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ESSAY

ESSAY SERIES: EQUITY, DIVERSITY AND INCLUSION

A reflection of life – my tale of microdiversity, equity and inclusion in cell biology (and beyond)

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Just as an organism depends on a multitude of different factors to function, from biochemical to environmental, a society depends on various dimensions of diversity to survive, but even more so to thrive. This concept was not lost on me when I moved to the USA. I started my scientific journey in my home country of Japan, where I trained in various disciplines. This transdisciplinary experience enabled me to grow and succeed as a researcher in cell and developmental biology. As I reframed my cross-cultural and cross-disciplinary experiences, I learned to incorporate an array of diverse fields into my daily life and research philosophy. Japan is a relatively homogenous society with a tradition of following established protocols and rules, thereby rarely changing. By comparison, the USA is a confluence of different backgrounds, experiences and perspectives. The change in exposure to diversity not only helped me to expand my social life but also my 'science life'. This essay is a testament to the growth in my appreciation for diversity at all levels; I will share my thoughts and experiences about the parallels that can be drawn between cellular diversity and its innate model for societal diversity.

Academic society

Increasing equity, diversity and inclusion is crucial for academic science and education. A diverse environment (including diversity in race, ethnicity, gender, religion, sexual orientation and socioeconomic status) is a true reflection of what life in any typical society should be (Hollins and Govan, 2015). Diversity is what makes us a rich community – by recognizing our differences. Embracing diversity is important because it gives us a chance to validate who we are individually and how we are different. Yet, we are equal, and we should keep things equal, because diversity should not limit someone's access to opportunity; in fact, it may even fuel it. Therefore, diversity in academic society enables the reaction and combination of unique ideas when equity and inclusion support all those activities. As a cell biologist, I am proud that the scientific community continues to make strides to be more diverse and to be functionally united. Overall, I am committed to advancing equity, diversity and inclusion by treating everyone respectfully and equally so that everyone can reach the full potential of academic society. And I believe having diversity provides the community with a scientifically active environment and innovation (Fig. 1). I could not be more proud to take a leadership role to further diversity.

Cell society

Like our society, a living organism uses complex and sophisticated systems that are diversified and that have been acquired evolutionarily to appropriately process information from both the inside and outside. Such systems are the key to organogenesis, regeneration and homeostasis, and any abnormality in the system or failure of the related molecular machinery can lead to congenital abnormalities and serious diseases. Cells are the building blocks of our bodies, and yet each cell type has its own specific role. The technology available for working with cells has enabled a reductive approach to understanding the whole by breaking down the complex components into their parts and examining them. As a result, it becomes clear that these tiny cells are equipped with amazingly complex mechanisms for responding to the outside world and for intracellular processing. Furthermore, by integrating these functions at the tissue and organ levels, advanced and diverse functions that could not be attained on a cellular level can be achieved. I strongly believe that cell biology will continue to play a variety of roles in bridging between molecules and organisms. As our knowledge advances, more challenges must be addressed to support the merging of scientific disciplines and the act of consciously being more open-minded and inclusive. These efforts will bring us a new interpretation of pathology, breaking away from the classical interpretation.

My point of departure to microdiversity

I was born and raised in a rural town in Tokushima prefecture, Japan, called Iwazu, which had a population of ∼10,000. My grandparents, parents and I lived together in the same house as an extended family. I grew up surrounded by an abundance of nature and being attracted to, and learning from, many living creatures. I decided to pursue an academic career, becoming the first person in our family and relatives' history who chose to go to college. It took time for me to learn the concept of 'microdiversity'. I did not encounter the word 'cell' until much later, when I entered the University of Nagoya, where with great mentoring by Dr Yasunori Machida, I learned about diversity of cell types, including well-coordinated plant cells, and the explicit diversity of function driven by varieties of cell organelles and molecules, including genetic material. This initial study of plant genetics inspired me to learn quite a few lessons from the secret communication of molecular and cellular diversity under the microscope.

Diversity of the gene family

The diversity of gene families was my PhD story and first-ever published contribution to scientific society (Itoh et al., 2005; Takata et al., 2009). To gain more insights into biology, I took a unique approach with *C. elegans*, a type of nematode model and an evolutionarily old animal, in the lab of Dr Masato Okada. One of the reasons that the model struck me was that only ∼1000 somatic cells elegantly coordinate diverse functions during the life cycle (Sternberg and Horvitz, 1982), and it also made me realize the genetic diversity in this ancestral species. Furthermore, this simple animal has ∼20,000 genes, and this set of genes is sufficient to exert the diversity of roles of all gene categories, highlighting both the similarities and differences between the genetic material of different organisms. I learned particularly about the evolutionary role of a proto-oncogene family. Characterization of the genes that produce tyrosine kinases in multicellular organisms highlighted to our team what the simple animal starts with and how complex animals like human beings are.

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Fig. 1. Diversity is what makes cells and us who we are in our respective cellular and human societies. The illustration is reproduced with permission of United Japanese Researchers Around the World (UJA), https://www.uja-info.org/post/covid19-028 (accessed November 2021; doi:10.34536/covid19-028).

I was amazed to see the diverse functions of these proto-oncogenes in cell migration, nerve cell formation and cell–cell communication through receptor proteins on the surface of the cells (Itoh et al., 2005; Takata et al., 2009). Yet, it is clear that human beings have continued to diversify cellular and molecular functions. Because of such breathtaking complexity, I tackled this evolutionary question with powerful genetic and biochemical approaches. I remember that when I encountered such beautiful biology, I was excited and shared the results with the other lab members, helping the whole lab to address fundamental questions together.

From embryonic cells to cell diversity and inclusion

My long-term topic of research is regenerative biology, focusing on understanding organ morphogenesis at the cellular and molecular levels using a combination of *in vivo* (mouse models) and *in vitro* (mouse and human organoids; Yin et al., 2016) approaches. As we know, embryonic stem cells (ESCs) have an enormous capability to become all the germ layers, and they eventually contribute to all systems of our body, including the nervous, digestive, circulatory, skeletal, muscular and respiratory systems. This transformative potential brought me from point A to point B, where I am able to exploit stem cells to create cellular diversity by using all of my expertise in genetics, development, and molecular and cellular biology. As part of my training, I had an opportunity to be part of the laboratory of Dr Yoshiki Sasai (Cyranoski, 2012) in Japan at the moment that three-dimensional eye organoids derived from mouse ESCs were reported (Eiraku et al., 2011). This publication received worldwide recognition, as it is considered a pioneering report on the use of this tool to generate complex organs from ESCs in a dish. Through contributing to this work, I learned that the system visualizes immature embryonic cells as they transform into a wide variety of cells and allows them to locally communicate to achieve the body plan during organ formation (Sasai, 2013). Using this organoid model, I also uncovered the fundamental process of vertebrate neural cell patterning by applying powerful genome-editing tools to visualize the dynamics of active molecular and cellular communication upon stem cell diversification (Takata et al., 2017a).

Studying abroad – equity, diversity and inclusion in the culture and science of the USA

Due to the tragic death of Dr Sasai, I decided to move abroad and join the laboratory of Dr Guillermo Oliver at Northwestern University in Chicago. The Oliver Laboratory has been an internationally diversified group during my postdoctoral training, with researchers from Argentina, China, England, India, Japan, South Korea, Spain, Uruguay and the USA (Fig. 2). The quality and level of professional research experience of the lab members is high, and I have soaked up intellectual stimulation willingly from all of my colleagues. Dr Oliver's lab has two main areas of research – one is the study of eyes, and the other is study of the lymphatic vasculature – and aims to address fundamental issues and make discoveries that are translatable into clinical treatments. I was impressed by how these two seemingly different research areas have been included and managed equally in one laboratory. This may be the secret to discovering the surprising nature of the cell and its developmental biology, and to attracting a variety of collaborations. In fact, I was able to learn a lot from the environment through my daily activities, including joint lab meetings (particularly with the labs of Dr Beatriz Sosa-Pineda and Dr Susan E. Quaggin), research seminars and collaborations. As a result, I combined *in vivo* mouse models and *in vitro* stem-cell-derived mouse organoids to determine that eye organoids are a reliable tool and a complementary resource to evaluate the process of mammalian eye morphogenesis (Takata et al., 2017b).

Fig. 2. The year of my arrival at Dr Guillermo Oliver's lab in the USA. The author is third from the right, wearing a black jacket and tie.

Chicago is an oddly cohesive city that consists of 77 neighborhoods – despite its many different cultures and opportunities, its citizens are able to learn from each other and experience and maintain a unified international flavor. As a foreigner in the USA, I have always been amazed by the range of nationalities and ethnicities represented in this country. However, it is also true that there is still a large gap in equal representation in our society and in academic institutions. Therefore, it is essential that we, as individuals, and academic institutions, try our best to improve equity, diversity and inclusion.

Equity in scientific learning

To contribute to equity in the public arena, I have had some experience in dealing with some of these issues. For example, I taught the history of sciences to a socio-economically diverse group of high school students as part of a program supported by the Japanese government. At the RIKEN Institute, I also participated in events for children and families that had a focus on showing how science has impacted human health but also highlighted how not all countries have equal access to those technological advances. Additionally, at the Japan XR Science Forum 2020 (https://ssp.jst.go.jp/sns/news/sat/science21/06_2.html), where I was that year's chairman of the forum, the organizers and I created a new virtual science learning platform for adults and even children who could not go to school in-person during the COVID-19 pandemic (XR is a cross-reality technology to enable better communication of physical

and digital environments and experiences). Currently, I organize scientific community gatherings supported by the Consulate-General of Japan in Chicago to provide scientific lectures to adults, including those with non-scientific backgrounds. My desire is to continue with this type of outreach activity and try to provide equal opportunities for adults, students and children to understand scientific disciplines.

Conclusion

The meaning of diversity to me is accepting others and accepting their values. It is no secret that the USA is a multi-ethnic country, and this is undoubtedly a strong driving force that gives birth to a culture that is rich in ideas and diversity. Alternatively, when racism is displayed, the situation can be so confrontational that it can make a big city dysfunctional. To me, the same is true in cell biology: dysfunctional communication between diverse molecular, organelle and cellular systems may result in congenital disorders and devastating diseases. Therefore, to understand the issue more deeply and from different perspectives, we need to rethink our respective opportunities for equity, diversity and inclusion in cell biology.

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References

Cyranoski, D. (2012). Tissue engineering: the brainmaker. *Nature* **488**, 444-446. doi:10.1038/488444a

Eiraku, M., Takata, N., Ishibashi, H., Kawada, M., Sakakura, E., Okuda, S., Sekiguchi, K., Adachi, T. and Sasai, Y. (2011). Self-organizing optic-cup morphogenesis in three-dimensional culture. *Nature* **472**, 51-56. doi:10.1038/nature09941

Hollins, C. D. and Govan, I. M. (2015). *Diversity, Equity, and Inclusion: Strategies for Facilitating Conversations on Race*. Lanham: Rowman & Littlefield.

Itoh, B., Hirose, T., Takata, N., Nishiwaki, K., Koga, M., Ohshima, Y. and Okada, M. (2005). SRC-1, a non-receptor type of protein tyrosine kinase, controls the direction of cell and growth cone migration in *C. elegans*. *Development* **132**, 5161-5172. doi:10.1242/dev.02103

Sasai, Y. (2013). Cytosystems dynamics in self-organization of tissue architecture. *Nature* **493**, 318-326. doi:10.1038/nature11859

Sternberg, P. W. and Horvitz, H. R. (1982). Postembryonic nongonadal cell lineages of the nematode Panagrellus redivivus: description and comparison with those of *Caenorhabditis elegans*. *Dev. Biol.* **93**, 181-205. doi:10.1016/0012-1606(82)90251-2

Takata, N., Itoh, B., Misaki, K., Hirose, T., Yonemura, S. and Okada, M. (2009). Non-receptor tyrosine kinase CSK-1 controls pharyngeal muscle organization in *Caenorhabditis elegans*. *Genes Cells* **14**, 381-393. doi:10.1111/j.1365-2443.2008.01275.x

Takata, N., Sakakura, E., Eiraku, M., Kasukawa, T. and Sasai, Y. (2017a). Self-patterning of rostral-caudal neuroectoderm requires dual role of Fgf signaling for localized Wnt antagonism. *Nat. Commun.* **8**, 1339. doi:10.1038/s41467-017-01105-2

Takata, N., Abbey, D., Fiore, L., Acosta, S., Feng, R., Gil, H. J., Lavado, A., Geng, X., Interiano, A., Neale, G. et al. (2017b). An eye organoid approach identifies Six3 suppression of R-spondin 2 as a critical step in mouse neuroretina differentiation. *Cell Rep.* **21**, 1534-1549. doi:10.1016/j.celrep.2017.10.041

Yin, X., Mead, B. E., Safaee, H., Langer, R., Karp, J. M. and Levy, O. (2016). Engineering stem cell organoids. *Cell Stem Cell* **18**, 25-38. doi:10.1016/j.stem.2015.12.005

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