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Production of insulin gene knockout piglets using CRISPR/Cas9 system

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Diabetes mellitus is the chronic disease with severe complications including diabetic nephropathy, neuropathy, and cardiovascular disease. To investigate the pathophysiology of diabetes or develop the drugs for diabetes, various animal models have been used. Although rodent models are commonly used for diabetes research, the interest about the pig diabetic models is increasing because of their similarity with human in many aspects like size, pathology, physiology, and metabolism. There are some methods to generate diabetic pig model. The treatment of chemicals like streptozotocin is generally used and pancreatectomy is also one of the methods. Recently, genetically modified pigs which were modified genes related with pathogenesis to induce diabetes were reported. In this study, we have successfully generated insulin gene knockout piglets by targeting the porcine *INS* gene in somatic cells using CRISPR/Cas9 system combined with somatic cell nuclear transfer (SCNT). Single cell derived somatic cell colonies carrying a modified *INS* gene were generated using CRISPR/Cas9 system and their genotypes were confirmed by T7E1 assay and Sanger sequencing method; targeting efficiency was 40.4% (21/52). After SCNT and embryo transfer, eight piglets (including five stillborn piglets) were born. As expected, *INS* knockout piglets presented high blood glucose levels. Also, the expression of insulin in the pancreas was absent in those piglets. This study demonstrates effectiveness of CRISPR/Cas9 system in generating genetically modified pigs. We expect that these insulin gene knockout pigs can be used in diabetes research as an animal model for the efficacy and safety test of new drugs and the recipient of islet transplantation to investigate optimal strategies for islet transplantation.

Biography

Bumrae Cho has his expertise in genetic modification and generation of donor cells for somatic cell nuclear transfer. Especially, he is focusing on the generation of genetically modified pigs for xenotransplantation, disease resistance pigs, and various pig models to investigate human disease. His research interest is genetic modification of SCNT donor cells using CRISPR/Cas9 system to produce various pig models including human disease mimicking pig model, viral disease-resistant pig, pigs as an organ donor for the xenotransplantation. Now, he is developing genetically modified pigs such as pigs mimicking type I diabetes, porcine epidemic diarrhea resistant pigs, and dengue virus sensitive pigs.

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