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Technology Offer

Genome-Editing-Technologies

Single compound or compound mix dramatically improve Homology-Directed-Repair (HDR)

Ref.-No.: 1306-5734-LI & 1306-5288-LI

Precise genome editing demands for homology-directed repair (HDR) by aiming to introduce a new double stranded DNA substituting for a homologous sequence but partially defect one. This substrate dependent reaction does compete with direct non-homologous end joining (NHEJ) of the double strand breaks. NHEJ is error-prone and is therefor mainly used for gene inactivation.
The rate of NHEJ is directly limiting the rate of HDR. For this reason HDR in vitro does occur on a very low level only and the frequency of successfully edited cells remains very low.
To tip the balance between the two reactions one can try to increase HDR by inhibiting NHEJ.

Technology

Scientists at the Max-Planck Institute for Evolutionary Anthropology in Leipzig have developed two approaches to drastically enhance HDR efficiency by blocking NHEJ. Both do block kinases (DNA-PKcs) chemically or genetically (DNA-PKc mutant) that are promoting NHEJ.

1.) iCRISPY compound mix. Such mixture contains several inhibitors of DNA-PKcs (our reference: MI-5288) - or even just one (“M-compound-only” still enabling strong HDR; our reference: MI-5734). Both approaches enable strong and recently unseen HDR efficiencies up to 90% in cell culture. iCRISPY mix significantly increases HDR rates independently of cell types or CRISPR enzymes used, when transiently applied.
2.) Genetically modified cell lines harbouring mutated DNA-PKcs permit high HDR rates while confidently maintaining genome stability. DNA-PKc mutant cell lines from HEK293 cells, K562 cells and human pluripotent stem cells (409B2) are readily available.

Patent Information

1306-5288-LI: see WO18/189186
1306-5734-LI: see WO20/127738

Literature

(1) Targeting repair pathways with small molecules increases precise genome editing in pluripotent stem cells, Riesenberg and Maricic, Nat Commun. 2018 Jun 4;9(1):2164
(2) Simultaneous precise editing of multiple genes in human cells, Nucleic Acids Res. Riesenberg et al., 2019 Nov 4;47(19):e116

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