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S-Quatre Corporation
Dokkyo Medical University
HOYA Technosurgical Corporation

Joint research agreement signed for the development of a new treatment for ischemic bone diseases

S-Quatre Corporation (Headquarters: Chuo-ku, Tokyo; President and CEO: Yasuyuki Mitani; hereinafter referred to as "S-Quatre"), Dokkyo Medical University (Shimotsuga, Tochigi; President: Kenichiro Yoshida; hereinafter referred to as "DMU"), and HOYA Technosurgical Corporation (Headquarters: Shinjuku-ku, Tokyo; President and CEO: Yasuyuki Nitta; hereinafter referred to as "HOTS") are pleased to announce the signing of a joint research agreement (hereinafter referred to as "the Agreement") aimed at developing a new treatment for ischemic bone diseases.

Ischemic bone diseases are conditions in which bone tissue becomes necrotic due to ischemia, or reduced blood flow. The femoral head, which forms the hip joint, is particularly at high risk of ischemia, leading to conditions such as necrosis following fractures that fail to heal or the development of a disease known as idiopathic osteonecrosis of the femoral head¹, even in the absence of fractures. This disease is a designated intractable condition in which the femoral head undergoes ischemic necrosis, collapses, and leads to the loss of hip joint function. Currently, no treatment has been established to prevent the progression of this collapse.

The Agreement aims to develop a novel treatment for ischemic bone diseases by leveraging the expertise of the three parties involved: S-Quatre, which focuses on research and development of regenerative medical products using stem cells from human exfoliated deciduous teeth (SHED²); DMU, which has extensive clinical experience in treating bone diseases; and HOTS, which has a proven track record in the development of bone graft materials.

Previous research has demonstrated that S-Quatre's proprietary SHED (SQ-SHED) exhibits superior angiogenic potential. Moreover, a joint study between S-Quatre and Hokkaido University (hereinafter referred to as "HU") confirmed that combining SHED with certain bone graft materials significantly enhances bone regeneration in animal models. These findings suggest that the combination of SHED and bone graft materials could offer a promising treatment for ischemic bone diseases.

Following the relocation of the joint research lead from HU to DMU, the ongoing collaborative

research will now be continued at DMU.

The Orthopedic Surgery Department at DMU has long been actively involved in research to enhance treatment efficacy and develop new surgical techniques for fractures and bone diseases, with numerous achievements to date. Additionally, HOTS has contributed to the treatment of patients with fractures and bone diseases, as well as improving their quality of life (QOL), through the development and commercialization of various medical devices, including bone graft materials, based on its advanced technological and developmental capabilities.

This joint research agreement seeks to combine the knowledge, experience, technology, and products of S-Quatre, DMU, and HOTS to develop a groundbreaking treatment for ischemic conditions, including the prevention of femoral head collapse in idiopathic osteonecrosis of the femoral head. Building on the foundational research results, the collaboration will advance to clinical trial-oriented formulation development and investigation of implantation methods into the femoral head. The ultimate goal is to improve the QOL of patients suffering from ischemic bone diseases, for which no established treatment exists globally.

1. Idiopathic osteonecrosis of the femoral head refers to cases of femoral head necrosis where no clear cause, such as dislocation or fracture, is identified. In Japan, 2,000 to 3,000 new cases are reported annually, predominantly affecting people in their 30s to 50s. When femoral head collapse progresses, hip replacement surgery is performed, but regular follow-up is necessary to check for dislocation or loosening post-surgery, and reoperation may be required 10 to 20 years later.

*Source: Japan Intractable Diseases Information Center
(<https://www.nanbyou.or.jp/entry/160>)

2. SHED: Stem Cells from Human Exfoliated Deciduous Teeth. These stem cells are isolated and cultured from the dental pulp of deciduous teeth, characterized by their high proliferative capacity and secretion of various growth factors essential for tissue regeneration.

About S-Quatre Corporation

S-Quatre Corporation aims to develop and provide cell-based therapeutics for rare and intractable diseases by leveraging its proprietary system for the stable supply of stem cells from human exfoliated deciduous teeth. The company is dedicated to delivering innovative treatments and therapies to patients suffering from diseases, injuries, and disabilities, particularly children, to help create a society where they can live bright and happy lives. For more information, please visit the website.

<https://www.kidswellbio.com/en/s-quatre/>

About Dokkyo Medical University

Dokkyo Medical University, established in April 1973 in Mibu, Tochigi Prefecture, is committed to the education and research of general liberal arts, medicine, and nursing. The university aims to cultivate physicians, public health nurses, midwives, and nurses with advanced medical knowledge and skills, contributing to the development of medicine, nursing, and welfare. For

more information, please visit the website.

<https://www.dokkyomed.ac.jp/dmu/english>

About HOYA Technosurgical Corporation

HOYA Technosurgical Corporation is committed to providing superior products in the field of orthopedics through the manufacturing and sale of ceramic implants (e.g., artificial bones) and metal implants (e.g., bone fixation devices). In addition, we strive to further contribute to the advancement of medical care in the fields of neurosurgery, plastic surgery, and dentistry. For more information, please visit the website.

<https://www.hoyatechnosurgical.co.jp/en/index.html>

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