Department of Regenerative Science

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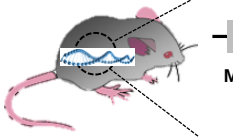
Analysis of the molecular biological features of mesenchymal stem cells *in vivo*

We are studying mesenchymal stem cells (MSCs), a type of tissue stem cells. In clinical studies, cultured MSCs have shown important therapeutic effects on disease, reducing neurological defects and regulating immune responses. However, *in vivo* MSC localization, function, and properties are poorly understood. To address these issues, we are developing a method that allows us to **visualize** MSCs *in vivo*, **manipulate** MSC function *in vivo*, and **understand** the molecular biology of MSCs *in vivo*. Using this approach will enable us to understand the molecular biology features of MSCs *in vivo*, leading to therapeutic applications for tissue repair and regeneration.

Main research techniques

Visualization

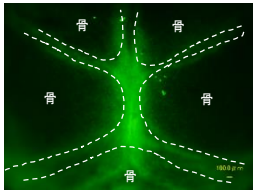


MSC specific promoter — Fluorescent protein

GFP(Green), tdTomato(Red) etc..

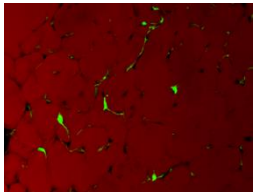
Generation of mouse for understanding the MSC localization

■Bone



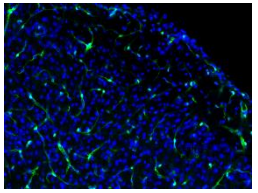
Green : MSC

■Fat



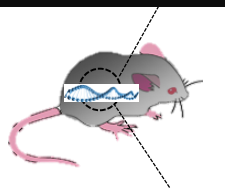
Red : Adipocyte, Green : MSC

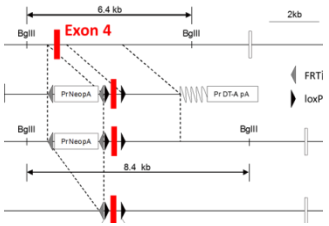
■Brain



Blue : Nuclei, Green : MSC

Manipulation





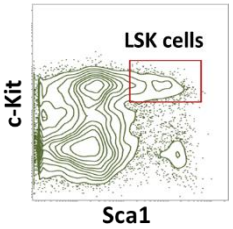
Generation of mouse for understanding the MSC function

■Skeletogenesis

WT

Deletion

■Hematopoiesis



■Metabolism

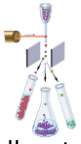
■Brain function

■Disease model

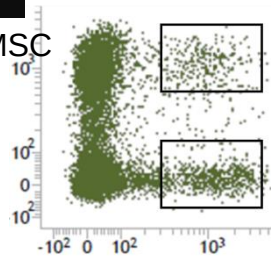
Bone disease
Metabolic disease
Cancer
Immunological disease
Neurological disease

Understanding

■Collect the MSC



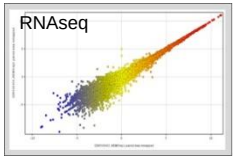
Cell sorter



■Molecular

Molecular biological techniques

Omics（RNAseq）



■Lineage

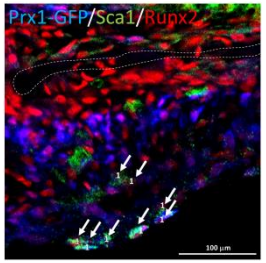
Hierarchy

Lineage determination

Stemness

XX+ ZZ +MSC

■Localization



Selected publications

#: corresponding author

Ryota Nakazato, Kenji Kawabe, Daisuke Yamada, Shinsuke Ikeno, Michihiro Mieda, Shigeki Shimba, Eiichi Hinoi, Yukio Yoneda and **Takeshi Takarada#** (2017) Disruption of Bmal1 impairs blood–brain barrier integrity via pericyte dysfunction. *J. Neurosci.* doi: 10.1523/JNEUROSCI.3639-16.2017.

Lifan Liao, Shanxing Zhang, Jianhong Gu, Weiwei Zhao, **Takeshi Takarada,** Yukio Yoneda, Jian Huang, Lan Zhao, Chun-do Oh, Jun Li, Mei-qing Wang, and Di Chen (2017) Deletion of Runx2 in Articular Chondrocytes Decelerates the Progression of DMM-Induced Osteoarthritis in Adult Mice. *Sci. Rep.* 7, 1:2371.

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Takeshi Takarada#, Cheng Xu, Hiroki Ochi, Ryota Nakazato, Daisuke Yamada, Saki Nakamura, Ayumi Kodama, Shigeki Shimba, Michihiro Mieda, Kazuya Fukasawa, Kakeru Ozaki, Takashi Iezaki, Koichi Fujikawa, Yukio Yoneda, Rika Numano, Akiko Hida, Hajime Tei, Shu Takeda and Eiichi Hinoi (2017) Bone resorption is regulated by circadian clock in osteoblasts. *J. Bone Miner. Res.* 32, 872-881.

Jianwen Wei, Junko Shimazu, Munevver P. Makinistoglu, Antonio Maurizi, Daisuke Kajimura, Haihong Zong, **Takeshi Takarada**, Takashi Iezaki, Jeffrey E. Pessin, Eiichi Hinoi and Gerard Karsenty (2015) Glucose uptake and Runx2 synergize to orchestrate osteoblast differentiation and bone formation. *Cell* 161, 1576-1591.

Takeshi Takarada, Eiichi Hinoi, Ryota Nakazato, Hiroki Ochi, Cheng Xu, Azusa Tsuchikane, Shu Takeda, Gerard Karsenty, Takaya Abe, Hiroshi Kiyonari, and Yukio Yoneda (2013) An analysis of skeletal development in osteoblast- and chondrocyte-specific Runx2 knockout mice. *J. Bone Miner. Res.* 28, 2064-2069.

Takeshi Takarada, Ayumi Kodama, Shogo Hotta, Michihiro Mieda, Shigeki Shimba, Eiichi Hinoi and Yukio Yoneda (2012) Clock genes influence gene expression in growth plate and endochondral ossification in mice. *J. Biol. Chem.* 287, 36081-36095.

Members (2017)

2 Assistant Professors
1 PhD course student,
5 Master course students