**The Science Breaker – Article**

**Gene edited “superpigs” resist devastating disease**

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**Articles referred to:**

**Burkard C, Lillico SG, Reid E, Jackson B, Mileham AJ, Ait-Ali T, Whitelaw CB, Archibald AL.** 2017. Precision engineering for PRRSV resistance in pigs: Macrophages from genome edited pigs lacking CD163 SRCR5 domain are fully resistant to both PRRSV genotypes while maintaining biological function. PLoS pathogens **13:**e1006206.

**Burkard C, Opriessnig T, Mileham AJ, Stadejek T, Ait-Ali T, Lillico SG, Whitelaw CBA, Archibald AL.** 2 018. Pigs Lacking the Scavenger Receptor Cysteine-Rich Domain 5 of CD163 Are Resistant to Porcine Reproductive and Respiratory Syndrome Virus 1 Infection. Journal of virology **92**.

Genome editors are simple tools that allow scientists to make very precise changes to the genome of any organism. This opens new avenues for investigating basic principles of biology but also to introduce novel traits to domesticated animal and plants. Here we present a use of these “gene scissors” that makes pigs resistant to a devastating disease.

Porcine reproductive and respiratory syndrome (PRRS), is arguably the most costly pig disease worldwide, and is present in almost every pig-producing country. The disease causes respirator distress, fever and reduced appetite in pigs of all ages and often results in death of suckling piglets. In pregnant sows it leads to the death of unborn fetuses or to complete abortions. The disease is caused by the PRRS virus (PRRSV) and to date vaccination strategies have been ineffective in preventing the spread. PRRSV is a master at incapacitating the pig’s immune system, leaving the door wide open for secondary infections by bacteria or other pathogens. This in turn leads to a poorer outcome following infection and increases the need to use antibiotics in pig breeding.

No pigs have been found in commercial breeding stocks that are naturally resistant to PRRSV infection. However, when investigating the interaction between PRRSV and pig cells in the lab, scientists found that there is a key-lock mechanism required for the virus to gain access. The lock, a protein called CD163, looks a bit like a string of nine beads on the surface of immune cells, the target for PRRSV infection. The virus only binds to bead number 5, and whilst all the other beads of are involved in important biological functions in protecting pigs from disease, bead 5 is not known to be involved in any. A very small segment of the pig genome (450 letters from the 2,700,000,000 letter genomic code) was found to be the genetic blueprint of CD163 bead 5. Using gene scissors that flanked this small segment it was possible to remove it from the pig genome.

To make the edited pigs a microscope was used to allow a very fine needle to be inserted into a fertilised pig egg, delivering the gene scissor reagents. After the DNA segment for bead 5 was removed both the segment and the reagents are degraded by natural cell processes within a few hours. The fertilised eggs were then transferred into a surrogate pig and almost 4 months later piglets were born naturally.

After confirming that the piglets contained the anticipated deletion, a small herd of animals lacking bead 5 of CD163 was produced by natural breeding. Cells from the animals were collected and exposed to PRRSV in the lab. By using cells rather than exposing pigs to the virus, multiple variants of PRRSV can be tested. The cells from pigs having a CD163 gene copy lacking pearl 5 from both mother and father were found to be completely resistant to infection with all tested variants of PRRSV. Having demonstrated that there was a good chance that the edited pigs would be resistant to infection by this devastating virus, a cohort of eight pigs (four edited and four unedited controls) were exposed to the virus by spraying virus into their nostrils, the natural route of infection. The animals were all housed together and whilst unedited pigs contracted the disease, pigs lacking bead 5 were completely resistant to infection. At the same time the CD163 protein lacking bead 5 was found to perform its natural functions in cells and in the pigs and animals were healthy and bred normally under standard farm conditions.

The creation of pigs lacking bead 5 holds tremendous opportunities for the pork industry worldwide to improve both animal welfare and productivity. PRRSV-resistant animals are not only free of disease but they also don’t spread the virus, which means they can shields other animals, opening avenues of PRRS erradication. PRRSV-resistant animals could also reduce the prevalence of bacterial infections (secondary infections are a big problem during PRRSV infection), reducing antibiotic use in pig production. At the same time these edited pigs don’t contain anything else but pig so there is no fear of novel allergens or other compounds that could be harmful to the consumer. This is a clear demonstration of the tremendous potential that genome editing technology offers as a tool to tackle animal disease. However, for the implementation of genome-editing techniques in animal production, both consumer acceptance and the legislative framework need to be in place.