Supramolecular Chemical Approach to Construction of Artificial Cell

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Exploring the boundary between a living and non-living matter is one of the most challenging problems for contemporary scientists. In order to understand a cell, which is a minimum unit of life, synthesis of an artificial cell from supramolecular chemical approach is a plausible strategy, because simple molecular assemblies evolved to a simple cell on prebiotic earth. As shown in Figure 1, the key elements of a cell are compartment, information and catalyst, *i.e.* metabolism. We have tackled the construction of a chemical artificial cell endowed with these three elements.

In our laboratory, we aim to construct the two artificial cells using giant vesicles (GV) as compartment. One is an artificial cell which can proliferate from generation to generation. This work is a collaboration with Sugawara group (Kanagawa Univ.). The other research is an artificial cell incorporating catalyst producing system. The GV system can generate catalyst and membrane molecule by transforming each precursors, which makes it possible for GVs to proliferate with producing catalyst.

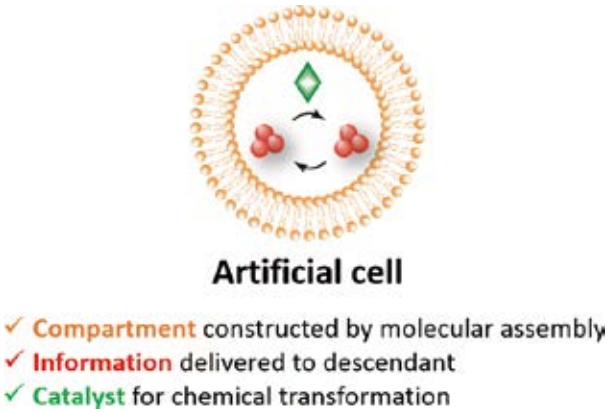

Figure 1. Artificial cell model
The replicating systems of compartment and the replicating system of information materials are combined. The reactions in the two replicating systems are accelerated by each proper catalysts.

Selected Publications

- K. Kurihara, M. Tamura, K-I. Shohda, T. Toyota, K. Suzuki and T. Sugawara, "Self-Reproduction of Supramolecular Giant Vesicles Combined with the Amplification of Encapsulated DNA," *Nat. Chem.* **3**, 775–781 (2011).
- T. Sugawara, K. Kurihara and K. Suzuki, "Constructive Approach towards Protocells," in *Engineering of chemical complexity*, world scientific lecture notes in complex systems, World Scientific Pub. Co. Inc., pp. 359–374 (2013).

1. An Artificial Cell with a Primitive Cell Cycle

One of the approaches for exploring the origin of life or elucidating of the functions of life is construction of an artificial cell from supramolecular chemical approach.[1,2] In collaboration with Sugawara's group, artificial cells which have three basic elements of a cell; information (DNA), compartment (giant vesicle (GV): A supramolecular assembly of amphiphiles) and metabolism (synthetic catalyst) have been constructed.[3] The artificial cellular system consisted of amplification of DNA by polymerase chain reaction and self-reproduction of GV by addition of membrane lipid precursor. Although this GV proliferated with distribution of internal amplified DNA, it ceased at the 2nd generation because of depletion of internal information substances.

Now, we construct a recursive vesicular artificial cell system with proliferation cycles, collaborating with Sugawara group. By using the vesicular transport system,[4] the 2nd generation of GVs which have no PCR reagents after self-reproduction was replenished by fusing with the conveyer GVs encapsulating the PCR reagents (Figure 2). The replenished GV can amplify the internal DNA and yield 3rd generation of the GV after addition of membrane lipid precursor. The GV system with replenishing system was constructed.[5] This system would lead to an evolvable artificial cellular system.

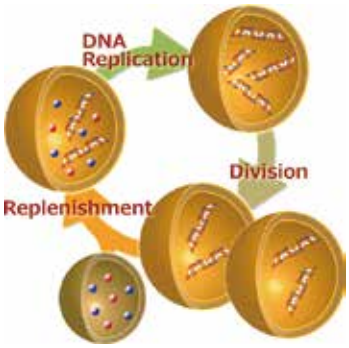

Figure 2. An artificial cell system with premitive cell cycle. After growth and division of GV, the substance-depleted GV was replenished by the vesicular fusion.

2. An Artificial Cell Containing a Catalyst-Producing System

A cell is a self-organized system which is able to maintain its state due to metabolism. The previous artificial cellular system have been so robust that it can self-reproduce only specific state in the any environments.

Here, we aim to realize a new artificial cellular system in which the GV self-organize its own composition spontaneously according to the environment. In order for GV to self-reproduce and self-maintain, it is necessary to combine metabolism and compartment. By introducing the cross-catalysis system (Figure 3), we construct an artificial cell in which catalysts are produced. After addition of membrane precursor aldehyde, the production of catalyst and membrane molecule was confirmed by NMR, microscopy observation. In this system, the GV was reproduced by the catalyst which catalyze the production of the GV membrane lipid molecule. The GV membrane provides the field where the catalyst is synthesized.

In addition, by changing the composition of the vesicular membrane, the production of catalyst and membrane molecule was oscillated by interacting each other. This means that the artificial cell incorporating the negative feedback is realized.

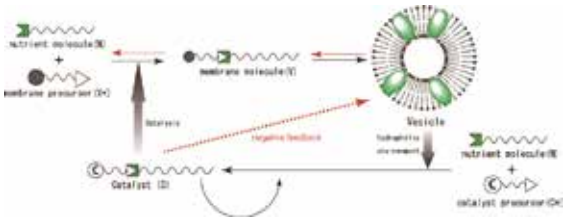

Figure 3. Scheme of new artificial cellular system. The membrane molecules of the GV was synthesized by the catalyst produced in the GV.

References

1) K. Takakura, T. Yamamoto, K. Kurihara, T. Toyota, K. Ohnuma and T. Sugawara, *Chem. Commun.* **50**, 2190–2192 (2014).
2) T. Sugawara, K. Kurihara and K. Suzuki, "Constructive approach towards protocells," in *Engineering of chemical complexity*, world scientific lecture notes in complex systems, World Scientific Pub. Co. Inc., pp. 359–374 (2013).
3) K. Kurihara, M. Tamura, K-I. Shohda, T. Toyota, K. Suzuki and T. Sugawara, *Nat. Chem.* **3**, 775–781 (2011).
4) K. Suzuki, R. Aboshi, k. Kurihara and T. Sugawara, *Chem. Lett.* **41**, 789–791 (2012).
5) K. Kurihara, Y. Okura, M. Matsuo, T. Toyota, K. Suzuki and T. Sugawara, *Nat. Commun.* **6**, Article number; 8352 (2015).