(Fiscal Year 2007-2009)

# Hirosaki Area

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#### Framework for Project Promotion

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Applied Research and Product Development of Proteoglycan to

#### **Core Research Organization**

Contribute to QOL Improvement

Hirosaki University

## **Major Participating Research Organizations**

Industry...Kakuhiro Co., Ltd., Sunstar Co., Ltd., Otsuka Pharmaceutical Co., Ltd. Academia...Hirosaki University Government····Aomori Industrial Research Center

# **Aims of Project**

Hirosaki University possesses a large amount of intellectual property and sophisticated proteoglycan bioengineering technology. Taking advantage of this know-how and the expertise of researchers, as a national and international pioneer we are pursuing collaborative research into the development of proteoglycan as functional foods, antiaging nursing materials, skin care products, oral care products, cosmetics, medicines, and medical materials based on the research results of the earlier Joint Platform Project.

## **Contents of Project**

# 1. Research and Development into the Commercialization of Proteoglycan-containing Functional Foods

We validated the usability of a proteoglycan-containing micro-powder, "Hirosaki University Natural Proteoglycan Powder," which was prepared using a production procedure established in the 2007 fiscal year. We also prepared prototype products via collaborative research with public research institutes in Aomori Prefecture. To develop and commercialize the products as functional foods, we analyzed the proteoglycan structure in the proteoglycan-containing material and prototype products. We then validated the functionality of the products and standardized them as food materials.

#### 2. Application of Proteoglycan to prevent Skin Anti-aging and as a Cosmetic

Skin anti-aging effects are studied by administering to hairless mice the proteoglycan derived from the nose cartilage of salmon in combination with hyaluronic acid, collagen (these first two products are extra-cellular matrix components), vitamins, and essential trace elements. The optimum combination of ingredients will soon be determined. Based on the results, we will apply the developed products in the fields of skin anti-aging and cosmetics.

#### 3. Application of Proteoglycan in the Discovery of New Drugs

We will analyze the functional region of proteoglycans based on our accumulated knowledge of this class of glycoprotein. Furthermore, we will establish a semi-automated reconstruction system of novel glycosaminoglycan oligosaccharides and proteoglycans. Based on this procedure, we will synthesize custom-made glycosaminoglycan oligosaccharides or proteoglycans, and determine their active components, leading to the discovery of new drugs.

#### 4. Research and Development of Proteoglycan-Containing Medicines and Medical Materials

We will seek to validate the safety of proteoglycan for use in medicines and medical materials. Thereafter, we will develop therapeutic applications against autoimmune diseases and allergic diseases (atopic diseases etc.), protective applications such as immunoregulatory potency, a thrombopoiesis-accelerating drug for the treatment of pancytopenia caused by radiation therapy for malignant tumor or chemotherapy, medical materials for cartilage repair in patients with osteoarthritis of the knee, and a diagnostic marker for bone metabolism disorders associated with aging and menopause.

### **Main Results**

# 1. Research and Development to Commercialize Proteoglycan-containing Functional Foods

We undertook the tasks of standardizing and reducing the production costs of proteoglycan-containing functional foods, and established the processing technology required for a proteoglycan micro-powder, "Hirosaki University Natural Proteoglycan Powder (NPGP)." The results of a basic toxicity test and sub-acute toxicity test confirmed the safety of this product.



Hirosaki University Natural Proteoglycan Powder



Apple Juice with PG, Apple Vinegar with PG (prototype)





29

2. Application of Proteoglycan in the Fields of Skin Anti-aging and Cosmetics

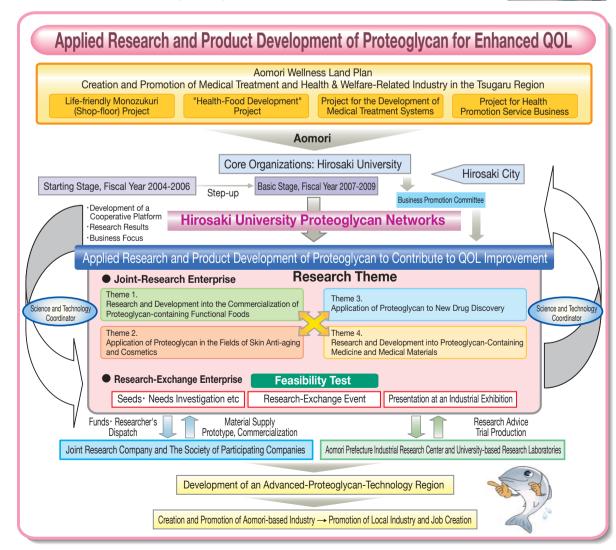
To determine the optimum effect of proteoglycan derived from the nose cartilage of salmon on skin anti-aging, we performed experiments in which hairless mice were administered proteoglycan combined with hyaluronic acid, collagen (as an extracellular matrix component), vitamins, or metal ions. Based on the experiment results, we began research and development into skin-related products taken by oral ingestion.

#### 3. Application of Proteoglycan for New Drug Discovery

We succeeded in the artificial synthesis of desired proteoglycans by the enzymatic and/or chemical reconstruction of glycosaminoglycan chains (of proteoglycans), representing a world-first technology. The reconstruction technology of glycosaminoglycan oligosaccharides and proteoglycans is not only useful for functional analysis, but also represents an important platform for applications in new drug discovery.

# 4. Research and Development into Proteoglycan-Containing Medicine and Medial Materials

We observed the protective effect of proteoglycan by treating model mice with experimental allergic encephalomyelitis, and found a suppressive effect of proteoglycan on the blood glucose level of a diabetic mouse model. We studied the effect of proteoglycan on cartilage regeneration and the mesenchymal stem-cell system, and found that treatment with proteoglycan-embedded collagen sponge showed an excellent cartilage-repair effect in an experimental model with damaged cartilage.



28