

## Healthcare industry BW

### Evolution caught in the act

**Mutations are the raw material of evolution. Charles Darwin already recognized that evolution depends on heritable differences between individuals: those who are better adapted to the environment have better chances to pass on their genes to the next generation. A species can only evolve if the genome changes through new mutations, with the best new variants surviving the sieve of selection. Scientists at the Max Planck Institute for Developmental Biology in Tübingen, Germany, and Indiana University in Bloomington have now been able to measure for the first time directly the speed with which new mutations occur in plants. Their findings shed new light on a fundamental evolutionary process. They explain, for example, why resistance to herbicides can appear within just a few years.**

"While the long term effects of genome mutations are quite well understood, we did not know how often new mutations arise in the first place," said Detlef Weigel, director at the Max Planck Institute in Germany. It is routine today to compare the genomes of related animal or plant species. Such comparisons, however, ignore mutations that have been lost in the millions of years since two species separated. The teams of Weigel and his colleague Michael Lynch at Indiana University therefore wanted to scrutinize the signature of evolution before selection occurs. To this end, they followed all genetic changes in five lines of the mustard relative *Arabidopsis thaliana* that occurred during 30 generations. In the genome of the final generation they then searched for differences to the genome of the original ancestor.

The painstakingly detailed comparison of the entire genome revealed that in over the course of only a few years some 20 DNA building blocks, so called base pairs, had been mutated in each of the five lines. "The probability that any letter of the genome changes in a single generation is thus about one in 140 million," explains Michael Lynch. To put it differently, each seedling has on average one new mutation in each of the two copies of its genome that it inherits from mum and dad. To find these tiny alterations in the 120 million base pair genome of *Arabidopsis* was akin to finding the proverbial needle in a haystack, says Weigel: "To ferret out where the genome had changed was only possibly because of new methods that allowed us to screen the entire genome with high precision and in very short time." Still, the effort was daunting: To distinguish true new mutations from detection errors, each letter in each genome had to be checked 30 times.

The number of new mutations in each individual plant might appear very small. But if one starts to consider that they occur in the genomes of every member of a species, it becomes clear how fluid the genome is: In a collection of only 60 million *Arabidopsis* plants, each letter in the genome is changed, on average, once. For an organism that produces thousands of seeds in each generation,



An Illumina sequencer is used to decipher the genome of *Arabidopsis thaliana*.  
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60 million is not such a big number at all.

Apart from the speed of new mutations, the study revealed that not every part of the genome is equally affected. With four different DNA letters, there are six possible changes-but only one of these is responsible for half of all the mutations found. In addition, scientists can now calculate more precisely when species split up. *Arabidopsis thaliana* and its closest relative, *Arabidopsis*

lyrata, differ in a large number of traits including size and smell of flowers or longevity: Arabidopsis lyrata plants often live for years, while Arabidopsis thaliana plants normally survive only for a few months. Colleagues had previously assumed that only five million years had passed by since the two species went their separate ways. The new data suggest instead that the split occurred already 20 million years ago. Similar arguments might affect estimates of when in prehistory animals and plants were first domesticated.

On a rather positive note, the results of the US-German team show that in sufficiently large populations, every possible mutation in the genome should be present. Thus, breeders should be able to find any simple mutation that has the potential to increase yield or make plants tolerate drought in a better manner. Finding these among all the unchanged siblings remains nevertheless a challenging task. On the other hand, the new findings easily explain why weeds become quickly resistant to herbicides. In a large weed population, a few individuals might have a mutation in just the right place in their genome to help them withstand the herbicide. "This is in particular a problem because herbicides often affect only the function of individual genes or gene products," says Weigel. A solution would be provided by herbicides that simultaneously interfere with the activity of several genes.

Turning to the larger picture, Weigel suggests that changes in the human genome are at least as rapid as in Arabidopsis: "If you apply our findings to humans, then each of us will have on the order of 60 new mutations that were not present in our parents." With more than six billion people on our planet, this implies that on average each letter of the human genome is altered in dozens of fellow citizens. "Everything that is genetically possible is being tested in a very short period," adds Lynch, emphasizing a very different view than perhaps the one we are all most familiar with: that evolution reveals itself only after thousands, if not millions of years.

#### **Original work:**

Stephan Ossowski, Korbinian Schneeberger, José Ignacio Lucas-Lledó, Norman Warthmann, Richard M. Clark, Ruth G. Shaw, Detlef Weigel and Michael Lynch  
The rate and molecular spectrum of spontaneous mutations in Arabidopsis thaliana. Science, January 1, 2010

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#### **Press release**

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