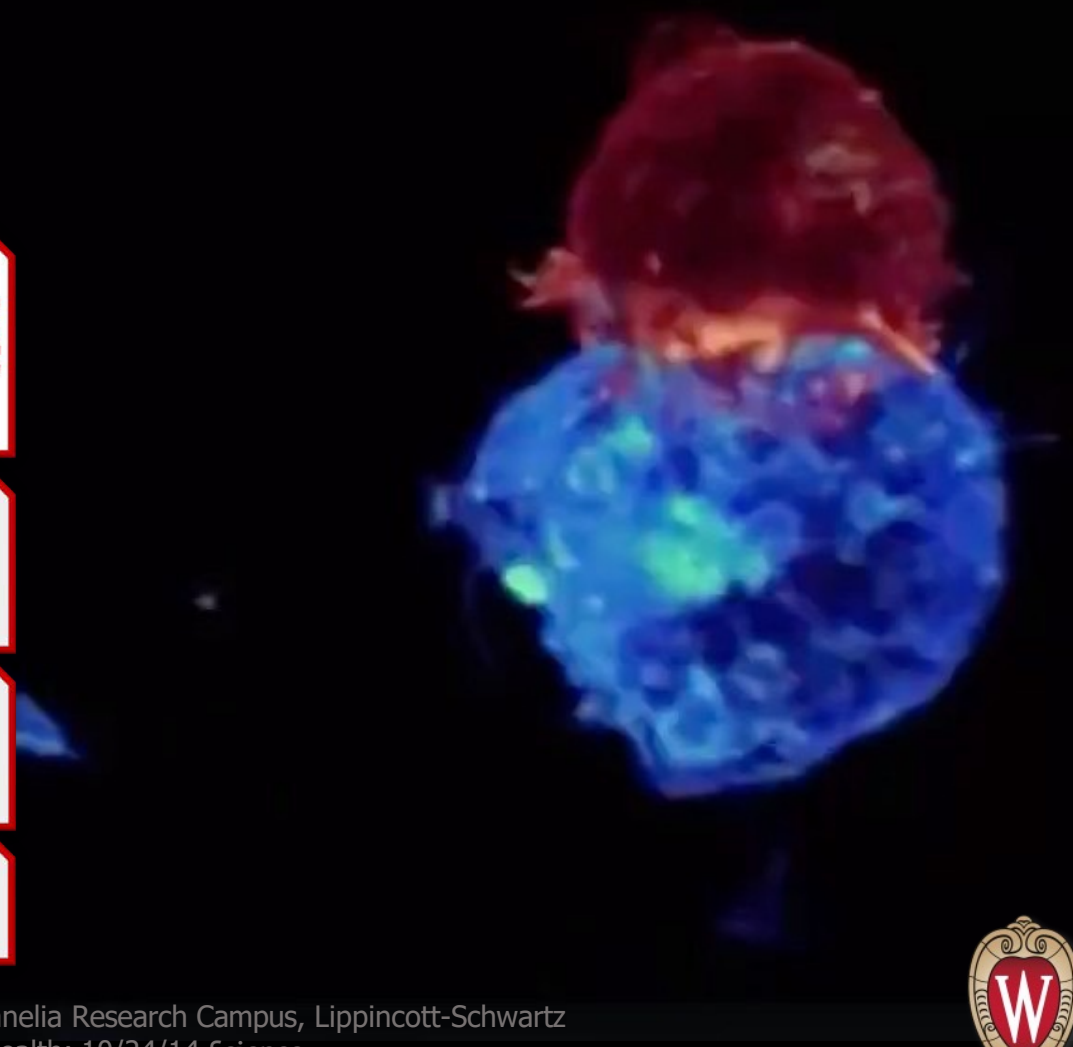
From Reading to Writing the Genome



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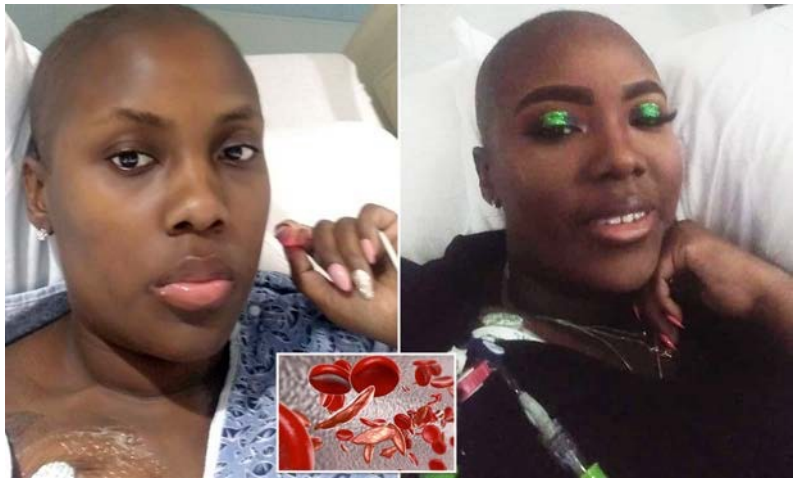
Stem Cell and Regenerative Medicine Center, Carbone Cancer Center, Grainger Institute for Engineering, Precision Medicine Center, Global Health Institute

Credit: Betzig Lab, HHMI/Janelia Research Campus, Lippincott-Schwartz Lab, National Institutes of Health; 10/24/14 *Science*.

From reading to writing the genome

Writing the sickle cell gene in stem cells



Victoria Gray, sickle cell patient, treated with gene-edited stem cells; Source: Daily Mail

Writing new genes into T cells

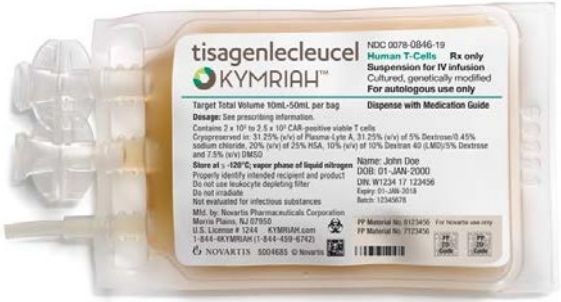
Emily Whitehead, blood cancer patient treated with CART cells; Source: Children's Hospital Philadelphia

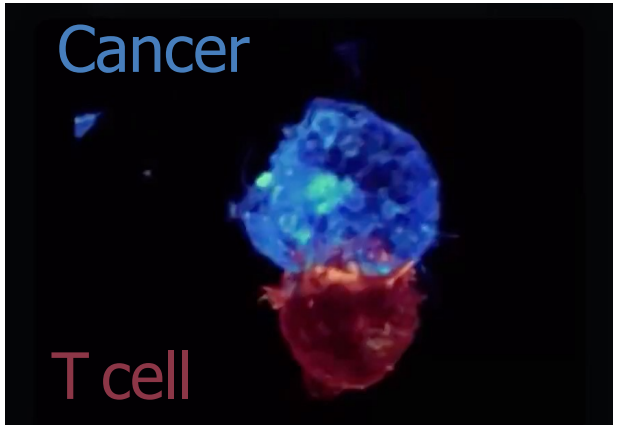
Correcting mutation within the eye

Michael Kalberer, retinal disease patient, treated with gene editing therapy; Saw colored lights at cousin's wedding…"joyous moment"; Source: Michael Kalberer

Drugs

Living cell therapy
$0.37M/dose





Viral gene therapy
$0.4M/eye

LUXTURNA®
voretigene neparvovec-rzyl
for subretinal injection

Illuminating possibilities.

Two drug modalities enabled by genome editing

Cell/gene therapy: infusion of CRISPR'd cells

In my lab: Solid Tumors (sarcoma, glioblastoma), blood cancers, Alzheimer's, aging

At UW-Madison: Retinal disorders, Diabetes, Parkinson's, Down's syndrome…

In the field: Autoimmune disease, Lupus, fungal infections, multiple sclerosis…

CMaT

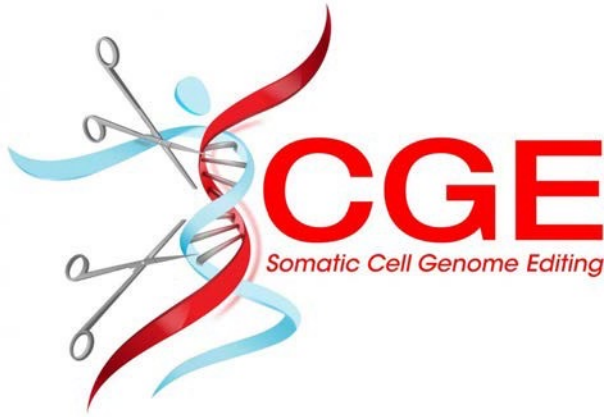
National Science Foundation
Center for Cell Manufacturing Technologies

Gene therapy: direct injection of CRISPR

In my lab: Best Disease, Inherited Retinal Disorders (eye), Pompe Disease (muscle, liver), Alzheimer's, Neurodegeneration (brain)

At UW-Madison: Muscular Dystrophy, Metabolic Diseases…

In the field: Infectious Disease, Cardiovascular, Cystic Fibrosis,…



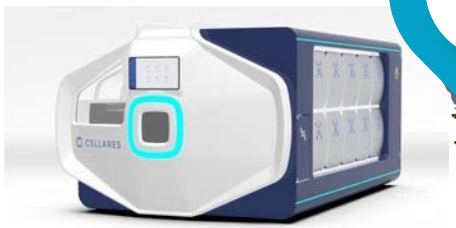
National Institutes for Health
Somatic Cell Genome Editing Consortium

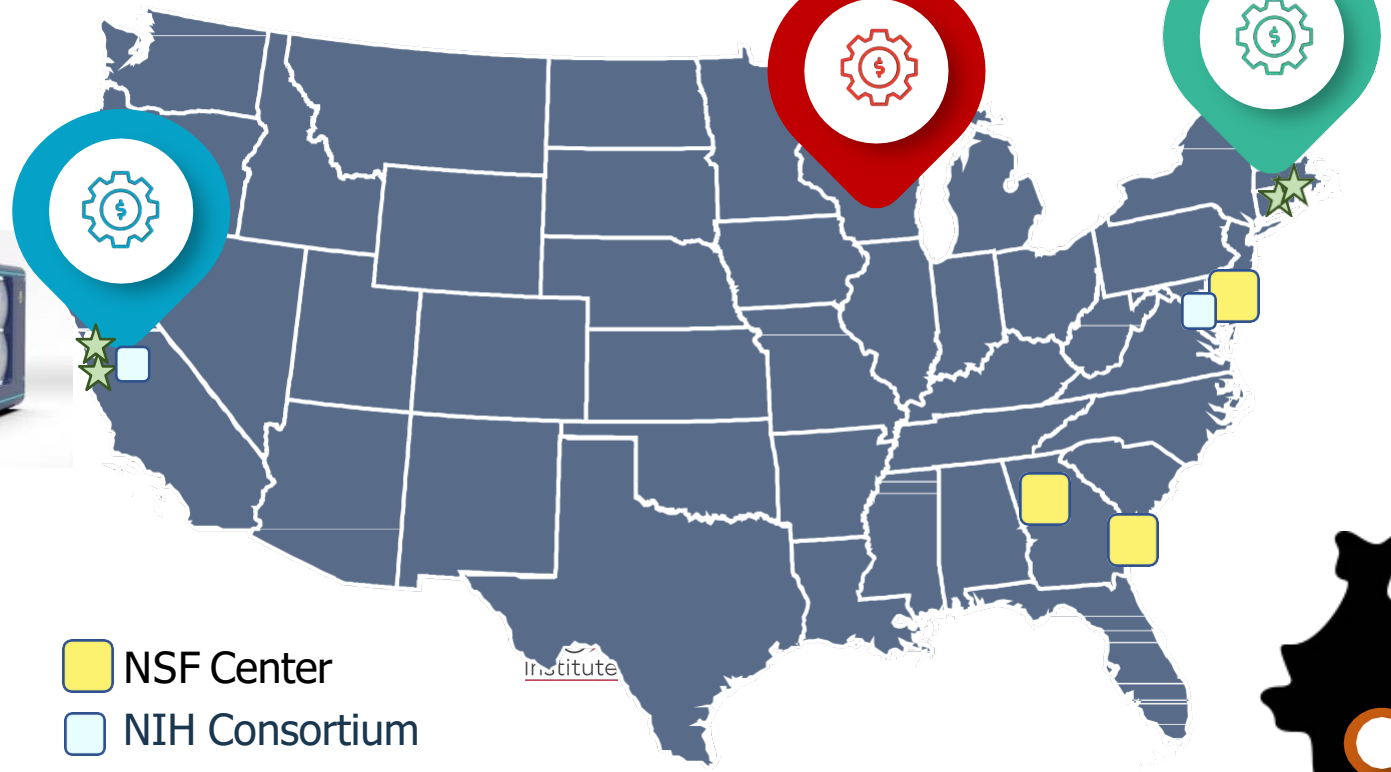
Rapid biomanufacturing of CRISPR cell/gene therapies

Univ. of Wisconsin-Madison
Morgridge Institute, Danaher

Univ. of Mass., Danaher, Gingko Bioworks, Mass Biologics

Spotlight Tx, IQVIA, CIRM, Synthego, Cellares



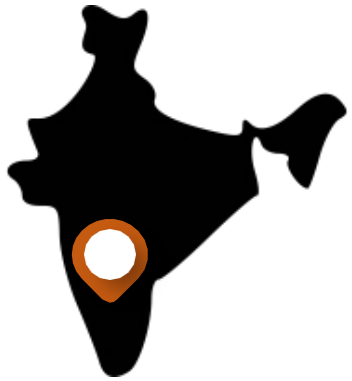


NSF Center
NIH Consortium
U19 Board Member

UW Madison Global Health Institute: One Health India, Immuneel, Science Gallery Bengaluru, Mazumdar Shaw Cancer Center

One Health India Cell/Gene Therapy

Improving access to "cures" and developing the next generation of therapies



UW Madison Global Health Institute: One Health India, Immuneel, Science Gallery Bengaluru, Mazumdar Shaw Cancer Center

Manufacture cellular therapies at 10-fold lower costs with novel supply chains.

- Move away from problematic supply chains involving viral vectors by leveraging CRISPR
- Utilize growing donor blood supply for manufacturing allogeneic products
- Develop novel automated manufacturing systems with advanced analytics
- Expand scope from blood cancers to solid tumors
- Freedom to operate for CRISPR and other tech may be greater in India

Perform clinical trials with novel cohorts and trial designs.

- Larger and more diverse cohorts than in many areas of the US
- Benefit—risk calculations evaluated relative to a different standard of care
- Potential to explore combination therapies more quickly (e.g., checkpoint mAb + CART, NK +CART, cancer vaccines +CART)

Integrate digital health and genomics into the design of new therapies.

- Characterize the mutational profile of most common solid tumors (e.g., perform mutational analysis on fresh tumor samples via oncogene panel)
- Discover new drug targets (e.g., CART targets)
- Deepen understanding of new One Health cases (e.g., develop the capacity to see unique connections among human, animal, and environmental health in India)