Laboratory of Regeneration Biology

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Comparative Regenerative Biology

We use animals that demonstrate a high ability in regenerating body parts, such as planarians and newts, to understand the principle of regeneration. In particular, we investigate the difference between regenerative and non-regenerative animals to evoke abilities from non-regenerative animals. We have already succeeded in achieving this with planarians, which were able to regenerate their heads through RNAi (Umesono *et al*., 2013 Nature), and accomplishing functional joint regeneration in frogs through the activation of reintegration systems (Tsutsumi *et al*., 2016 Regeneration). We are currently trying to induce functional joint regeneration in mouse and to characterize adult pluripotent stem cells in planarian at a single cell level.

Trials for evoking functional joint regeneration in mouse

Mouse can't regenerate joint structures at all. However, we expect that functional joints might be evoked by the activation of reintegration systems since we found that the remaining tissues after amputation at the joint level possessed the ability to regenerate joint tissues (Hotta *et al*., unpublished data). That is, the mouse might lose their regenerative abilities due to non-cell autonomous reasons. Therefore, we are now investigating how to activate reintegration systems in mice after amputation at the joint level for evoking functional joint regeneration.

Isolation of the viable planarian aPSC (adult pluripotent stem cells) and characterization of these cells at the single cell level.

We tried to develop an isolation method for viable adult pluripotent stem cells (aPSC) from planarians using FACS. In the previous method, isolated aPSC were unhealthy after staining with several fluorescence dyes. Recently, we found a condition to be able to isolate viable aPSC by FACS sorting without staining with dyes. The single cell transcriptome analyses using these isolated aPSC showed unique properties of planarian aPSC (Kuroki *et al*., unpublished).

We also found that these aPSC showed the collective migration property (branch-like patterns in Fig.1) after RNAi treatment of the *MTA* (*Metastatic Tumor Antigen*) family genes, suggesting that planarian might have unique niche for maintain aPSC in the adult bodies (Sato *et al*., 2022).

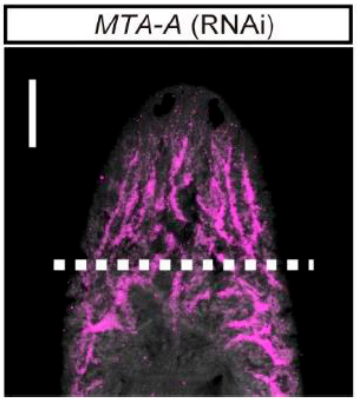

Figure.1 RNAi treated animal of the *MTA-A* gene showed the branch-like distribution patterns of aPSC (magenta stained with the PIWI-A antibodies).

Now, we are investigating differences of these cellular systems between highly- and lower- regenerative animals.

Publication List:

〔Original papers〕

- Bando, T., Okumura, M., Bando, Y., Hagiwara, M., Hamada, Y., Ishimaru, Y., Mito, T., Kawaguchi, E., Inoue, T., Agata, K., Noji, S., and Ohuchi, H. (2022). Toll signalling promotes blastema cell proliferation during cricket leg regeneration via insect macrophages. Development *149*, dev199916. DOI: 10.1242/dev.199916
- Finet, C., Kassner, V.A., Carvalho, A.B., Chung, H., Day, J.P., Day, S., Delaney, E.K., De Re, F.C., Dufour, H.D., Dupim, E., Izumitani, H.F., Gauterio, T.B., Justen, J., Katoh, T., Kopp, A., Koshikawa, S., Longdon, B., Loreto, E.L., Nunes, Maria D.S., Raja, K.K.B, Rebeiz, M., Ritchie, M.G., Saakyan, G., Sneddon, T., Teramoto, M., Tyukmaeva, V., Vanderlinde, T., Wey, E.E., Werner, T., Williams, T.M., Robe, L.J., Toda, M.J., and Marletaz, F. (2021). DrosoPhyla: Resources for Drosophilid Phylogeny and Systematics. GENOME Biol. Evol. *13*, evab179. DOI: 10.1093/gbe/evab179
- Inoue, T., and Agata, K. (2022). Quantification of planarian behaviors. Dev. Growth & Differ. *64*, 16–37. DOI: 10.1111/dgd.12765
- Lee, H., Hikasa, K., Umesono, Y., Hayashi, T., Agata, K., and Shibata, N. (2022). Loss of plac8 expression rapidly leads pluripotent stem cells to enter active state during planarian regeneration. Development *149*, dev199449. DOI: 10.1242/dev.199449
- Sato, Y., Umesono, Y., Kuroki, Y., Agata, K., and Hashimoto, C. (2022). Proliferation maintains the undifferentiated status of stem cells: The role of the planarian cell cycle regulator Cdh1. Dev. Biol. *482*, 55–66. DOI: 10.1016/j.ydbio.2021.12.006
- Takeuchi, T., Matsubara, H., Minamitani, F., Satoh, Y., Tozawa, S., Moriyama, T., Maruyama, K., Suzuki, K.T., Shigenobu, S., Inoue, T., Tamura, K., Agata, K., and Hayashi, T. (2022). Newt Hoxa13 has an essential and predominant role in digit formation during development and regeneration. Development *149*, dev200282. DOI: 10.1242/dev.200282