Custom Model Creation

• Genome engineering services in rat & mouse
• *In vivo* liver gene delivery
• Breeding & phenotyping
• Lead optimization services
## About Hera BioLabs

**Precision Toxicology™ & Efficacy**: utilizing precisely gene-edited models such as SCID rats, humanized rodents and engineered cell lines for producing more rapid, consistent and clinically-relevant data

<table>
<thead>
<tr>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2017/18 plan</th>
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<tbody>
<tr>
<td>Hera spun-out of Transposagen &amp; licenses IP for gene editing technology; development of SCID rats begins; awarded phase II SBIR grant</td>
<td>Completion of a 10,000 ft² facility; Scientific team assembled with <em>in vitro</em> &amp; <em>in vivo</em> efficacy &amp; toxicity capabilities</td>
<td>Introduction of SDR™ &amp; SRG™ SCID rats and efficacy services; Engineered HepG2 and MDCK cells; <em>in vivo</em> toxicity studies and humanized liver mice; custom gene editing, breeding and screening services in mouse and rat</td>
<td>Humanization of the liver &amp; immune system of SRG™ rats for toxicity and immuno-oncology services</td>
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Gene editing technology & capabilities

Hera’s gene editing tool box for product development

Custom gene editing, phenotyping and screening services in cells, rats & mice available
Comprehensive services with data delivery each step of the way

- Model creation: design, genetic engineering, breeding and colony maintenance, phenotyping

- Lead optimization: dosing and sample collection, serum chemistry panels for clinical pathology, PK/PD, full necropsy of all organs, fixation or flash freezing of organs, histopathology, immunohistochemistry
Pronuclear injection (PNI) of CRISPR reagents targeting Rag2 and Il2rg in the rat

<table>
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<tr>
<th>Embryos injected</th>
<th>Embryos transferred</th>
<th>Total born</th>
<th>Rag2 het</th>
<th>Il2rg het</th>
<th>Double het</th>
</tr>
</thead>
<tbody>
<tr>
<td>314</td>
<td>187</td>
<td>32</td>
<td>4</td>
<td>2</td>
<td>2</td>
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Rag2\textsuperscript{tm2hera} (8bp del):

gttactttccgtgta\textsuperscript{agt}gagat\textsuperscript{gtc}ctgaagccag\textsubscript{ata}tggcc attcattgacgtggtatatagccgaggaaaaagtg

Il2rg\textsuperscript{tm1hera} (16bp del):
cggctccgaaccggaatgtgtacagttccttgtcatccacacttaggcagg\textsubscript{aga}aatctaggctcat gatccactattttgccctagggagaagaag
Immunophenotype of Rag2/Il2rg double KO rats, the SRG™ rat

Analysis of immune populations in SRG™ rats. A) CD4+/CD8+ mature T cells are absent from SRG™ rat thymocytes (bottom panel), compared to a wild-type control (top panel). The lack of thymus tissue in the SRG™ rat results in a low recovery of thymocytes. B) The SRG™ spleen contains no mature B cells as demonstrated by lack of CD45R (B220)+/IgM+ cells (bottom panel), compared to WT spleen (top panel). C) The Il2rg knockout in the SRG™ rat results in a reduced NK cell population (bottom panel) compared to the SDR™ rat, which only has a Rag2 knockout (compare to figure 1, panel C). NK cells in the SRG™ rat are similar to or less than the amount of NK cells in the WT rat (top panel).
In vivo gene & viral delivery

Transgenes and virus can be delivered to humanized liver or wild type mice & rats

- Disease model creation
- *In vivo* gene delivery efficacy testing
- Therapeutic gene efficacy screening
- Gene therapy toxicology screening

AAV-GFP – 7 days post injection

AAV-GFP – 28 days post injection

Non-injected

A nearly 100% GFP delivery rate in adult mouse liver as a result of episomal delivery of GFP with AAV-GFP. AAV-GFP refers to the AAV vector without piggyBac transposase. GFP expression is present at 7 and 28 days post injection in adult mice.
Hera’s facility and scientific team

- Dosing by multiple routes including i.p., oral and i.v.
- ACLAM and AALAS certified staff
- Digital data acquisition via StudyLog® systems software

- Vivarium featuring all 100% HEPA filtered, disposable IVC caging specifically designed for immunocompromised animals
- Molecular and cell culture facility
Hera’s products & services

Cancer Xenografts
- Xenograft/PDX Efficacy studies
- Off-the-shelf SCID rats models

In Vivo & In Vitro
Lead Optimization, Toxicity and Metabolism
- HepG2-CYP™ metabolism and toxicity cell panel
- hu-MDCK™ humanized transporter cells
- Humanized liver rodent models
- In vivo early discovery services

Disease Modeling
- In vivo liver gene delivery for disease model creation and gene therapy efficacy
- Custom genome engineering in rat and mouse
- Colony management and phenotyping

Links for specific product and service information above
Hera has the freedom to operate through multiple licenses to issued and pending patents for CRISPR, piggyBac and TALEN gene editing technologies.

Hera’s SCID rats are covered under issued patents claiming knockout rat phenotypes for immune system disorders, SCID and cancer. US Patent Numbers: 8,558,055; 9,314,005; 8,722,964.
Hera BioLabs Leadership

Jack Crawford, M.S.
CEO
Formerly directed the Sales, Marketing, and Business Development Divisions at Transposagen. Experience in product development, licensing, technology and patent evaluation, and fundraising.

Tseten Yeshi, Ph.D.
VP, R & D
Former Director of R&D at Transposagen. An expert in genome editing with well-developed scientific program management skills and experience.

Chris Chengelis, Ph.D., DABT
Senior Scientific Advisor
Former CSO at WIL Research. 35 years+ experience in the preclinical toxicology industry, facility design, study design and execution

Fallon Noto, Ph.D.
Senior Scientist
10+ years working with mice and rats, expertise in rodent humanization, cell and tissue transplantation, microsurgery, and ethical animal care.

Kamesh Ravi, Ph.D.
Senior Scientist
10+ years of experience in preclinical oncology, cancer xenograft models, tumor efficacy studies and onco-nephrology.

Goutham Narla, M.D., Ph.D.
SAB Member & Consultant
The Pardee Gerstacker Professor of Cancer Research and a Medical geneticist at Case Western Reserve University. CSO and Scientific Founder of Dual Therapeutics, Inc. Expertise in cancer genetics and xenograft and transgenic models of cancer with over 58 publications in the field.

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