Logical control of CRISPR gene editing system

Researchers at the University of Oxford have developed a control system that allows spatio-temporal activation of CRISPR, based on an engineered RNA guide strand.

CRISPR/Cas9 approaches and limitations

CRISPR is described as “the technology of the century” and brings the hope of treatments for currently incurable diseases, by excising or silencing genes that drive tumour proliferation, repair of faulty genes, or by killing diseased cells.

However, unwanted DNA cuts, resulting from non-specific delivery to off-target cells, remain a serious problem in the successful clinical translation of CRISPR-based therapeutics. Exact spatio-temporal control of CRISPR/Cas9 activity would lead to the development of new therapies and new tools for biotechnology with great translational potential.

Improvement on current methods with the Oxford technology

Oxford academics have developed an innovative control system allowing gene editing to be activated only in response to precisely defined combinations of biomolecular signals in targeted cell populations.

This technology is based on engineered Cas9 guide strands that incorporate sensor motifs that allow the nuclease Cas9 to cut DNA only when conditions characteristic of target cells are met. By improving the CRISPR/Cas9 constructs with the use of these modified guide-RNAs (gRNA) containing the blocking module, a nucleic-acid dependent activation of the Cas9 enzyme is allowed.

Furthermore, this unique design provides Cas9 sensing abilities with minimal leakage of activity, which is desirable for precise enzyme activity.

Several RNA guide strands have already been developed in the laboratory. Efficiency and selectivity of the system has been succesfuly tested *in vitro* and in cellular models.

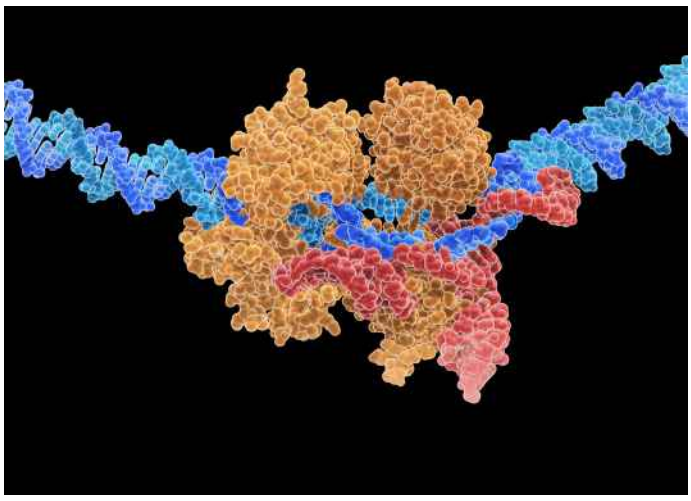
Main applications of conditional regulation

This new approach improves the current CRISPR/Cas9 gene editing applications and it can be applied to any gene regulation technique but with improved implementation and results:

- Use in biomedical applications for cell-type specific activation of the CRISPR/Cas9 system
- Tool for synthethic biology: genetic circuits or nucleic-acid nanotechnology
- Production of other conditionally activated CRISPR/Cas9 systems based on the use of other activation molecules, such as proteins or small molecules

Commercialisation

This technology is subject to a patent application. Oxford University Innovation is interested in hearing from companies that would like to license this technology.



For further information please contact:
Bénédicte Menn
benedicte.menn@innovation.ox.ac.uk
+44 (0)1865 280906
www.innovation.ox.ac.uk
Project number: 14361

Technology Transfer from the University of Oxford