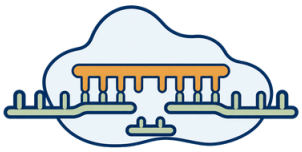
DESIGN FOR THE MODALITY

The therapeutic mechanism should guide the *in vivo* model design

When a therapeutic behaves differently against human and mouse targets, a useful model must support target engagement while preserving the expression, signaling, and physiology relevant to the study. The research question determines whether a focused target change or broader humanization is needed.

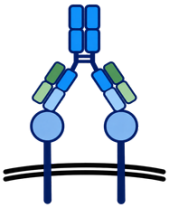
Where it makes a difference:

ASOs and RNAi:



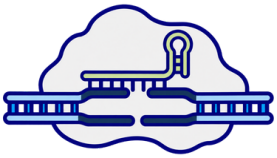
These therapies act on a specific RNA sequence, which may differ between mouse and human in an exon, splice junction, or regulatory region. A humanized allele can put the intended target sequence into an *in vivo* model, establishing a preclinical platform for testing these modalities.

Antibodies and other biologics:



A clinical antibody may not bind the mouse epitope, or a human protein may interact differently with mouse ligands. Humanizing the relevant domain can let the clinical molecule be tested *in vivo* without relying on a surrogate antibody.

Genome and base editing:



Guide RNAs, PAM sites, and disease variants are sequence-specific. Adding the relevant human target sequence can enable direct testing of an editor *in vivo*.

Which human feature must the mouse carry for your next decision?

It may be a binding epitope, splice junction, disease allele or larger genomic region. The right design depends on the modality, readout and biology that must remain intact.

Tell us your target, modality and decisive *in vivo* readout. Ozgene can help define the model before you commit to building it.

GENETIC HUMANIZATION

Humanized by design. Guided by biology.



Genetic humanization introduces selected human sequences into the mouse genome to support studies of human biology and therapeutic activity. Strategies range from replacing a small target sequence or protein domain to introducing an entire human gene or a larger genomic region containing regulatory elements.

Five common approaches *and the trade-offs that matter when selecting a strategy*

1 Partial humanization

A small human gene segment replaces the homologous mouse sequence. Most mouse regulation and protein sequence remain, while human features outside the segment are not modeled.



2 Random transgenic

A full human gene or protein can be introduced. Useful when a human homolog is not obvious. The insertion site and copy number can alter the expression level and pattern. The orthologous mouse gene remains expressed.



3 Targeted transgenic

A defined locus allows single-copy insertion and flexible construct design. Expression levels may differ from the physiological pattern. The orthologous mouse gene remains expressed.



4 cDNA knock-in

The human coding sequence is expressed instead of the mouse sequence under the endogenous promoter. Human splice isoforms may be absent.



5 Genomic replacement

Human genomic sequence replaces the mouse locus. It can preserve human isoforms and support physiological expression, but locus design and size need careful evaluation.



For more details or to book a meeting with one of our experts to discuss your target and study goals, please go to our website at www.ozgene.com or scan: