Report of “Research Award of Oral Sciences”

Major: Oral Sciences
Grade: 4
Department: Orthodontics and Dentofacial Orthopedics
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Title: Co-Administration of Myostatin-Targeting siRNA and ActRIIB-Fc Fusion Protein Increases Masseter Muscle Mass and Fiber Size

1. Aim of research and results obtained (Approximately 400 words):

Myostatin, a member of the TGF-ß superfamily, is a negative regulator of skeletal muscle cell growth and differentiation, and binds with high affinity to the activin type IIB receptor (ActRIIB). The soluble ligand-binding domain of Activin RIIB fused to the Fc domain of IgG (ActRIIB-Fc) potently binds and inhibits TGF-ß family members in muscle, leading to rapid and marked muscle growth.

The present study was designed to assess the effectiveness of the co-delivery of myostatin-targeting siRNA (Mstn-siRNA) and ActRIIB-Fc into skeletal muscle as a potential treatment of atrophic myopathies. Eleven-week-old, male C57BL/6 mice were injected with atelocollagen (ATCOL)-mediated Mstn-siRNA with/without ActRIIB-Fc locally into the masseter muscle twice a week.

Inhibition of myostatin function by the combination of Mstn-siRNA and ActRIIB-Fc increased muscle weight and myofibril size in murine masseter muscle. Realtime PCR analysis revealed significant downregulation of myostatin mRNA expression in both Mstn-siRNA-treated and the combination treatment group. Furthermore, myogenin mRNA expression was upregulated in the combination treatment group, while MuRF-1 and Atrogin-1 mRNA expression was downregulated compared to administration of each compound alone. These findings suggest that double inhibition of myostatin is a potentially useful treatment strategy to increase muscle mass and fiber size and could be a useful treatment of patients with various muscle atrophies, including muscular dystrophy.

2. Self-evaluation of research achievement:

I am writing to express my sincere gratitude to Tokushima University Graduate School of Oral Sciences for making the “Bronze” winner (Research Award of Oral

Science) possible. This award has given me chance to attend the annual meeting of "The study group-aiming at structuring fundamentals of muscular dystrophy clinical trial" on December 6-7th 2016, Tokyo, Japan. It was great opportunity for me. This award has allowed me to not only maintain focus on my studies and research, but to also contribute to my community.

3. Meeting presentation:
   * Title, conference, venue, date, co-author, presentation (oral/ poster).
   (Underline the speaker.)
   - Effectiveness of myostatin targeting siRNA and ActRIIB-Fc fusion protein in skeletal muscle mass, *第 75 回日本矯正歯科学会大会プログラム・抄録集*, p.316, Nov. 2016, Bayarsaikhan Od, Nobuhiko Kawai, Hiroyo Mori, Nao Kinouchi, Takeshi Nikawa, Eiji Tanaka, (Poster).

4. Journal publication:
   * Title, journal, volume, number, paragraph, date, co-author.
   (Underline the speaker.)
   - Effects of co-transfection with myostatin-targeting siRNA and ActRIIB-Fc fusion protein on skeletal muscle growth, *Journal of Oral Health and Biosciences*, in press, Bayarsaikhan Od, Nobuhiko Kawai, Hiroyo Mori, Nao Kinouchi, Takeshi Nikawa, Eiji Tanaka.