

European court ruling -Regulates Gene editing

By [Erik Stokstad](#) Jul. 25, 2018 , 4:40 PM

Hopes for an easier regulatory road for genetic engineering in European agriculture were **dashed today by the Court of Justice of the European Union**. In a **closely watched decision**, the court ruled that plants created with new gene-editing techniques that don't involve transferring genes between organisms—such as CRISPR—must go through the same lengthy approval process as traditional transgenic plants. Many researchers had argued that regulators should take a lighter touch when evaluating products created with the new technologies, but environmental groups **and their allies successfully argued that they should be subject to the same EU rules that apply to other genetically modified organisms**. “We applaud the European Court of Justice for this forward-thinking decision,” said Dana Perls, senior food and agriculture campaigner at Friends of the Earth (FOE) in Washington, D.C., in a statement. **“All products made with genetic engineering, including ones made with gene-editing tools like CRISPR, should be regulated, assessed for health and environmental impacts, and labeled.”** FOE’s affiliate in France was part of a coalition of groups that brought the case. Many researchers were less pleased. “This is going to impact plant breeding in Europe hugely and negatively,” predicted Cathie Martin, a group leader at the John Innes Centre in Norwich, U.K., in **a statement distributed by the Science Media Centre in London**. The ruling is “the death blow for plant biotech in Europe,” said Sarah Schmidt of the Heinrich Heine University of Düsseldorf in Germany. **It will force gene-edited plants to go through a regulatory process that typically costs about \$35 million, she said, meaning only large companies will be able to foot the bill, effectively pricing out universities, nonprofits, and small companies.** The case focused on crops that have been made resistant to herbicides without transferring genes from other species. (The transgenic technique has been the typical way of creating herbicide-tolerant crops.) The French government had passed a law exempting these new gene-edited crops from regulation under the European Union’s directive on genetically modified organisms (GMOs), which requires an assessment of risks to health and the environment, as well as labeling, tracking, and monitoring of the products. **Confédération Paysanne, a French union in Bagnole representing small farms, and eight other groups, sued and charged that the plants modified with gene-editing techniques should be regulated under the GMO directive, because they could cause significant harm.** The court decided that gene-editing techniques are covered by the GMO directive because they “alter the genetic material of an organism in a way that does not occur naturally.” **(The court exempted conventional mutagenesis—the unnatural use of chemicals or radiation to create mutations for plant breeding—because it has “a long safety record.”)** It also said the new

Comment [i]: **and the usda did not regulate this like the GM's or GE's like they were going to ---the question is why---when clearly any editing or manipulating any genome is a form of genetic engineering and there has been as well studies showing how crispr causes genteic and dna damage with unforeseen effects**

gene-editing techniques have risks that could be similar to those of transgenic engineering. Those findings drew criticism from some researchers. "To classify gene-edited crops as GMOs and equivalent to transgenic crops is completely incorrect by any scientific definition," said Nick Talbot, a molecular geneticist at the University of Exeter in the United Kingdom. "Precise modern gene-editing technologies allow accurate, predictable changes to be made in a genome." The court also asserted that gene-editing techniques "make it possible to produce genetically modified varieties at a rate out of all proportion to those resulting from the application of conventional methods of mutagenesis." Schmidt said she was "shocked" by this claim. Maurice Moloney, CEO of the Global Institute for Food Security in Saskatoon, Canada, called it "logically absurd" that gene editing was riskier than the random mutagenesis used in conventional breeding. In its statement, FOE said it hopes U.S. regulators would follow the lead of the European court. So far, however, U.S. officials have said they have no plans to subject most gene-edited crops to the same regulatory process used for transgenic crops.

Genome damage from CRISPR/Cas9 gene editing higher than thought

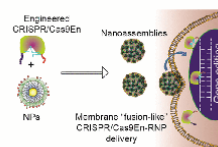
Scientists at the Wellcome Sanger Institute have discovered that CRISPR/Cas9 gene editing can cause greater genetic damage in cells than was previously thought. These results create safety implications for gene therapies using CRISPR/Cas9 in the future as the unexpected damage could lead to dangerous changes in some cells. Reported today (16 July 2018) in the journal *Nature Biotechnology*, the study also revealed that standard tests for detecting DNA changes miss finding this genetic damage, and that caution and specific testing will be required for any potential gene therapies. CRISPR/Cas9 is one of the newest genome editing tools. It can alter sections of DNA in cells by cutting at specific points and introducing changes at that location. Already extensively used in scientific research, CRISPR/Cas9 has also been seen as a promising way to create potential genome editing treatments for diseases such as HIV, cancer or sickle cell disease. Such therapeutics could inactivate a disease-causing gene, or correct a genetic mutation. However, any potential treatments would have to prove that they were safe. Previous research had not shown many unforeseen mutations from CRISPR/Cas9 in the DNA at the genome editing target site. To investigate this further the researchers carried out a full systematic study in both mouse and human cells and discovered that CRISPR/Cas9 frequently caused extensive mutations, but at a greater distance from the target site. The researchers found many of the cells had large genetic rearrangements such as DNA deletions and insertions. These could lead to important genes being switched on or off, which could have major implications for CRISPR/Cas9 use in therapies. In addition, some of these changes were too far away from the target site

Comment [i]: Europe is correct --Canada is retarded and so are the States to think when editing it is different then GE or GM --when it fact it is exactly the same the procedure differs but the end result is a modification from the original template and the involvement of tampering

Comment [i]: or the opposite ---create genetic Mutations

to be seen with standard genotyping methods. Prof Allan Bradley, corresponding author on the study from the Wellcome Sanger Institute, said: **"This is the first systematic assessment of unexpected events resulting from CRISPR/Cas9 editing in therapeutically relevant cells, and we found that changes in the DNA have been seriously underestimated before now."** It is important that anyone thinking of using this technology for gene therapy proceeds with caution, and looks very carefully to check for possible harmful effects." Michael Kosicki, the first author from the Wellcome Sanger Institute, said: "My initial experiment used CRISPR/Cas9 as a tool to study gene activity, **however it became clear that something unexpected was happening.** Once we realised the extent of the genetic rearrangements we studied it systematically, looking at different genes and different therapeutically relevant cell lines, and showed that the CRISPR/Cas9 effects held true." **The work has implications for how CRISPR/Cas9 is used therapeutically and is likely to re-spark researchers' interest in finding alternatives to the standard CRISPR/Cas9 method for gene editing.** Prof Maria Jasin, an independent researcher from Memorial Sloan Kettering Cancer Centre, New York, who was not involved in the study said: "This study is the first to assess the **repertoire of genomic damage arising at a CRISPR/Cas9 cleavage site.** While it is not known if genomic sites in other cell lines will be affected in the same way, this study shows that further research and specific testing is needed before CRISPR/Cas9 is used clinically." -**Story Source-** [Materials](#) provided by [Wellcome Trust Sanger Institute](#). **Journal Reference-** Michael Kosicki, Kårt Tomberg, Allan Bradley. **Repair of double-strand breaks induced by CRISPR–Cas9 leads to large deletions and complex rearrangements.** *Nature Biotechnology*, 2018; DOI: [10.1038/Nbt.4192](#) -Wellcome Trust Sanger Institute. "Genome damage from CRISPR/Cas9 gene editing higher than thought: Caution required for using CRISPR/Cas9 in potential gene therapies." ScienceDaily. ScienceDaily, 19 July 2018. <www.sciencedaily.com/releases/2018/07/180719165032.htm>.

~~~~~ Researchers develop nanoparticle delivery system for gene-editing tool



Researchers from the [University of Massachusetts Amherst](#) have designed a **nanoparticle delivery system to assist the gene-editing tool known as CRISPR/Cas9 across the cell membrane and into the cell nucleus, effectively avoiding the cell's natural defense mechanisms.** The team's work was published in [ACS Nano](#). "CRISPR has two components: **a scissor-like**

protein called Cas9, and an RNA molecule called sgRNA that guides Cas9 to its target gene. Once the Cas9-sgRNA pair gets to the destination gene in the nucleus, it can interrogate its genetic mistakes and correct them with the help of the host cell's repair machinery,"

principal investigator Rubul Mout said in prepared remarks. Since CRISPR was discovered in 2012, gene editing has emerged as a means to treat otherwise incurable genetic diseases by manipulating diseased genes. "However, to achieve this, biotech and pharmaceutical companies are constantly searching for more efficient CRISPR delivery methods," Mout added. **The team of researchers engineered the Cas9 protein, Cas9En, and carrier nanoparticles to develop a delivery system. "By finely tuning the interactions between engineered Cas9En protein and nanoparticles, we were able to construct these delivery vectors,"** co-principal investigator Vincent Rotello explained. "The vectors carrying the **Cas9 protein and sgRNA come into contact with the cell membrane, fuse, and release the Cas9:sgRNA directly into the cell cytoplasm."** "Cas9 protein also has a **nuclear guiding sequence that ushers the complex into the destination nucleus.** The key is to tweak the Cas9 protein," he added. "We have delivered this Cas9 protein and sgRNA pair into the cell nucleus without getting it trapped on its way. We have watched the delivery process live in real time using sophisticated microscopy." With their nanoparticle delivery system, the team claimed they could deliver the Cas9 protein and **sgRNA pair into 90% of cells with an editing efficiency of 30%.** "90% cytosolic/nuclear delivery is a huge improvement compared to others methods," Mout said. The team's engineered nanoparticle system could serve to deliver other materials including **polymers, lipid nanoparticles or self-assembling peptide, the team suggested.** "Now that we have achieved efficient gene editing in cultured cells, we are aiming to edit genes in pre-clinical animal models. We are also interested in gene editing for adoptive therapies, where a diseased cell is isolated from a patient, corrected by CRISPR in the lab, and delivered back to the patient," Rotello said.

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in scientific research, CRISPR/Cas9 has also been seen as a promising way to create potential genome editing treatments for diseases such as HIV, cancer or sickle cell disease. **Such therapeutics could inactivate a disease-causing gene, or correct a genetic mutation.** However, any potential treatments would have to prove that they were safe. **Previous research had not shown many unforeseen mutations from CRISPR/Cas9 in the DNA at the genome editing target site.** To investigate this further the researchers **carried out a full systematic study in both mouse and human cells and discovered that CRISPR/Cas9 frequently caused extensive mutations,** but at a greater distance from the target site. **The researchers found many of the cells had large genetic rearrangements such as DNA deletions and insertions. These could lead to important genes being switched on or off,** which could have major implications for CRISPR/Cas9 use in therapies. In addition, **some of these changes were too far away from the target site to be seen with standard genotyping methods.** Prof Allan Bradley, corresponding author on the study from the Wellcome Sanger Institute, said: **"This is the first systematic assessment of unexpected events resulting from CRISPR/Cas9 editing in therapeutically relevant cells, and we found that changes in the DNA have been seriously underestimated before now.** It is important that anyone thinking of using this technology for gene therapy proceeds with caution, and looks very carefully to check for possible harmful effects." Michael Kosicki, the first author from the Wellcome Sanger Institute, said: "My initial experiment used CRISPR/Cas9 as a tool to study gene activity, **however it became clear that something unexpected was happening.** Once we realised the extent of the genetic rearrangements we studied it systematically, looking at different genes and different therapeutically relevant cell lines, and showed that the CRISPR/Cas9 effects held true." **The work has implications for how CRISPR/Cas9 is used therapeutically and is likely to re-spark researchers' interest in finding alternatives to the standard CRISPR/Cas9 method for gene editing.** Prof Maria Jasin, an independent researcher from Memorial Sloan Kettering Cancer Centre, New York, who was not involved in the study said: "This study is the first to assess the **repertoire of genomic damage arising at a CRISPR/Cas9 cleavage site.** While it is not known if genomic sites in other cell lines will be affected in the same way, this study shows that further research and specific testing is needed before CRISPR/Cas9 is used clinically." -**Story Source-**[Materials](#) provided by [Wellcome Trust Sanger Institute](#). **Journal Reference-**Michael Kosicki, Kärt Tomberg, Allan Bradley. **Repair of double-strand breaks induced by CRISPR–Cas9 leads to large deletions and complex rearrangements.** *Nature Biotechnology*, 2018; DOI: [10.1038/Nbt.4192](#) -Wellcome Trust Sanger Institute. "Genome damage from CRISPR/Cas9 gene editing higher than thought: Caution required for using CRISPR/Cas9 in potential gene therapies." ScienceDaily. ScienceDaily, 19 July 2018. <[www.sciencedaily.com/releases/2018/07/180719165032.htm](#)>.

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