

Public Abstract

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Graduation Term: SP 2015

Department: Animal Sciences

Degree: PhD

Title: Genetic Linkage of Multiple Modifications in the Pig

Genetic engineering facilitates heritable modification of target genomes. Modifications can be site-specific or random. Though inefficient, homologous recombination allows for precise genome modification. Random integration can be very efficient, but lacks the opportunity to control the orientation and location of the introduced DNA. Thus, an efficient method for site-specific integration into a predetermined location would have utility. The ability to precisely modify the genome has and will continue to have profound effects in the fields of agriculture and human medicine. The current protocols used are effective, but additional enhancements in the efficiencies are desirable. In particular, any added efficiency to modify the genomes in livestock species will have a profound impact. This is due in large part to the expenses related to husbandry of large animals in comparison to that of small animals. The aim of this dissertation was to develop an efficient system(s) to precisely modify the pig genome and to develop a system(s) that would link multiple modifications, both a gene knockout and additional transgenes. There were three main topics that were evaluated: 1) Phic31 recombinase-mediated gene stacking in pigs, 2) the effect of donor DNA length in nuclease-mediated gene targeting, and 3) CRISPR/Cas9-mediated gene stacking and gene targeting.