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Technology Offer

Genome-Editing-Technologies

GOLD gRNA - allows robust genome editing regardless of spacer sequence composition by super stable hairpin technology

Ref.-No.: 1306-6101-LI

A Cas nuclease such as Cas9 can introduce a DNA double strand break in a sequence target that is complementary to a 20-nt spacer sequence of its bound guide RNA (gRNA) when a protospacer adjacent motif (PAM) is present. The gRNA can be provided as duplex of spacer containing CRISPR RNA (crRNA) and trans-activating crRNA (tracrRNA). Or as a single gRNA (sgRNA) where crRNA and tracrRNA are fused by an artificial loop.
Hence a gRNA consists of the target-specific spacer and a constant part typically comprised of distinct motifs including the nexus, and a first and second hairpin.
Genome editing efficiencies vary strongly from sequence target to sequence target and some sequence targets are totally intractable to genome editing. This results in a need to pre-screen several gRNAs to find an efficient one. In addition numerous gRNA efficiency algorithms have been employed to allow in-silico prescreening. But their accuracy is far from satisfying.
Investigation of certain biological questions or precise repair of disease alleles can be prevented or limited to the use of a potentially inefficient single target site. Or large scale Crispr screens could not be harnessed with optimally covering gRNA libraries.

Technology

Scientists at the Max-Planck Institute for Evolutionary Anthropology in Leipzig demonstrated that low cleavage efficiency of targets can be due to non-canonical gRNA secondary structures (“misfolding”) provoked by certain spacer sequences.
They have developed a guide RNA (gRNA) backbone comprising an elongated super stable (first) hairpin that does not interact with a Cas enzyme but locks the secondary structure of the whole gRNA in order to suppress such misfolding and thereby to enforce and enable correct base pairing of the spacer sequence to its target sequence in otherwise failing gRNAs.
This GenOme-Editing-Locked-Design (GOLD-tracr/gRNA) **allows robust genome editing regardless of spacer sequence composition**. By introduction into unbiased gRNA libraries it can help to make them more efficient in their cleavage capabilities in CRISPR knock-out, activation or repression screens without compromising already well behaving gRNAs in general.

Patent Information

A priority application protecting a stabilized hairpin and its use has been filed in 2021. More information is available under confidentiality only for the time being.

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