Report of "Research Award of Oral Sciences"

Major: Oral Sciences
Grade: 4

Department: Pediatric Dentistry
Name: Anrizandy Narwidina

Title: Iroquois homeobox 3 regulates odontoblast proliferation and differentiation mediated byWnt5a expression

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

Iroquois homeobox (Irx) genes are TALE-class homeobox genes that are evolutionarily conserved across species and have multiple critical cellular functions in fundamental tissue development processes. Previous studies have shown that Irxs genes are expressed during tooth development. However, the precise roles of genes in teeth remains unclear. Here, we demonstrated for the first time that Irx3 is an essential molecule for the proliferation and differentiation of odontoblasts. Using cDNA synthesized from postnatal day 1 (P1) tooth germs, we examined the expression of all Irx genes (*Irx1-Irx6*) by RT-PCR and found that all genes except *Irx4* were expressed in the tooth tissue. *Irx1-Irx3* a were expressed in the dental epithelial cell line M3H1 cells, while *Irx3* and *Irx5* were expressed in the dental mesenchymal cell line mDP cells. Only *Irx3* was expressed in both undifferentiated cell lines. Immunostaining also revealed the presence of IRX3 in the dental epithelial cells and mesenchymal condensation. Inhibition of endogenous *Irx3* by siRNA blocks the proliferation and differentiation of mDP cells. *Wnt3a*, *Wnt5a*, and *Bmp4* are factors involved in odontoblast differentiation and were highly expressed in mDP cells by quantitative PCR analysis. Interestingly, the expression of *Wnt5a* (but not *Wnt3a* or *Bmp4*) was suppressed by *Irx3* siRNA. These results suggest that Irx3 plays an essential role in the proliferation and differentiation of dental mesenchymal cells by regulating Wnt5a expression during odontoblastic differentiation.

2. Self-evaluation of research achievement:

First, I would like to express my sincere gratitude to Prof. Otto Baba as the Dean, of the Graduate School of Oral Sciences for the "Research Award of Oral Sciences" to encourage me as a Ph.D student to support the research work. During my research work, I learn a lot of things. Life experience has taught me that a successful outcome is always determined by many small things that should be well-prepared before performing research work. Sometimes, unexpected results come, but I always remind myself that ***"nothing good comes easy"***. Fortunately, I was surrounded by an excellent research environment that widened my paradigm about sciences. Continuous supervision and discussion with Professor Tsutomu Iwamoto, DDS, Ph.D , Professor Tomonori Iwasaki, DDS, Ph.D, Aya Miyazaki, DDS, Ph.D, and other colleagues also stimulate critical thinking and improve the capability of the latest research technologies.

Research Achievement
1. International Education and Research Fund Awardee, Fujii Otsuka, 2021
2. Futoku Foundation-International Grant, 2021
3. The Excellent Presenter of Interim Presentation, Graduate School of Oral Sciences, Tokushima University. 2021
4. 1st Prize of Scientific Literature Review Award, Indonesia Association of Pediatric Dentistry. Indonesia 2019
5. 1st Prize of Scientific Research Award, Indonesia Association of Pediatric Dentistry, Indonesia 2021
6. The Excellent Presenter/ Winner of Tokushima Bioscience Retreat. 2022
7. 1st Prize of Scientific Award, Indonesia Association of Pediatric Dentistry, Indonesia, 2023
8. Scientific Poster Presenter and Delegate, "Iroquois 3 plays an essential role in odontogenesis". International Genomics Conference, Lorne-Melbourne, Australia, 2023

3. Meeting presentation:

The presentations with this award's support

1. Iroquois 3 plays an essential role in odontogenesis, International Genomics Conference, Lorne- Melbourne, Australia, 9-11 February 2023, **Anrizandy Narwidina**, Aya Miyazaki, Kokoro Iwata, Rika Kurogoshi, Tomonori Iwasaki, Tsutomu Iwamoto. presentation (poster).
2. Iroquois homeobox 3 regulates odontoblast proliferation and differentiation mediated by Wnt5a expression, Scientific Meeting of Indonesia Association of Pediatric Dentistry, Indonesia, 9-11 March 2023, **Anrizandy Narwidina,** Aya Miyazaki, Kokoro Iwata, Rika Kurogoshi, Tomonori Iwasaki, Tsutomu Iwamoto. presentation (poster).

4. Journal publication:

The presentations with this award's support

1. **Narwidina A**, Miyazaki A, Iwata K, Kurogoushi R, Sugimoto A, Kudo Y, Kawarabayashi K, Yamakawa Y, Akazawa Y, Kitamura T, Nakagawa H, Yamaguchi-Ueda K, Hasegawa T, Yoshizaki K, Fukumoto S, Yamamoto A, Ishimaru N, Iwasaki T, Iwamoto T. Iroquois homeobox 3 regulates odontoblast proliferation and differentiation mediated by Wnt5a expression. Biochem Biophys Res Commun. 2023 Apr 2;650:47-54. doi: 10.1016/j.bbrc.2023.02.004. Epub 2023 Feb 4. PMID: 36773339.