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LockSeq: Ensuring genomic safety in gene therapies through high-fidelity NGS validation

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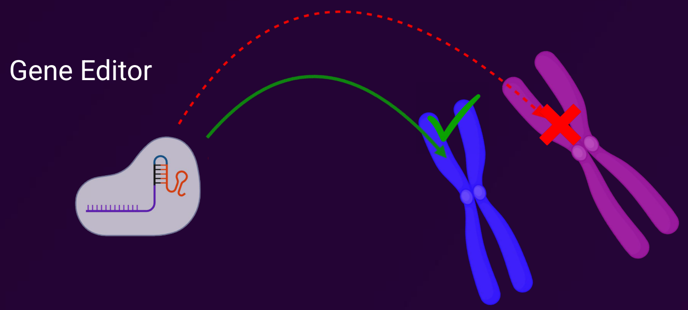
Off-Target Confirmation Is Critical For Safety Assessment



01 CRISPR ideally generates **one intended clean edit** — at the same time, there are **hundreds of potential off-target sites** across the genome.

02 Current methods trade sensitivity for scale: **the more sites are surveyed the more dropouts***, leaving regulatory blind spots.

03 Off-targets detected late can **cost 6–50× more** to resolve than at pre-clinical stage.

PRE-CLINICAL	PHASE I	PHASE II/III
€2–5M	€30M	€100M+
Cost of off-target discovery	If discovered post-IND	Trial halt, programme rework

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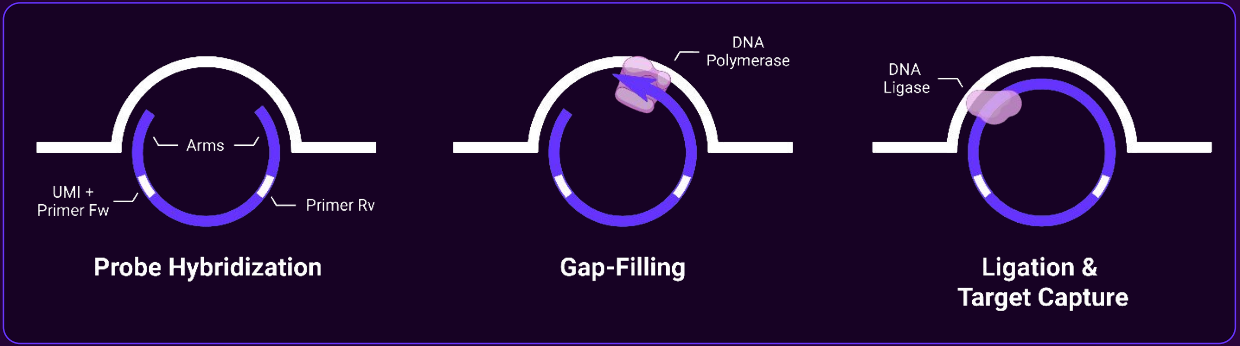
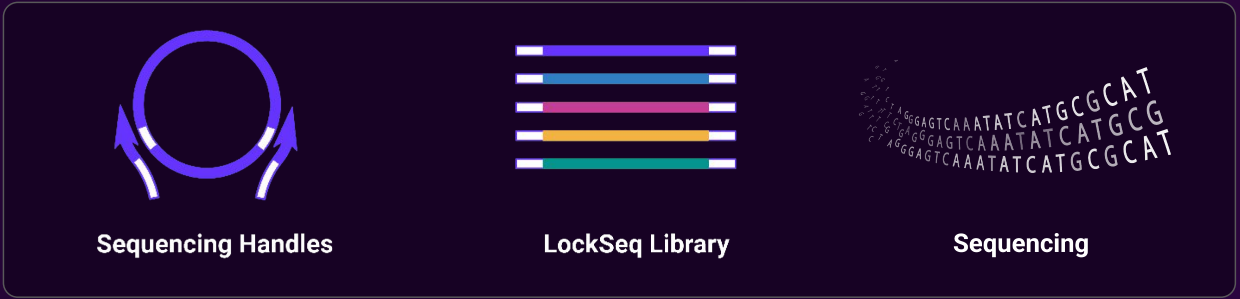
* Dropout = The stochastic or systematic failure to capture a genomic locus during off-target validation.

LockSeq: High-Fidelity Molecular Lock Capture Chemistry

I. Target Capture



II. Library Preparation



One probe per target. No primer competition. No amplification bias.

Hiatt et al, 2013: https://doi.org/10.1101/gr.147686.112. Pending Patents.

COUNTAGEN

Robust Variant Detection Across Platforms

0.1%

VAF sensitivity limit

= 1in 1,000 alleles

R^2>0.99

ONT x Illumina x expected

Excellent correlation across platforms

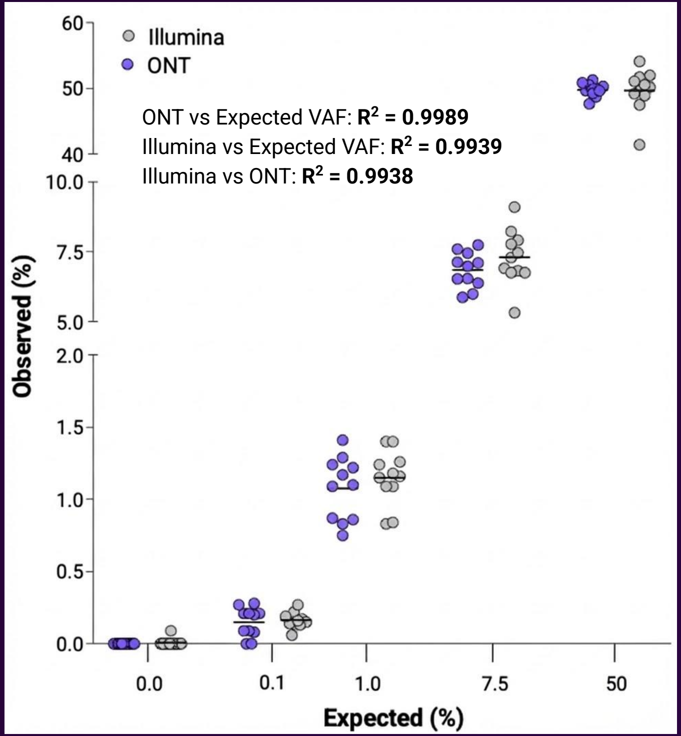
>98%

Indel profiling accuracy

High confidence variant calling

ALSO VALIDATED

- Cas9
- Base editing
- Prime editing
- Transposon systems



OBSERVED VS. EXPECTED VAF · ILLUMINA × ONT

Acknowledgements

NIST NATIONAL INSTITUTE OF STANDARDS AND TECHNOLOGY U.S. DEPARTMENT OF COMMERCE

Manuscript in review at Nature Biotechnology

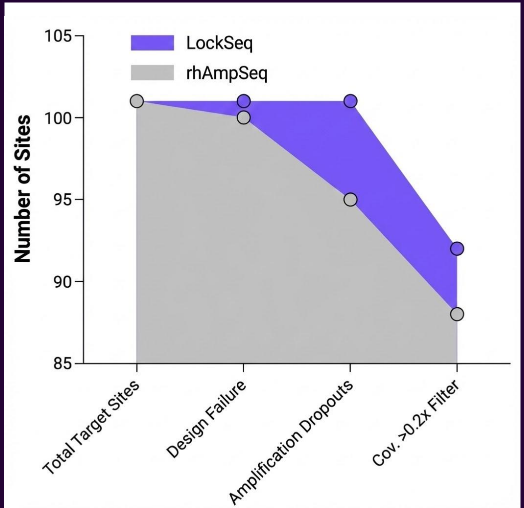
Minimal Target Dropout & Uniform Capture

0 **LockSeq Dropouts**
Across 101 designed sites

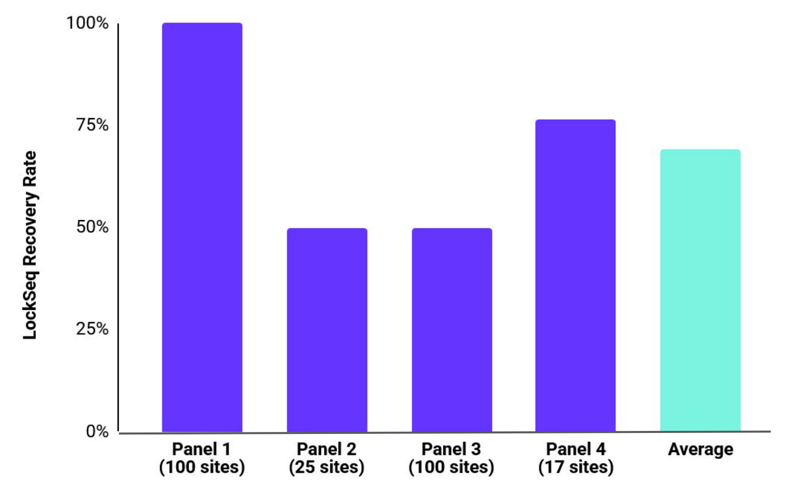
6 **rhAmpSeq Dropouts**
On same panel, same DNA

70% **Recovery Rate**
Reduced Blind Spots

90% **Coverage Uniformity**
Bias reduction



Site-retention through the panel pipeline

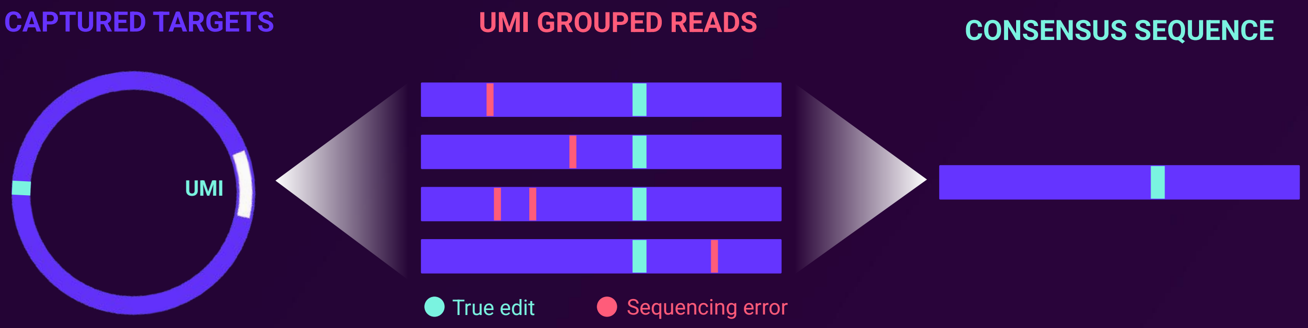


Recovery Rate Across 4 Panels

EMX1 canonical gRNA off-target sites adapted from: Dobbs, F.M., van Eijk, P., Fellows, M.D. et al. Precision digital mapping of endogenous and induced genomic DNA breaks by INDUCE-seq. Nat Commun 13, 3989 (2022). https://doi.org/10.1038/s41467-022-31702-9

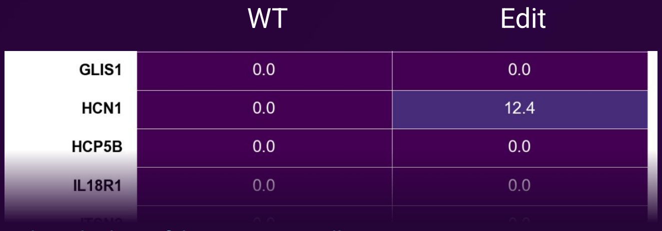
High Confidence Through Consensus Sequencing

Each captured site is tagged with a UMI. Consensus sequencing across reads grouped with UMI corrects stochastic and systematic errors – leaving only biologically true variants.



	WT	Edit
GLIS1	3.2	4.0
HCN1	4.6	16.8
HCP5B	4.4	5.3
IL18R1	6.6	6.8
ITSN2	8.3	12.5

noisy, many false positives



	WT	Edit
GLIS1	0.0	0.0
HCN1	0.0	12.4
HCP5B	0.0	0.0
IL18R1	0.0	0.0
ITSN2	0.0	0.0

clean, high-confidence variant calls

Acknowledgement: Cathomen Lab @ Freiburg University

Two Ways To Start – Today

Full LockSeq Service

DNA-in → Report in 15 days. Custom panels up to 1,000+ sites.

1. Panel Design
2. Target Capture
3. Sequencing
4. Reporting

- → Bring DNA, walk away with data
- → Sequencing platform of your choice

Strategic Partnerships

For teams thinking about integrating LockSeq in their own pipelines – long-term.

- → Early-stage conversations open for facilities and CROs evaluating in-house deployment
- → Karolinska CFG core facility already offers LockSeq for their customers – backend service offering
- → Let's talk – we want to understand how can we support your off-target confirmation!

Trusted by

GenE-HumDi

Karolinska Institutet

Danish Cancer Institute

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UNIVERSITÄTS KLINIKUM FREIBURG

& more

Every edit.
Every site.
No blind spots.

Let’s Connect!

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