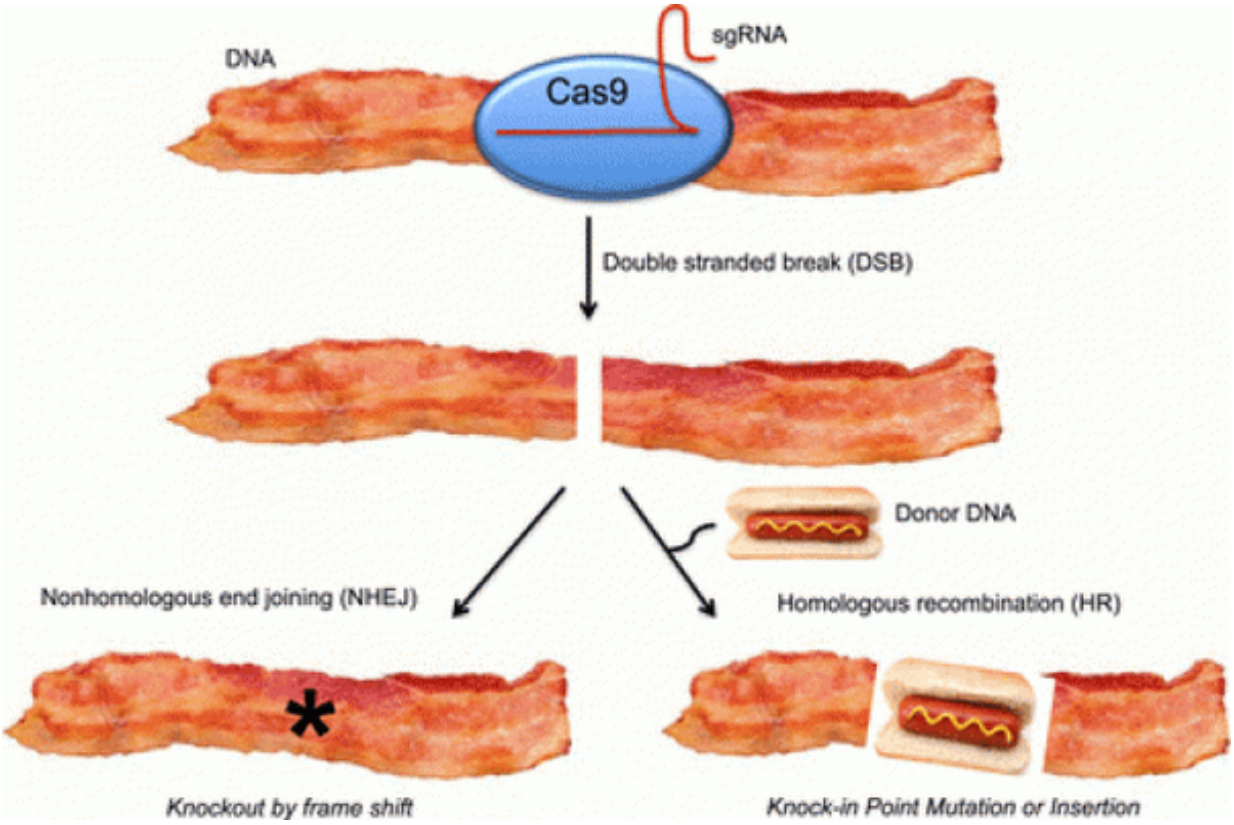
Researchers massively edit the genome of pigs to turn them into perfect human organ donors

October 8 2015, by John Hewitt



CRISPR gene editing of the pig genome. Credit: Editors-in-Chief Franco J. DeMayo and Thomas Spencer, Biology of Reproduction

(Phys.org)—One benefit of the closeness between pigs and humans is

the potential to be organ donors. There are however, just a few nagging uncertainties that still stand in the way. The big one, the possibility of porcine endogenous retroviruses (PERVs) getting reactivated inside the human organ recipient, is no longer the concern it once was. That comes thanks to the recent groundbreaking work of the one-man army of genetics, George Church, and his lab at Harvard. The latest news, just reported in *Nature*, is that the group was able to use CRISPR gene-editing techniques to inactivate 62 PERVs in pig embryos.

The one other big concern is rejection of donor organs by the human immune system. Church has reportedly tackled that problem too, by modifying over 20 genes in additional embryos that make the proteins that irritate our immune cells. Although many of these proteins typically reside on the cell surface, they can also be interior proteins which ultimately get chopped up into representative 'tags' that are exposed at the surface. We don't yet know exactly which genes these all are (and they will hopefully soon be published), but one might be able to make a few good guesses.

Researchers in China, have also had recent successes in making multiple CRISPR edits to pig genomes. They were even able to combine the technique with somatic cell nuclear transfer (the method used correct various mutations in the creation of multi-parental embryos) without mosaic mutation or any of the usual undesirable 'off-target' effects. Perhaps the most arresting news from the Chinese pig geneticists has been their creation of custom pet rainbow micropigs. Not only are these pigs miniature due to inactivation of one copy of their growth hormone receptor gene, but they can be ordered in different colors.

Clearly the genomes of all the higher forms of multicellular life must be no strangers to retroviruses. Not only did these genetic inserts co-evolve with their hosts, they orchestrated many of the primary genetic rearrangements that drove key physiologic adaptations—signature

innovations like, for example, placentas. Primate genomes are littered with over a million copies one particular class of repeat elements that are believed to be retroviral derivatives. These elements, known as Alu's, seem to have evolved from various signal recognition RNAs, and possibly a few transfer RNAs.

What is particularly interesting here, is that it was recently shown that pigs devote roughly the same percentage of their genome as primates (about 11%) to a repeat that is almost the same as the Alu's. These porcine repeat elements (known as PRE-1) are structurally and functionally very similar to the primate Alu's and as the authors report, hint at a much closer relationship between us and swine than had former been appreciated.

It has been shown some time ago that human receptors for pig PERVs exist. However if PERVs can just be genetically inactivated, then we don't have to worry too much about trying to make vaccines against them. At this point in the game it is probably important to be sure not only that all the important PERVs have been inactivated, but that their loss doesn't compromise the animal. We might note that despite the clear benefits, making just a single alteration to create genetically-modified plants can still affect their fitness at some level. There probably won't be cataclismic unintended consequences to the environment, or even to the modified organism, but a little caution won't hurt. In every sense of the word, these pigs are GMO's.

Church, and his startup company eGenesis, hope to begin implanting gene-edited pig embryos into mother pigs as soon as it is possible. For an animal that is so close to humans to at once serve not just as food and pet, but also as a organ backup—and do all at once—should give some pause for concern. If the gene editors can also give the pig vocal chords, they might then be able negotiate a deal to serve in the latter two capacities, but perhaps forgo the former.

More information: Gene-editing record smashed in pigs, *Nature* DOI: 10.1038/nature.2015.18525 , www.nature.com/news/gene-editi … shed-in-pigs-1.18525