

Genetically Engineered Swine Models to Study Diseases like Cystic Fibrosis

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Swine have become important in biomedical research as they are excellent models for a variety of diseases including cardiovascular disease, atherosclerosis, cutaneous pharmacology, wound repair, cancer, diabetes, ophthalmology, toxicology research, lipoprotein metabolism, pathobiology of intestinal transport, injury and repair, as well as being considered potential sources of organs for xenotransplantation. Cystic Fibrosis (CF) is caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The CFTR protein is responsible for chloride ion transport. Disruption of the function in humans results in meconium ileus, focal biliary cirrhosis, pancreatic destruction, liver lesions, and lung disease. Unfortunately disruption of this gene in mice, while affecting chloride transport, does not result in any of the symptoms that humans develop. In collaboration with the University of Iowa we have created pigs with either a knockout of the CFTR gene or a mutated version that is similar to 70% of the people with CF ($\Delta F508$). These pigs are born with meconium ileus, focal biliary cirrhosis, pancreatic destruction, liver lesions and they develop lung disease. Finally there is a model to invasively study the development of CF, to monitor disease progression, and to develop treatments and therapies without experimenting on children with CF.