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Interview

An Interview with Dr. Masahiro Sato

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Dr. Masahiro Sato

Dr. Masahiro Sato obtained PhD in Biochemistry from the Kagoshima University School of Medicine, and later spent ten years at the Laboratory for Pathobiology, Pharma Research Laboratories, Hoechst Japan Ltd. (Kawagoe, Saitama, Japan), where he has engaged in the production of disease mouse models for Alzheimer's disease and osteoporosis. In April 1996 - March 2006, He spent at the Department of Molecular Life Science, Tokai University School of Medicine (Isehara, Kanagawa, Japan) as Professor (Assistant), where he engaged in developing novel technologies, as exemplified by cell-lineage analysis in mammals using Cre-*loxP* system and testis-mediated gene transfer (TMGT), a technique without using microinjection-based transgenesis. In April 2006 - March 2021, Dr. Sato spent at the Gene Expression Regulation Section, Frontier Science Research Center, Kagoshima University (Kagoshima, Japan) as Professor, where he engaged in developing novel technologies related to reproduction and molecular biology as well as producing genetically modified piglets suitable for xenotransplantation. Notably, during these periods, Dr. Sato and his colleague Prof. Masato Ohtsuka (Tokai University School of Medicine) succeeded in developing improved Genome-editing via Oviductal Nucleic Acids Delivery (*i*-GONAD), a novel method for creating genome-edited animals through *in vivo* genome editing. In April 2021 – Present, he is studying reproduction engineering-related research at NCCHD as Senior Fellow.

1. Please Tell Us Your Scientific Background?

My scientific background is Molecular Biology, Developmental Biology, Theriogenology, and Assisted Reproductive Technology with biotechnology skills and expertise such as recombinant DNA technology (including plasmid construction and its propagation and purification, Northern/Southern blotting, Sanger sequencing and transfection with non-viral vectors *in vitro* and *in vivo*), histochemical staining technology (including immunological staining and preparation of cryostat and paraffin sections) and reproductive technology [including *in vitro* fertilization, zygote microinjection, embryo culture, embryo transfer (implantation), gamete cryopreservation and manipulation of embryonic stem cells].

2. What Is Your Main Research Area? How Did You First Become Interested in It? Is There a Particular Case Which Has Influenced You the Most?

My main research area is reproduction engineering (creation of gene-engineered mice, development of novel techniques for simple and efficient production of those mice and development of an *in vivo* genome editing system towards preimplantation mouse embryos) and molecular biology. My first scientific concern related to the above subjects was to know that mouse zygotes (fertilized eggs) could be successfully manipulated through pronuclear microinjection of exogenous DNA about 40 years ago by Gordon et al. [1]. The resulting gene-engineered mice were called "transgenic mice" and can be classified as "artificial mice with gain-of-function". This finding means that it is possible to alter the natural phenotype of mice through chromosomal integration of exogenous DNA (called "transgene"). Unfortunately, it requires an expensive manipulator system and highly skilled person to operate it. To bypass this laborious process, I and my colleague have attempted to develop several methods (i.e., testis-mediated gene transfer (TMGT) [2], GONAD [3] and *i*-GONAD [4]) to create gene-engineered mice in more convenient manner.

3. Which Topics Are Included? In Your Opinion, What Developments and Opportunities Can We Expect to See in among These Topics?

I have a great interest in gene delivery using "nanoparticles (NPs)", which are now reported to enable efficient genome editing *in vivo.* The DNA/mRNA (including genome editing components) complexed with NPs can be easily introduced *via* tail-vein or local administration into mice. Indeed, using these approaches a number of genetically inherited diseases could be successfully cured. I believe that using these NPs mouse early embryos and fetuses can be easily genome-edited in future. Furthermore, NPs may be widely used as gene therapeutic reagents in near future.

4. How Do Patients Benefit from Your Research?

My research area involved in genetic alteration of experimental animals such as mice through gene introduction to early embryos and fetuses as well as *in vivo* organ/tissue genome editing at adult stage. Particularly, I believe that NPs are potentially useful for curing genetic disorders, cancers and immunologic defects. Thus, my research area will be easily accessible to the preclinical application and its advance will provide support for patients with diseases and their families.

5. Considering the Progress in Your Research Area, Could You Please Share Us Some Major Advances or Cutting-edge Technologies in Your Research Field?

Advance of our research area may be helpful for rescuing patients with diseases that are thought be difficult to cure using the presently available technique. This can be potentially achieved by the "precise genome editing technology". For this purpose, it is prerequisite to correct the mutation site without any side effect (off-target). Base editor and prime editor systems are now considered promising for this purpose. It is highly likely that more precise and convenient systems for precise genome editing will appear in near future.

6. Do You Also Offer Training and/or Further Education in Your Area?

In my area, the training of *i*-GONAD (a more advanced type of GONAD) method has been officially offered from our Japanese Society for Genome Editing, since 2020.

7. What Are the Biggest Roadblocks and Challenges in Your Research Work?

Before 2019, I did not feel any impediment that results in stoppage of my scientific action. However, since early 2020, our social behavior has been extensively restricted by the appearance of COVID-19. We were asked to prohibit direct mutual communication between outside collaborators, which caused a decreased motivation to proceed experimental plans. On the other hand, I newly learned that vaccination against COVID-19 is useful for expression of a target protein from the injected site (muscular cells) after simple intra-muscular injection of lipid-encapsulated mRNA. This approach greatly inspired my future *in vivo* gene delivery experiments.

8. Let Us Know How You Balance Your Job with Privacy? What Are Your Secrets of Success for This?

The balance between my job and privacy may be 4:1. I am always thinking of experiments, idea for scientific approach and papers.

9. What Are Your Future Plans and Long-term Research Goal?

My long-term research goal is to cure genetic disorder in patients by simple methods, like COVID-9 vaccination. For example, it is desirable to make normal protein (continuously produced from the transgenes integrated into the genome of the patients) secrete into blood stream through intra-muscular injection of a solution carrying knock-in type genome-editing reagents.

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