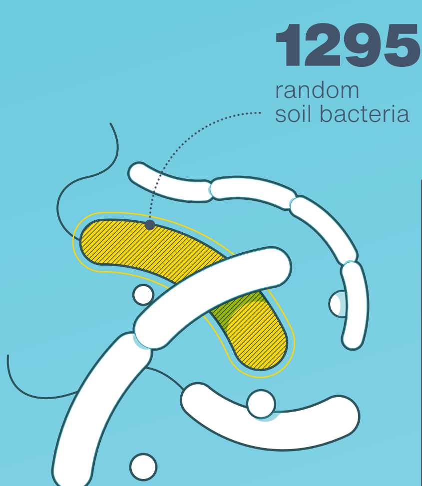
IN 5 STEPS

FINDING NEW ANTIBIOTICS

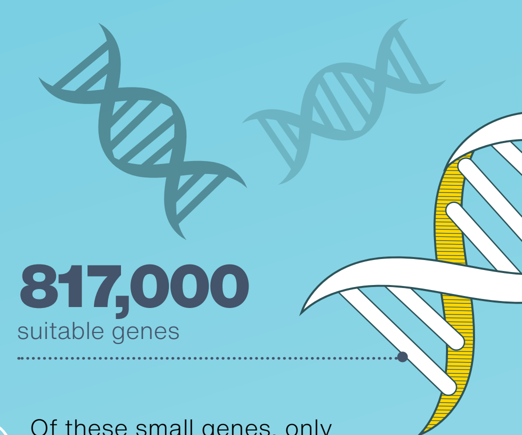
Until now, scientists have looked for new antibiotics among the relatives of bacterial strains that are known to make antibiotics. WUR bio-information scientist Marnix Medema and his Leiden colleagues are now using artificial intelligence and algorithms to look for new antibiotics in thousands of bacteria at the same time.

Text Albert Sikkema • Infographic Pixels&inkt



1 The researchers collect a large set of bacterial strains from a soil sample. In the example used here, they isolate 1295 soil bacteria at random, some of which are known to make antibiotics.

2 The researchers select small genes and fragments of DNA that may be small genes from the genomes of these bacterial strains, because it is known that such small genes can code for the 'raw materials' for antibiotics. By doing this, they obtain 7.2 million possible small genes from the 1295 bacterial strains.

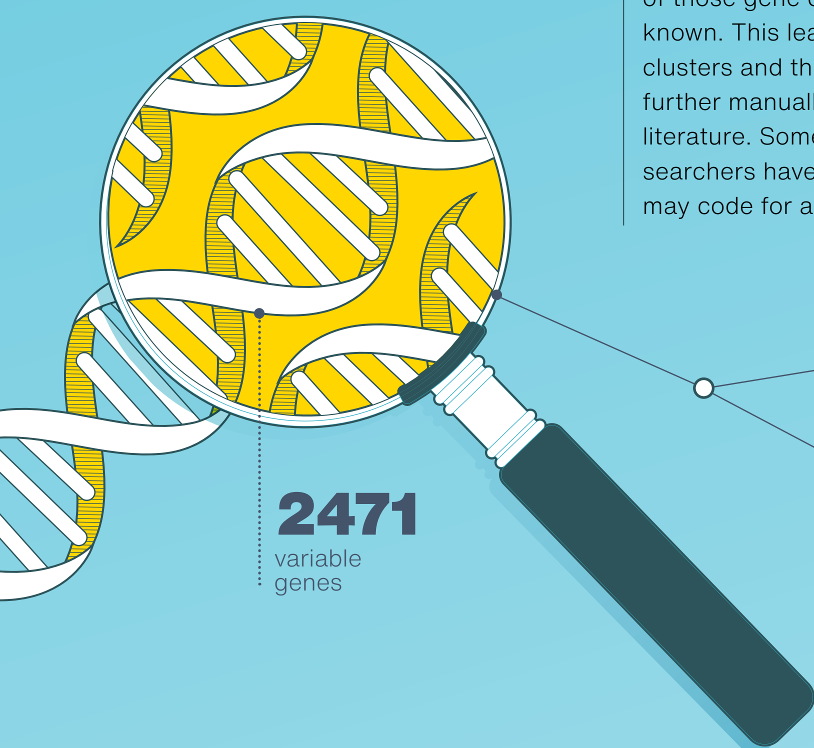


3 Of these small genes, only genes with particular amino acids and characteristics can make antibiotics. The researchers have created an algorithm that 'learns' to recognize and select these genes. This leaves them with 817,000 genes.

4 Not all bacteria can make antibiotics, as this is a specialized function. So if you compare the DNA of bacteria, the antibiotics gene is a variable gene. The machine therefore selects the variable genes from the 817,000 genes and checks where they are located on the genome. If they are surrounded by other variable genes, that suggests an antibiotic. This is because an antibiotic gene needs to have genes around it that code for enzymes that can 'taper off' the antibiotic. So the machine selects variable gene clusters that make enzymes too. There are 2471 of those.

42
gene clusters that may code for an antibiotic.

5 Next, the researchers do a network analysis to rule out duplicates. They end up with 187 unique gene clusters that may make antibiotics. After that, they check to see which of those gene clusters are already known. This leaves them with 151 new clusters and this group is assessed further manually and on the basis of literature. Some months later, the researchers have 42 gene clusters that may code for an antibiotic.



Many variable genes together suggests an antibiotic

Usable antibiotic

Medema and his colleagues have studied one of the 42 highly promising gene clusters. They characterized the molecule made by this gene cluster. That molecule may be an antibiotic. They also studied the enzyme route: the chemical reactions of the supporting genes that lead to this molecule. Medema does not yet know which bacteria switch off this molecule and whether it is therefore a usable antibiotic. That will require more research into the way the molecule works.