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Session 2SHP report - Decoding intracellular architecture using visualizing device development and mathematical modeling

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Cells carry highly organized architectures. In this session, Invited (4) and selected (2) speakers introduced their frontier research findings determining the actual image of intracellular architectures, such as structural change of chromatin or nucleic acids, enzymatic activity, and signal transduction process via posttranslational modification, by visualization using optical imaging and microscopic control devices, or mathematical modeling.

Dr. Soya Shinkai (RIKEN) talked about the microrheology of 3D genome organization (Shinkai et al., bioRxiv 756965). He developed a simulation tool, polymer dynamics deciphered from chromosome conformation change data (PHi-C) (Shinkai et al., bioRxiv 574962). PHi-C mainly consists of three steps: (i) normalization of input Hi-C data, which is formatted by the Juicer tool developed by Aiden's laboratory (Durand et al., 2016); (ii) optimization of the Hi-C data followed by determination of optimal interaction parameters from Hi-C data; (iii) simulation and analysis of polymer dynamics and conformations. Accordingly, the 3D genome structure can be linked to its function.

Dr. Kazuya Kabayama (Osaka University) introduced several new techniques that his laboratory has developed to analyze single cells. Especially, to visualize intracellular Ca^{2+} change in floating cells, they developed a nano-wrapping system (Zhang et al., 2018). In the system, wrapping floating cells using a porous nanosheet can be readily observable because the cells have kept not to flow. Moreover, they elucidate the action mechanism of volatile anesthetic using a microfluidic device. To measure the molecular movement in the lipid membrane, they also used fluorescence recovery after photobleaching (FRAP) (Ono et al., 2018).

Dr. Ryo Iizuka (The University of Tokyo) introduced techniques for the isolation and analysis of single cells, organelles, and intracellular supramolecular complexes using microfluidic microdroplets. The techniques facilitate microbial single-cell genomics (Nakamura et al., 2016) and single-organelle analysis, and can be applied to directed enzymatic evolution. The total microfluidic system itself is homemade, surprisingly. They emphasized that even using such a simple system, it enables analysis

of trace or minor samples.

Dr. Chikara Sato (National Institute of Advanced Industrial Science and Technology) introduced bone tissue mineralization in natural aqueous buffer, visualization of axonal segmentation controlling neuron trafficking, and methicillin-resistant Staphylococcus aureus (MRSA) biofilm formation monitoring by using Atmospheric Scanning Electron Microscope (ASEM) (Sato et al., 2019; Sugimoto et al., 2016).

Dr. Fumihiko Hakuno (The University of Tokyo) talked about their studies on the regulatory mechanism of Insulin-like growth factor (IGF)-I signaling (Hakuno and Takahashi, 2018) including a feedback loop, using a numerical model to simulate the IGF-I signaling in the constant presence of IGF-I. The IGF-I signaling showed completely different behavior between high and low IGF-I concentration.

Dr. Akira Kitamura (Hokkaido University) introduced the principle of transient state (TRAST) monitoring microscopy (Kitamura and Kinjo, 2018; Sanden et al., 2007) and its application to determine the intracellular folding state of RNA. TRAST monitoring microscopy has a great potential to read out the conformation of fluorophore-labeled biomolecules such as RNA and proteins because microenvironment around fluorophores can affect its photochemical reaction.

In the last of the session, Dr. Kitamura, an organizer of the session provided an overall summary of all the talks within it. He questioned what ‘dark matter’ in cell biology is. He proposed three candidates for dark matter in cell biology: (i) Detection of native and naïve biochemical reactions; (ii) realistic physical principles and parameter in the cells (e.g., realistic theory of phase separation, excluded volume effect, and so on); (iii) weak but significant interaction between biomolecules. Elucidation for such ‘dark matters’ using biophysical techniques and/or mathematical models is important.

Finally, Dr. Yasuhiro Hirano (Osaka University) participated in this session as a chairperson and actively discussed with the speakers throughout the talks.

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