Organ Fabrication is achievable *in vitro*?

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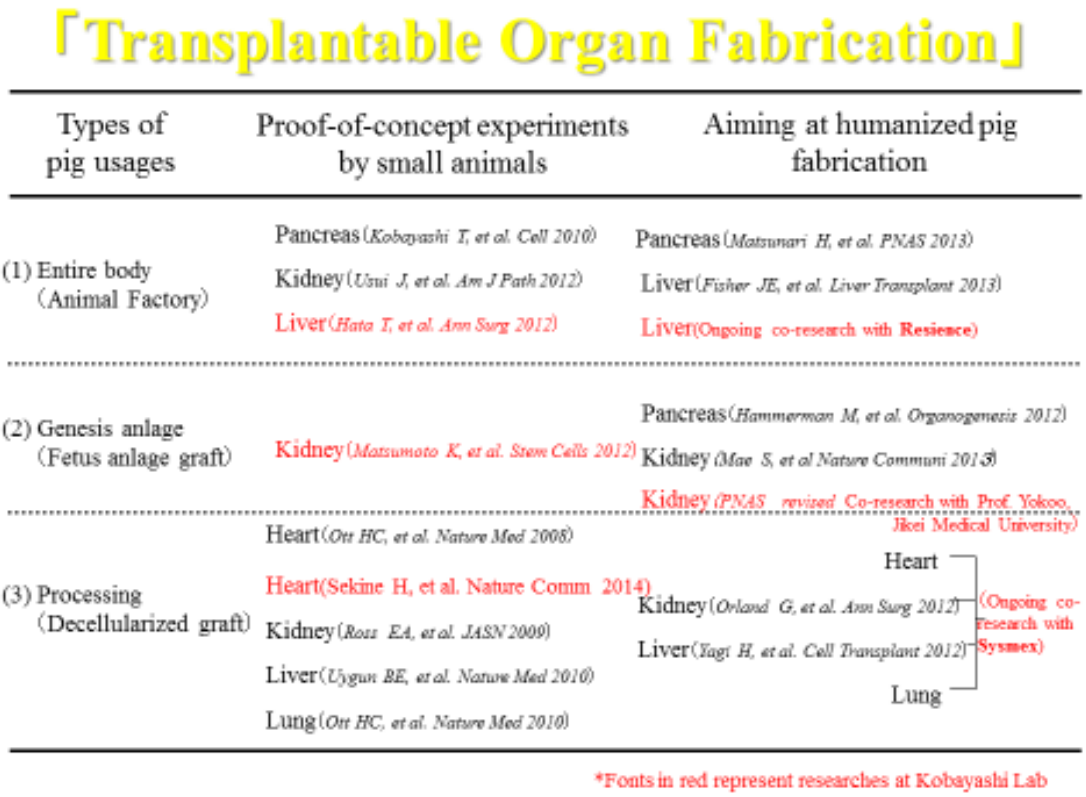
In recent years the basic researches for stem cells such as world-first iPS have been reported one after another from Japan. Based on these excellent results, the zeal for fabricating organs *in vitro* has been accelerated. The author up to now has been disclosing on manuscripts that there are three methods to fabricate transplantable organs [1] [2] [3].



It will be explained in this seminar how much progress has been made so far for the regulations of Organ Bud Generation and upcoming challenges based on reviewing the researches originally started for fabricating organs *in vitro* by Dr. Makoto Asashima, Executive Director of Japan Society for the Promotion of Science.

In later years of 20th Century, Dr. Asashima found out that various kinds of cells could be generated by adding Activin to frog's undifferenciated embryonic cells in the non-fertilized eggs (animal cap) [4]. Also he succeeded in cloning Nodal-5 for pancreas and Xsal-3 for kidney, which were essential for initialization. These research results have been disclosed to the world as organogenesis molecule mechanism and have enlightened the viability of fabricating organs *in vitro*.

However, it has taken time to relate animal cap to the finding of human pluripotent cells because there exist differences in gene functions between animal and human. In 1998 ES cells were generated from human fertilized egg, furthermore, in 2007 iPS cells were developed skipping the process of utilizing fertilized eggs. It has all ignited the possibilities of fabricating organs *in vitro*. In 2013 Prof. Osafune has generated kidney precursor cells *in vitro* out of iPS and proposed cell transplantation therapy against kidney malfunction [5]. Prof. Nishinakamura also has succeeded in fabricating 3-D kidney structure *in vitro* based on his research that cell group which emerges Sall1 is precursor cells for Nephron (Minimum functioning score of kidney which consists of glomerulus and renal tubules) [6]. And at the same time Dr. Takebe has developed cultivation method to form liver anlage from human iPS cells. It was different from the conventional method which was to induce differentiation to stem cells. It is a mixed culture method of 3 kinds of cells; endodermal, vascular endothelial and mesenchymal cells. And it leads to a clarification that to fabricate cubic organ anlage requires following conditions; 1. To exist mesenchymal cells, 2. To physically establish external environment in culture system, which triggers multicellular contraction phenomenon [7].

Currently it has become almost possible to acquire human organ bud. The utmost challenge is how we culture organ buds to apply them to the patients with organ malfunction. The technology exists how we set up organ buds *in vitro* as Tissue/Organ Fabrication. This seminar will be focused on the above issues how we apply these new technologies to clinical practices.

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