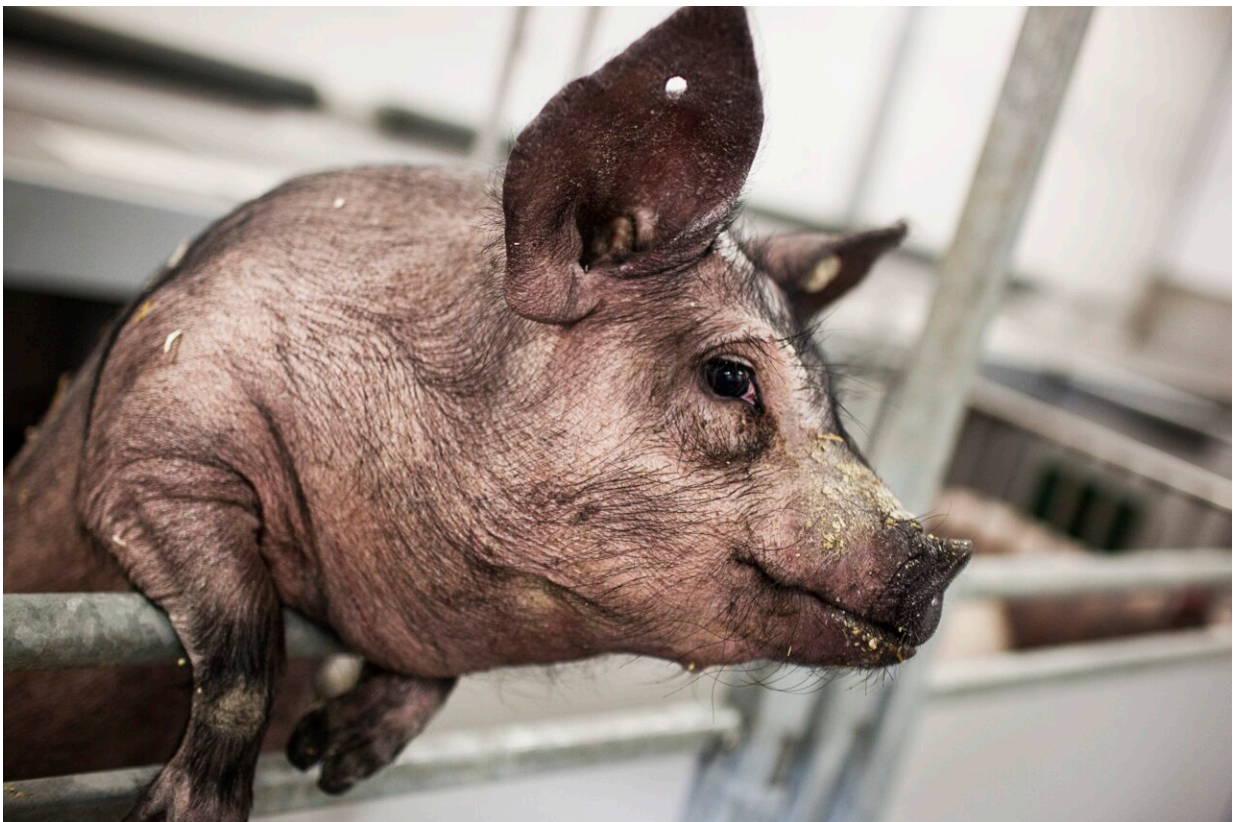


Large-scale mapping of pig genes could lead to greener agriculture, pave the way for new human medicines

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Pigs and humans are very similar. Human and pig organs are almost the same size, and many tissue types are almost identical. This is why pigs are useful when developing and testing new drugs. Thanks to the new findings, we now have even better knowledge about the similarities between pigs and humans. Credit: Jesper Rais, AU Communication.

Researchers from Aarhus University have carried out complex genetic analyses of hundreds of pigs and humans to identify differences and similarities. This new knowledge can be used to ensure healthier pigs for farmers and can help the pharmaceutical industry breed better laboratory pigs for testing new medicines.

It may sound strange, but we can actually learn more about ourselves by studying [pigs](#). Pigs and humans are pretty similar. Our organs, our skin, and the way many diseases develop are largely the same.

Pigs have, therefore, long been used to develop and test [new medicines](#), even though pigs are larger, more expensive, and more difficult to use in experiments than rats and mice.

And now, pigs may become even more valuable as laboratory animals because researchers from the Center for Quantitative Genetics and Genomics at Aarhus University have mapped the most important genetic similarities between pigs and humans. Their research is [published](#) in *Nature Genetics*.

The researchers have not only identified the [genes](#) that are the same in humans and pigs; they have also identified the so-called 'transcriptome' across a number of tissue types. Where the genome includes all the genes found in the DNA of our [cells](#), whether active or inactive, the transcriptome includes the genes that are active in the different types of cells in our body, says Lingzhao Fang, one of the prominent researchers behind the new findings.

"We examined which genes are active and how they are regulated in 34 different tissue types in pigs and compared this with similar studies in humans. We looked at everything from testicular tissue to skin cells and various brain cells," he says. He continues, "No one has ever conducted a study at this scale and comprehensiveness, and we hope the new

knowledge can make a difference in agriculture and the pharmaceutical industry."

More useful knowledge from RNA

A little more than 20 years ago, a group of more than 1,000 researchers succeeded in mapping the entire human genome. After completing the project, the researchers hoped they could now develop treatments for nearly all diseases, because they now knew the code and could identify the errors.

But that is not how the story went.

The researchers soon discovered that there is a big difference between the genes in an individual's recipe book and the recipes that are actually used and translated by the various cell types.

This is what is also referred to as genotype and phenotype, with phenotype referring to the traits or symptoms that can be observed in an individual. Because of the greater role played by the transcriptome, a person can have the genetic disposition for a disease without actually suffering from the disease.

In other words, two people who, on paper, have the same disease mutation do not necessarily become ill to the same extent. With greater knowledge about the role of the transcriptome in various diseases, it is possible to develop better and more targeted medicines.

This is one area in which the results from Lingzhao Fang's study can be useful regarding pigs as laboratory animals.

"Pigs become more suited as animals for testing new medicines. As the various tissue types in pigs and humans are very similar, in fact, more

similar than we thought, the pharmaceutical industry can test the safety of new medicines in pigs with much higher accuracy," he says.

DNA, RNA and transcriptomes

In the center of every human and pig cell, inside a small nucleus, are the long, two-stranded DNA molecules that make up the chromosomes. The strands consist of almost endless rows of four small molecules that we abbreviate to A, C, G, and T.



Pigs resemble humans more than mice and rats do. But because pigs are more expensive to use as a model organism in research into new medicines, the small rodents are used more often. However, better knowledge about what makes pigs and humans similar could make pigs even more valuable in developing new medicines for humans. The photo shows a pig that has been bred to study

atherosclerosis. Credit: Jesper Rais/AU Communication

The sequence of the four molecules is what forms our genes. A gene is a sequence of four molecules, and it serves as a recipe for a protein.

However, the sequence must be translated before the cell can produce one of the many different proteins for which it has recipes in its DNA. This happens when the two strands of DNA unwind where the recipe is located, and a so-called RNA strand binds to this place and copies the part of the code that makes up the gene. In simple terms, RNA is single-stranded DNA.

RNA leaves the cell nucleus and transports the code to the cell's protein factories, the ribosomes, where the code is then translated into a protein.

All cells in our body have the same DNA, but the parts of the DNA code that are translated and activated differ from cell to cell. Liver cells have other [active genes](#) than skin cells, for example. Not all RNA sequences transport code to the protein factories. Instead, some bits attach themselves to other RNA sequences to stop them from being translated into proteins or to ensure that the body produces even more of the protein in question.

The RNA sequences that are active in a specific type of cell are called the transcriptome. This is what the researchers have been studying in this research project.

Can also help agriculture become greener

The [pharmaceutical industry](#) is not the only industry to potentially benefit from the new results. Agriculture can also use the results in their

efforts to breed pigs with a reduced climate impact, according to Lingzhao Fang.

"There's never before been such a comprehensive mapping of the genes that are active in various tissue types. Our results make it possible to more precisely pinpoint the genetic mechanisms that lead to different desirable traits in pigs," he says and continues, "For example, traits that make them more climate-friendly."

"Our mapping also paves the way for researchers to edit pig genes far more precisely and, in this way, develop entirely new properties in the future. Because we now know more about a wide range of traits in pigs, other researchers can more easily use gene-editing techniques such as CRISPR to change genes or insert new sequences with greener properties."

Mapping other animals as well

Pigs are actually not the first animal whose transcriptome Lingzhao Fang and his colleagues have mapped. They started with cows a few years ago, and they plan to map a number of other animals in the coming years.

"We already have a study on chickens in the pipeline. It's currently being peer-reviewed, but we hope to publish it early next year," he says.

In addition to chickens, pigs, and cows, the research team is studying goats, sheep, horses, and ducks using the same method. He explains that the ultimate objective is not only to make agriculture greener but also to obtain a better understanding of fundamental animal and human biology.

"Once we've completed the project, we'll have gained a greater basic understanding of the biology and evolution of a number of animals. This knowledge can be useful in other areas," he says and continues:

"For example, we have problems with disease transmission between humans and farm animals. Our mapping may provide us with the necessary knowledge to limit and prevent outbreaks in the future."

One of the reasons why Lingzhao Fang is studying [farm animals](#) and not [wild animals](#) is that it is easy to access tissue samples and large amounts of data. However, the knowledge obtained can also be used in relation to wild and even extinct animals.

"We will gain a fundamental understanding of the biology of several different animals, and these all have wild cousins who basically function in the same way," he concludes.

More information: Jinyan Teng et al, A compendium of genetic regulatory effects across pig tissues, *Nature Genetics* (2024). [DOI: 10.1038/s41588-023-01585-7](#)

Provided by Aarhus University

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