

Study on the mechanisms of alternative mRNA splicing that regulates the regulation of angiogenesis and diabetic complication susceptibility

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2006 Fiscal Year Final Research Report Summary

Study on the mechanisms of alternative mRNA splicing that regulates the regulation of angiogenesis and diabetic complication susceptibility

Research Project

Project/Area Number

17590241

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

General medical chemistry

Research Institution

Kanazawa Medical University (2006)

Kanazawa University (2005)

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Project Period (FY)

2005 – 2006

Keywords

angiogenesis / diabetic complications / alternative 3'-end processing / alternative splicing / regulatory element / vascular endothelial cell / soluble VEGF receptor / soluble RAGE

Research Abstract

In this research, we studied the mechanisms of alternative pre-mRNA splicing/processing by which mRNAs for soluble RAGE and soluble VEGF receptor are produced, and their roles in the regulation of diabetic vascular complications and angiogenesis. Soluble RAGE has a protective activity against AGE-induced vascular cell injury and soluble VEGF receptor acts as a potent anti-angiogenic factor.

(1) We isolated the marine equivalent of soluble RAGE by RT-PCR cloning. This study will provide an animal orthologue of soluble RAGE to clarify its roles in health and disease.

(2) We investigated the expression of soluble RAGE protein in human organs and tissues by immunohistochemical analysis, and found that soluble RAGE was widely distributed in various organs and tissues including vascular endothelium, neurons, pancreatic β cells, macrophages/monocytes, bile ducts, salivary glands, digestive tracts, renal tubules, prostate, skin, and thyroid.

(3) We developed enzyme-linked immunosorbent assay (ELISA) for human soluble RAGE and examined the association of plasma soluble RAGE level with atherosclerosis, and found that it inversely correlated with carotid or femoral atherosclerosis.

(4) We established an assay system for RAGE alternative splicing using a human RAGE mini-gene and HEK293T cells. Transfection experiments with various mutant RAGE mini-genes identified cis-acting elements on RAGE pre-mRNA, which regulated the alternative splicing of soluble RAGE mRNA. We also found the involvement of hnRNP-H in the regulation of soluble RAGE mRNA production.

(4) We established an assay system for alternative 3'-end processing of VEGF receptor-1 (Flt-1) mRNA using a human Flt-1 mini-gene and primary cultured human vascular endothelial cells, and identified a cis-acting element on Flt-1 pre-mRNA, which regulated the production of soluble Flt-1 mRNA.

Research Products (47 results)

	All	2007	2006	2005	Other
	All	Journal Article	Book	Patent(Industrial Property Rights)	
[Journal Article] Endogenous secretory receptor for advanced glycation endproducts levels are correlated with serum pentosidine and CML in patients with type 1 diabetes.		2007			▼
[Journal Article] Endogenous secretory receptor for advanced glycation end products in non-small cell lung carcinoma.		2007			▼
[Journal Article] Inhibition of diabetic leukostasis and blood-retinal barrier breakdown with a soluble form of a receptor for advanced glycation end products.		2007			▼
[Journal Article] Short-chain aldehyde-derived ligands for RAGE and their actions on endothelial cells.		2007			▼
[Journal Article] Assaying soluble forms of receptor for advanced glycation endproducts.		2007			▼
[Journal Article] RAGE in diabetic nephropathy.		2007			▼
[Journal Article] Endogenous Secretory Receptor for Advanced Glycation Endproducts - a Novel Prognostic Marker of Chondrosarcomas.		2007			▼
[Journal Article] Endogenous secretory receptor for advanced glycation endproducts levels are correlated with serum pentosidine and CML in patients with type 1 diabetes.		2007			▼
[Journal Article] Endogenous secretory receptor for advanced glycation end products in non-small cell lung carcinoma.		2007			▼
[Journal Article] Inhibition of diabetic leukostasis and blood-retinal barrier breakdown with a soluble form of a receptor for advanced glycation end products		2007			▼
[Journal Article] Short-chain aldehyde-derived ligands for RAGE and their actions on endothelial cells.		2007			▼
[Journal Article] Assaying soluble forms of receptor for advanced glycation endproducts.		2007			▼
[Journal Article] RAGE in diabetic nephropathy.		2007			▼
[Journal Article] Endogenous Secretory Receptor for Advanced Glycation Endproducts-a Novel Prognostic Marker of Chondrosarcomas.		2007			▼
[Journal Article] A severe diabetic nephropathy model with early development of nodule-like lesions induced by megsin overexpression in RAGE/iNOS transgenic mice.		2006			▼
[Journal Article] Isoflavones Inhibit Nicotine C-Oxidation Catalyzed by Human CYP2A6.		2006			▼
[Journal Article] Isolation and expression analysis of mouse endogenous secretory receptor for advanced glycation endproducts (esRAGE).		2006			▼
[Journal Article] Receptor for advanced glycation endproducts is involved in impaired angiogenic response in diabetes.		2006			▼
[Journal Article] RAGE control of diabetic nephropathy in a mouse model : effects of RAGE gene disruption and administration of low-molecular weight heparin.		2006			▼

[Journal Article] Development of an ELISA system for a circulating decoy receptor for AGE and its application to type 1 diabetic patients.	2006	▼
[Journal Article] A severe diabetic nephropathy model with early development of nodule-like lesions induced by megsin overexpression in RAGE/iNOS transgenic mice.	2006	▼
[Journal Article] Isoflavones inhibit nicotine C-oxidation catalyzed by human CYP2A6.	2006	▼
[Journal Article] Isolation and expression analysis of mouse endogenous secretory receptor for advanced glycation endproducts (esRAGE).	2006	▼
[Journal Article] Development of an ELISA system for a circulating decoy receptor for AGE and its application to type 1 diabetic patients.	2006	▼
[Journal Article] Roles of the receptor for advanced glycation endproducts in diabetes-induced vascular injury.	2005	▼
[Journal Article] Expression profiling of endogenous secretory receptor for advanced glycation end products in human organs.	2005	▼
[Journal Article] Blockage of diabetic vascular injury by controlling of AGE-RAGE system.	2005	▼
[Journal Article] Receptor for advanced glycation end products is a promising target of diabetic nephropathy.	2005	▼
[Journal Article] Plasma level of endogenous secretory receptor for advanced glycation endproducts (esRAGE) is associated with components of the metabolic syndrome and atherosclerotic arterial wall thickness.	2005	▼
[Journal Article] 糖尿病血管合併症の分子機構-糖化蛋白受容体(RAGE)の役割-	2005	▼
[Journal Article] 糖尿病腎症におけるAGE-RAGE相互作用	2005	▼
[Journal Article] AGE-RAGE系	2005	▼
[Journal Article] Roles of the receptor for advanced glycation endproducts in diabetes-induced vascular injury.	2005	▼
[Journal Article] Expression profiling of endogenous secretory receptor for advanced glycation end products in human organs.	2005	▼
[Journal Article] Blockage of diabetic vascular injury by controlling of AGE-RAGE system.	2005	▼
[Journal Article] Receptor for advanced glycation end products is a promising target of diabetic nephropathy.	2005	▼
[Journal Article] Plasma level of endogenous secretory receptor for advanced glycation endproducts (esRAGE) is associated with components of the metabolic syndrome and atherosclerotic arterial wall thickness.	2005	▼
[Journal Article] Molecular Mechanism of Diabetic Angiopathy-Roles of the receptor for advanced glycation endproducts in diabetes-induced vascular injury-(in Japanese)	2005	▼
[Journal Article] AGE-RAGE interaction in diabetic nephropathy. (in Japanese)	2005	▼
[Journal Article] AGE-RAGE system in diabetic microangiopathy. (in Japanese)	2005	▼
[Journal Article] Gene screening by antisense DNA-Principle and application of the antisense display method.		▼
[Book] アンチセンスDNAを用いた機能的遺伝子同定法-アンチセンスディスプレイ法の原理と適用-(RNAi法とアンチセンス法-RNAの科学と応用)(pp. 189-199)(関根光雄,多比良和誠編)	2005	▼
[Patent(Industrial Property Rights)] RAGE阻害剤	2006	▼
[Patent(Industrial Property Rights)] RAGEポリペプチドの新規用途	2006	▼
[Patent(Industrial Property Rights)] RAGEポリペプチドの新規用途	2006	▼
[Patent(Industrial Property Rights)] アルツハイマー病の診断方法	2006	▼
[Patent(Industrial Property Rights)] 早期肺癌の術後予後検査方法	2005	▼

