CRISPR/Cas in animals: Unintended changes and unexpected patterns of inheritance

Findings relevant for planned marketing of GE laying hens

10 February 2022 / In experiments with zebrafish, researchers have shown that unintended effects of CRISPR/Cas applications are inherited in subsequent generations. They also found unusual patterns of inheritance. According to the scientists, the findings show that the effects of CRISPR/Cas applications on subsequent generations need to be examined in much greater detail.

In a preprint version, CRISPR/Cas in zebrafish was already shown to cause large structural changes at off-target sites. This means that the gene scissors can cut genomic regions outside of the target site, and thus cause specific unintended mutations. The experiments are part of basic research. In this context, zebrafish are seen as important model organisms. The researchers assume that unintended genetic changes at off-target sites can be more concerning compared to those at on-target regions, as the effects may go unnoticed.

Many of the unintended genetic alterations have now been observed in the subsequent generation. Surprisingly, in some cases, not all the bodily cells of the fish were affected. In addition, again in some cases, the researchers found non-Mendelian patterns of inheritance, with some alterations being homozygous while others were heterozygous. The findings show that unintended effects caused by the gene scissors can lead to specific effects and new risks.

Consequently, the offspring of animals manipulated with CRISPR/Cas for use in agriculture, need to be examined in greater detail to detect unintended genetic alterations. The first of these animals might be genetically engineered laying hens: researchers in Israel have used CRISPR/Cas to alter hens so that they do not produce male offspring. A deadly gene is passed on to any male offspring, which should cause these chicks to die in the egg before they hatch. A patent for the process and the resulting animals has already been filed. The chicken could in due course be marketed in cooperation with a US company.

According to some media reports, there are also plans to market the hens and their eggs in the EU. Regulation in the EU requires mandatory risk assessment and labelling of offspring from genetically engineered organisms. The recent research on zebrafish shows just how important these legal requirements are. It provides evidence that if animals are engineered with ‘New GE’, their offspring also may suffer from unintended genetic changes that are associated with specific risks.

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Further information: Recent publication on CRISPR/Cas-zebrafish [2]
Previous news on research with CRISPR/Cas zebrafish [3]
Patent application on genetically engineered chicken [4]

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