Visceral and gonadal fat participate more than subcutaneous fat in hypoleptinemia. ► Oxidative-soleus muscle appears to be more sensitive to ghrelin and leptin than glycolytic-gastrocnemius muscle. ► Only subcutaneous fat express the active LEPR form. ► Chronic hyperghrelinemia prevents lipid loss on visceral and subcutaneous fat by inducing GHS-R1a expression.
Expression of kisspeptins and kisspeptin receptor in the kidney of chronic renal failure rats

Original Research Article

Pages 1920-1925

Itaru Shoji, Takuo Hirose, Nobuyoshi Mori, Keisuke Hiraishi, Ichiro Kato, Akiko Shibasaki, Hajime Yamamoto, Koji Ohba, Kiriko Kaneko, Ryo Morimoto, Fumitoshi Satoh, Masahiro Kohzuki, Kazuhiro Totsune, Kazuhiro Takahashi

Research highlights

► Kisspeptins and kisspeptin receptor are expressed in the kidney. ► They are expressed mainly in tubular cells and collecting duct cells. ► The expression levels are altered in the kidney tissues of chronic renal impairment. ► The expression levels of kisspeptin mRNA and peptide are not parallel. ► The expression levels of kisspeptin receptor mRNA and protein are also not parallel.

Lactoferricin B-derived peptides with inhibitory effects on ECE-dependent vasoconstriction

Original Research Article

Pages 1926-1933

Ricardo Fernández-Musoles, José Javier López-Díez, Germán Torregrosa, Salvador Vallés, Enrique Alborch, Paloma Manzanares, Juan B. Salom

Research highlights

► LfcinB-derived peptides inhibit endothelin-converting enzyme (ECE) activity. ► LfcinB-derived peptides inhibit ECE-dependent vasoconstriction. ► LfcinB-derived peptides are dual vasopeptidase (ACE/ECE) inhibitors. ► LfcinB-derived peptides are potentially antihypertensive peptides of milk protein origin.

Altered cardiovascular reflexes responses in conscious Angiotensin-(1-7) receptor Mas-knockout mice

Original Research Article

Pages 1934-1939

Marina Matos de Moura, Robson Augusto Souza dos Santos, Maria José Campagnole-Santos, Mihail Todiras, Michael Bader, Natalia Alenina, Andréa Siqueira Haibara

Research highlights

► Genetic deletion of the Ang-(1-7) receptor Mas impaired the baroreflex bradycardia. ► Cardiovascular responses of Bezold–Jarisch reflex were lower in Mas-knockout mice. ► Mas-deficiency in mice increased the pressor and bradycardic
chemoreflex responses. ▶ Actions of Ang-(1-7) on cardiovascular reflexes seem to oppose those mediated by Ang II.

23 ▶ Mechanism of cigarette smoke-induced kinin B₁ receptor expression in rat airways  Original Research Article

*Pages 1940-1945*

James Chi-Jen Lin, Sébastien Talbot, Karim Lahjouji, Jean-Philippe Roy, Jacques Sénécal, Réjean Couture, André Morin

**Research highlights**

▶ Expression of kinin type 1 receptor (B₁R) and IL-1β is enhanced in rat lung slices treated with total particulate matter (TPM) of cigarette smoke. ▶ Induction of kinin type 2 receptor (B₂R) and TNF-α gene by TPM is not significant. ▶ Protein expression of B₁R is totally blocked by a co-treatment with IL-1Ra, a IL-1 receptor antagonist. ▶ B₁R is involved in cigarette smoke-induced airway inflammation through a mechanism mediated by IL-1β.

**Short communication**

24 ▶ B-type natriuretic peptide in outpatients after myocardial infarction: Optimized cut-off value for incident heart failure prediction  Pages 1946-1948

Mina Radovanovic, Zorana Vasiljevic, Nebojsa Radovanovic, Jelena Marinkovic, Branko Beleslin, Predrag Mitrovic, Sanja Stankovic, Goran Stankovic

**Review**

25 ▶ Antioxidative peptides from food proteins: A review  Review Article  Pages 1949-1956

Bahareh H. Sarmadi, Amin Ismail