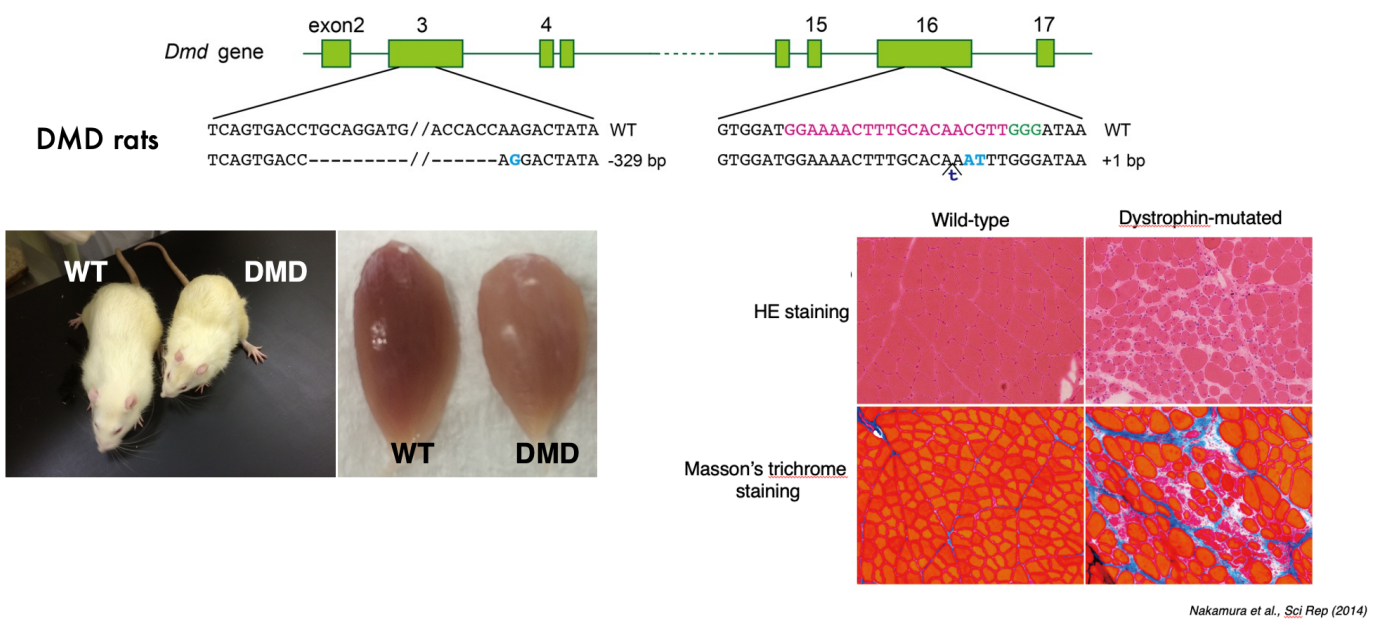
1. Identification of a new drug target for Duchenne muscular dystrophy

Duchenne muscular dystrophy is a X-linked genetic muscular disease caused by a mutation in Dmd gene. Dystrophin protein stabilizes the cell membrane of myofibers, and the lack of Dystrophin causes progressive loss of function in skeletal muscle and heart, eventually resulting in death.

We previously generated Duchenne muscular dystrophy model rats (DMD rats) with CRISPR/Cas9 (Nakamura et al., 2014). Unlike murine models, DMD rats show severe and degenerative phenotypes, which are close to human pathologies.

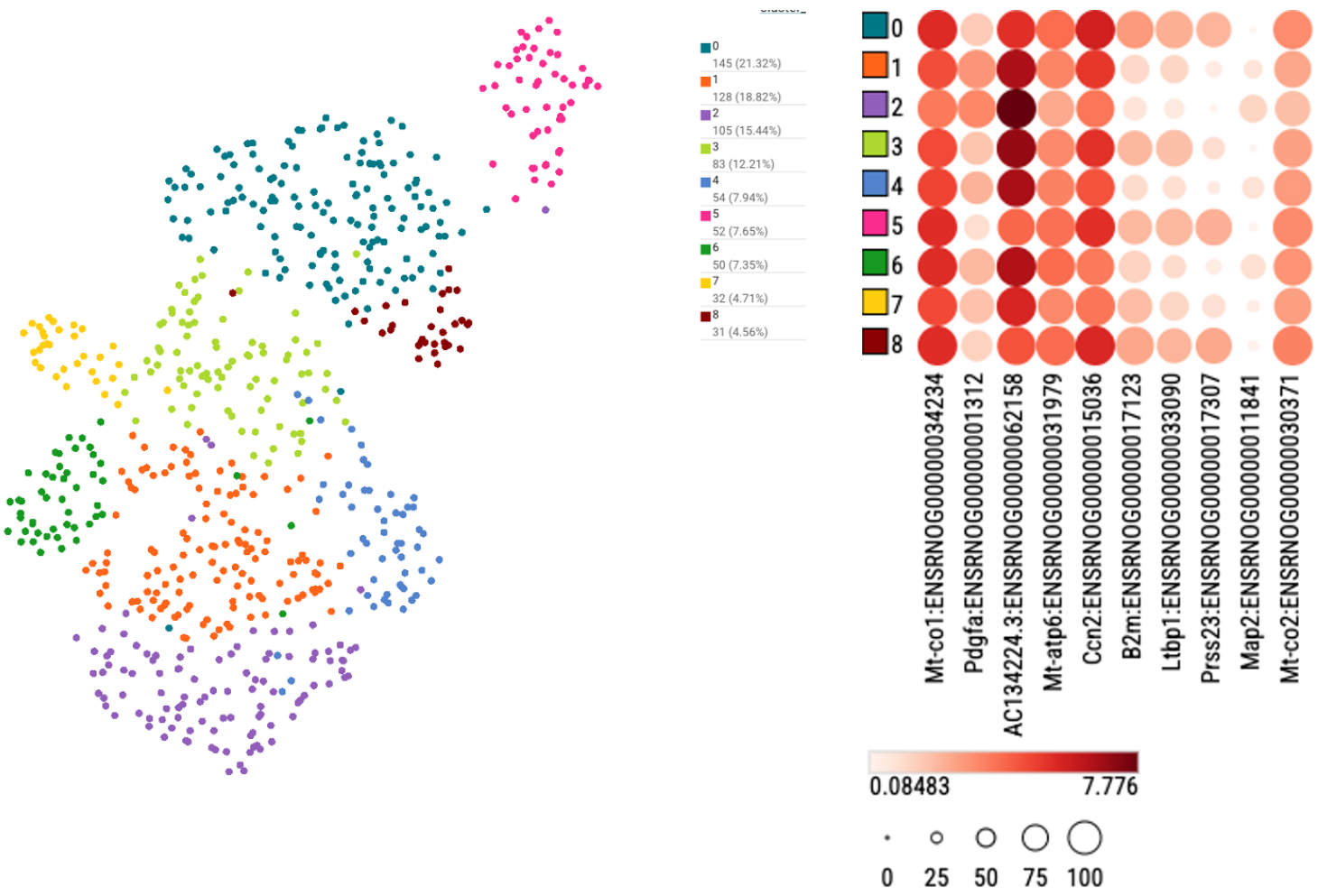


Generation of Duchenne muscular dystrophy model rats

Using this model, we are going to conduct the experiments to:

- Understand the molecular mechanism of DMD pathology.
- Explore a new drug target for DMD by scRNA-seq or metabolome analysis.

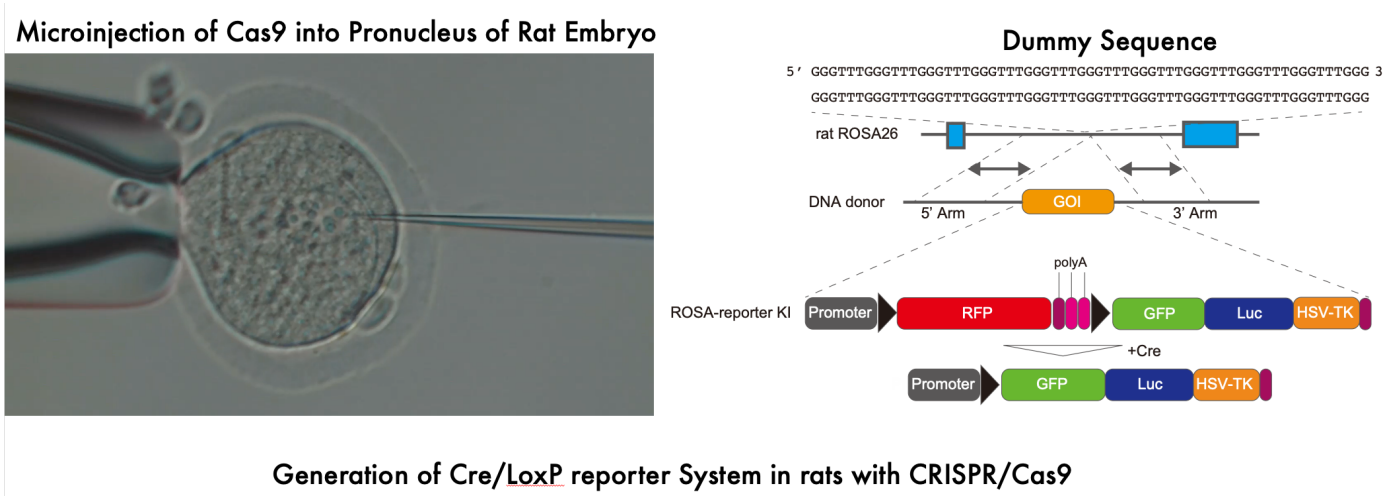
An example of scRNA-seq analysis



2. Establishment of a new preclinical tool for muscular diseases with CRISPR-based genome engineering in rats.

Rat is useful as a preclinical tool for translational research to develop a new drug. However, genetic tools are not as well-prepared as mice. Here, we generated Cre/LoxP reporter system by using CRISPR-based knock-in

technology in rat embryos.



Generation of Cre/LoxP reporter System in rats with CRISPR/Cas9

By crossing Cre driver rats, DMD rats and this ROSA-reporter KI rats, further analysis in more close pathological condition can be performed for reliable translational research.

3. Research for molecular mechanism of aging

Cellular senescence is one of the hallmarks of aging and now is focused as a new therapeutic target for aging and age-related diseases such as Sarcopenia or COPD. Cellular senescence is also related to Duchenne muscular dystrophy (Sugihara, Teramoto and Nakamura et. al., 2020 Sci Rep).

We are conducting preclinical research to:

- Disclose molecular mechanism of how senescent cells emerge in the pathology of DMD, progeria or chronological aging.
- Find a way to remove efficiently in pathological conditions of DMD, progeria or chronological aging.