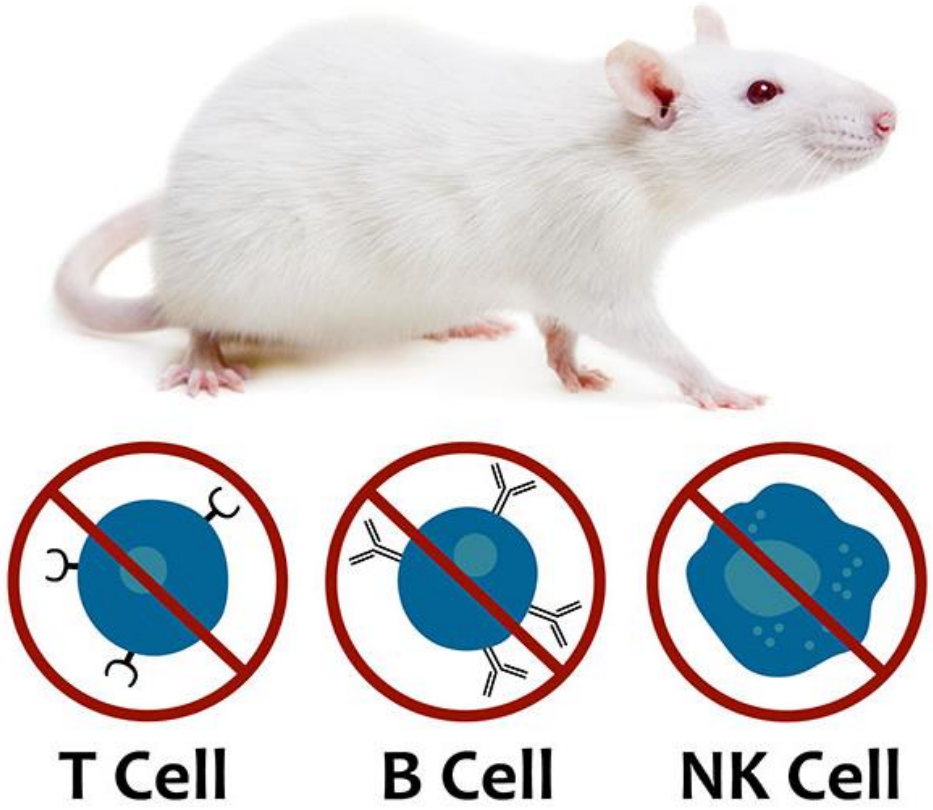
The *SRG OncoRat*®



SRG OncoRat: Building a Better Trap for Cancer

Developed using Hera Biolabs' advanced gene editing technology, is a **SCID** rat on the **Sprague-Dawley** background that harbors a **double knockout for the Rag2 and Il2Rγ genes**.

- Enhanced immunodeficiency: lacks B-cells, T-cells, and NK-cells.
- Enhanced engraftment rates
- Improved tumor growth for both cell-line tumor models and patient-derived xenografts (PDXs)
- Perform serial tumor biopsies
- Combine efficacy, pharmacokinetic (PK), biomarker, and toxicology studies

Noto et al. PLoS One. 2020 Oct 7;15(10):e0240169.

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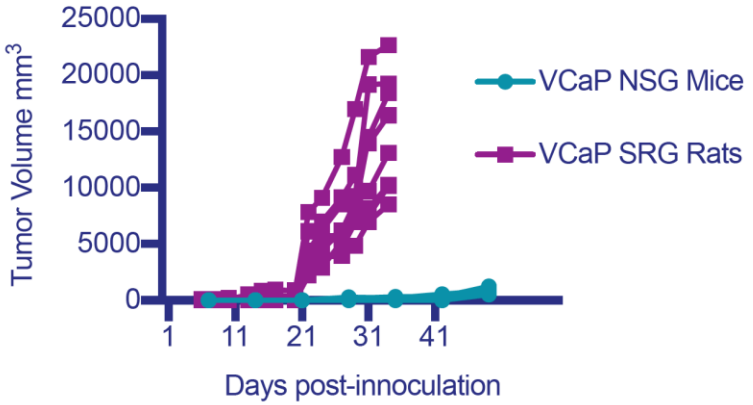
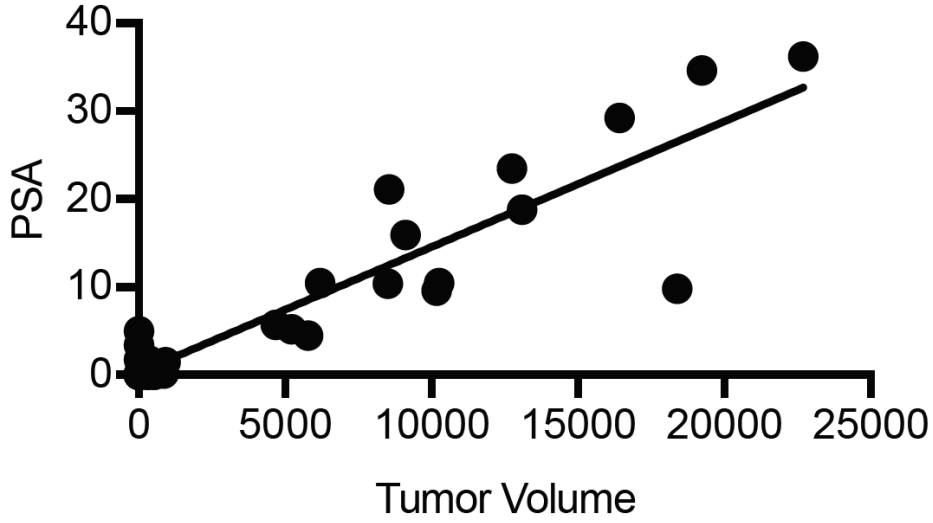
Cancer Xenograft Studies: Human Prostate Example

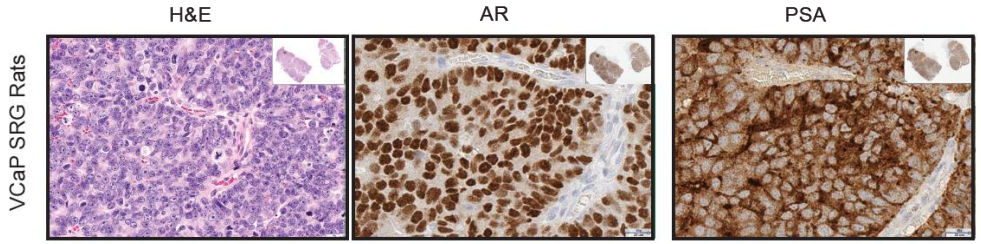
VCaP tumor kinetics rat vs. mice

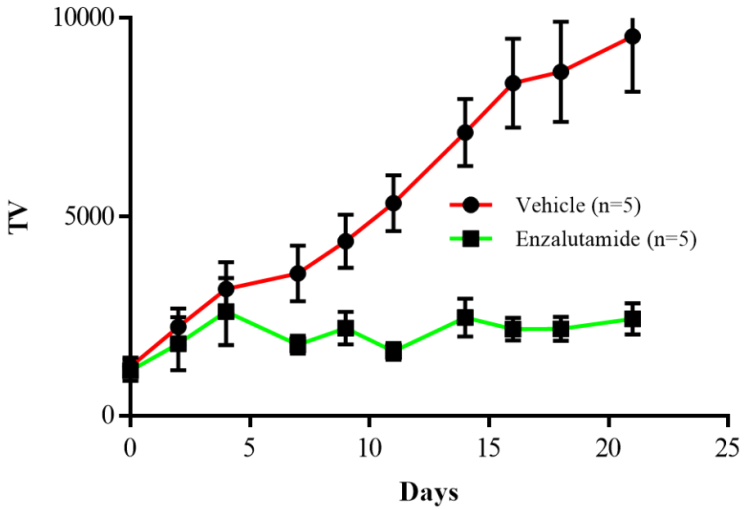




VCaP tumor serum PSA

IHC of VCaP tumors confirms AR and PSA





VCaP is responsive to Positive Control

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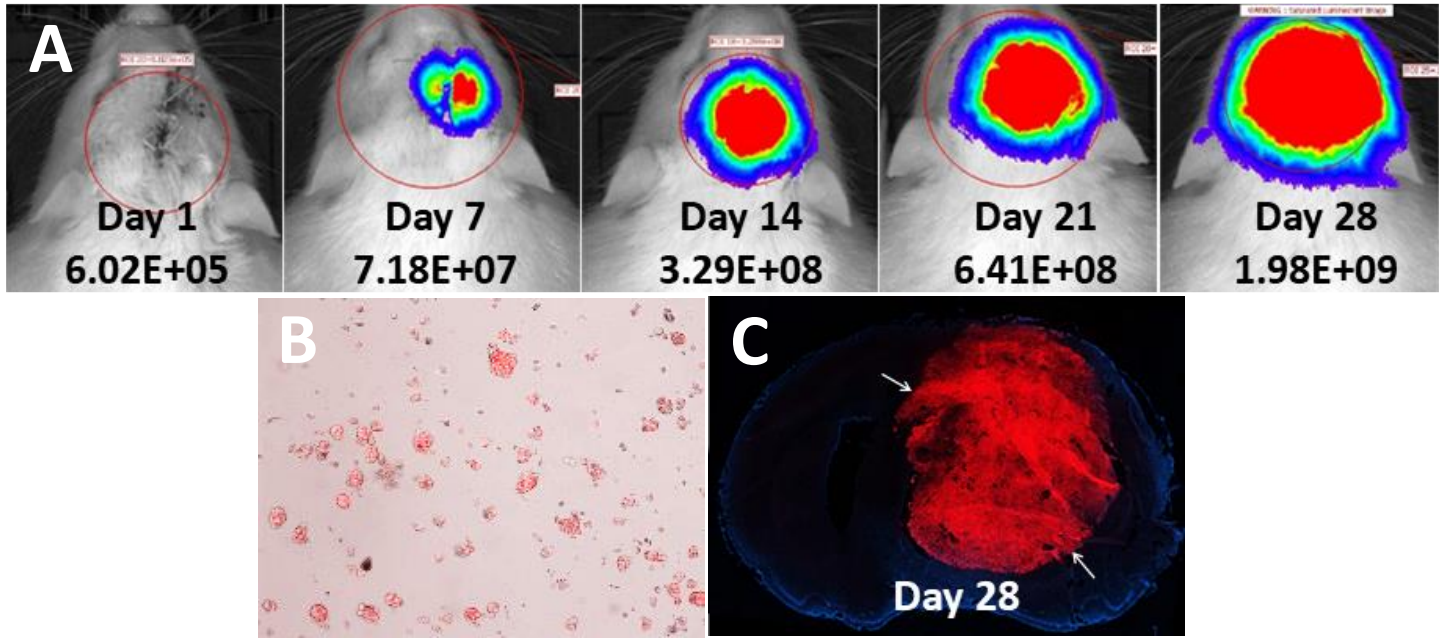
SRG rat brain size permits translational interventions and imaging

In vivo bioluminescent imaging to track tumor growth



A) signal expansion over 4 weeks. The tumors become symptomatic after ~4 weeks of growth.

B) Patient GBM stem-like cells (4x magnification) grown in spheres and transduced to express luciferase and tdTomato.

C) Day 28 GBM PDX histology showing the tdTomato against DAPI.

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List of cell-derived tumor models validated in the SRG rat

Model	Cancer Type	Notes
MOLM-13	Adult acute myeloid leukemia	Mutation in FLT3; Unexplicit; Internal tandem duplication
MDA-MB-231	Breast adenocarcinoma	Triple negative breast cancer; Mutations in CDKN2A, CDKN2B, BRAF, KRAS, TERT, TP53
MX-1	Breast adenocarcinoma	Mutation in TP53
HCC1954	Breast ductal carcinoma	HER2+ studies, ER- studies, AR inhibitors; Gene fusion CLTC-VMP1; Mutations in PIK3CA, TP53
MCF7	Invasive breast carcinoma	Derived from pleural effusion metastasis; Mutations in GATA3, PIK3CA, TP53
HCT-116	Colon carcinoma	Tumorigenesis, colorectal cancer metastasis, CDK inhibition, TGFβ+; Mutations in ACVR2A, BRCA2, CDKN2A, CTNNB1, EP300, KRAS, PIK3CA, TGFBR2
HT-1080	Fibrosarcoma	Cachexia studies; Gene deletion CDKN2A; Mutations in IDH1, NRAS
SNU-5	Gastric Carcinoma	Mutations in CDKN2A, TP53
U118-MG	Glioblastoma/Astrocytoma	Mutations in PTEN, TP53
U87-MG	Glioblastoma	Historic data comparisons (some model controversy); Mutations in NF1, PTEN, TERT
Hep3B	Hepatocellular carcinoma, pediatric	a.k.a Hep 3B2.1-7; Mutations in AXIN1, RB1
OCI-AML2	Leukemia, adult acute myeloid	NOS and VEGF signaling, angiogenesis inhibitors, DNA methylation; Gene fusion KMT2A-AFDN
K-562	Leukemia, blast chronic myelogenous	Cachexia studies; BCR-ABL1 positive. Gene fusion BCR-ABL1; Mutation in TP53
A-549	Lung adenocarcinoma	Mutations in KRAS, STK11, TP53
NCI-H1975	Lung adenocarcinoma	Mutations in EGFR, PIK3CA, TP53
NCI-H226	Lung, pleural epithelioid mesothelioma	Gene deletion CDKN2A
NCI-H322	Lung adenocarcinoma, minimally invasive	Mutation in TP53

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List of cell-derived tumor models validated in the SRG rat

Model	Cancer Type	Notes
HCC-95	Lung, squamous cell carcinoma	Derived from metastatic site: Pleural effusion
NCI-H2170	Lung squamous cell carcinoma	Mutations in RHOA and TP53
NCI-H1734	NSCLC, Lung adenocarcinoma	Mutations in ATM, KRAS, RB1, TP53
NCI-H2122	NSCLC, Lung adenocarcinoma	Mutations in KRAS, TP53
NCI-H358	NSCLC, Lung adenocarcinoma	KRAS & EGFR signaling, metastasis to lungs; Gene deletion TP53; Mutation in KRAS
NCI-H441	NSCLC, papillary adenocarcinoma	Mutations in KRAS, TP53
Daudi	Lymphoma, EBV-related Burkitt	Gene fusion MYC-IGH; Mutation B2M, CTNNB1, TP53
OV81*	Ovarian, serous	Mutation in BRCA2, *Developed by Hera BioLabs
Capan-2	Pancreatic ductal adenocarcinoma	Mutations in CDKN2A, KRAS, TP53
MIA PaCa-2	Pancreatic ductal adenocarcinoma	Epithelial-to-mesenchymal transition (EMT); Gene deletion CDKN2A. Mutations in KRAS, TP53
22Rv1	Prostate carcinoma	Mutations in KMT2D, PIK3CA, TP53
LNCaP	Prostate carcinoma	AR inhibtors, castration resistance studies; Mutations in AR, MEN1, PIK3R1, PTEN, TP53
NCI-H660	Prostate small cell carcinoma	Gene fusion TMPRSS2-ERG
PC-3	Prostate carcinoma	Derived from metastatic site: Bone. Mutation in TP53
VCaP-EnzR	Prostate carcinoma	Enzalutime drug resistance studies, castration resistant studies
VCaP	Prostate Carcinoma	AR resistance, castration resistant studies; Gene fusion TMPRSS2-ERG; Mutation MLH1; TP53;
786-O	Renal Cell Carcinoma	VEGF inhibition studies, bone metastasis development, hypoxia and tumor progression; Mutations in PTEN, TERT, TP53, VHL
SCC-090	Tongue squamous cell carcinoma	Cells are positive for Human Papilloma Virus (HPV)

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