

# Stopping Runaway CAR-T Cells

John Miller

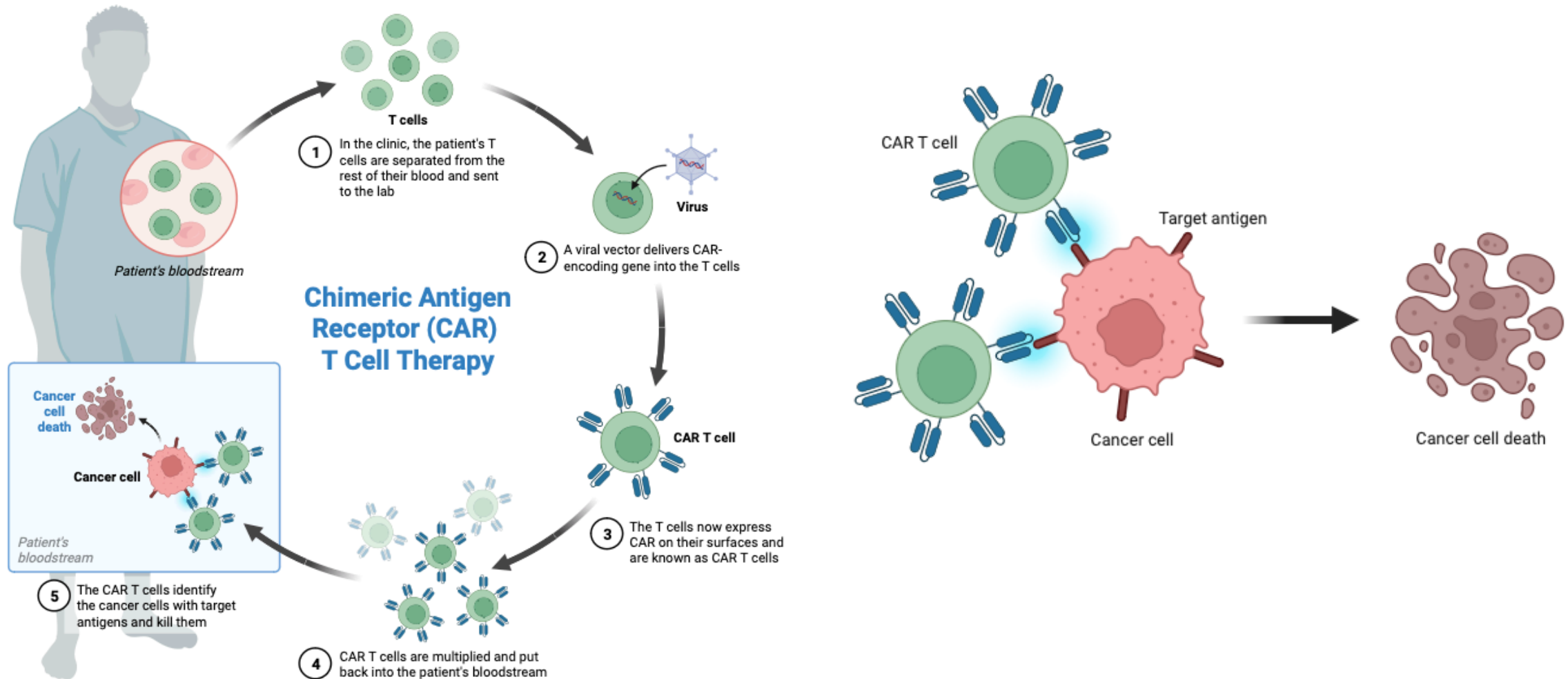
University of Rochester

Department of Microbiology & Immunology

*America's Got Regulatory Science Talent* Student Competition

# CAR-T cells are a promising cancer treatment

## CAR-T cell mediated cancer cell death



# Regulatory Science Focus Area

## Individualized therapies and precision medicine

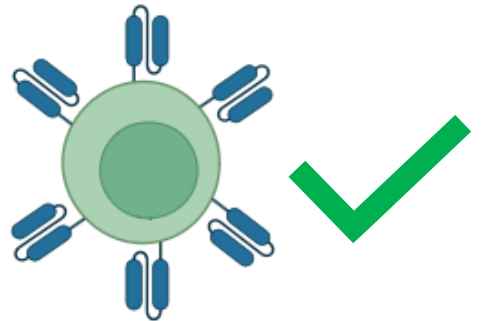
Goal: Provide new regulatory guidelines to address off-target effects of CAR-T cell therapies and improve the CAR-T cell review process

- Important for increasing review efficiency and the safety of these treatments

# The Problem with Runaway CAR-T cells

- Overactive CAR-T cells > Cytokine release syndrome, neurotoxicity

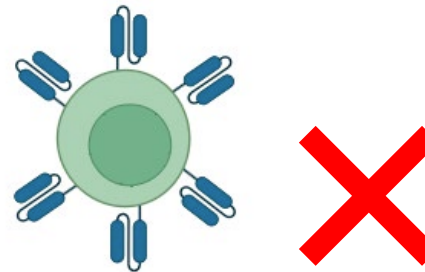
## On-target effects



Tumor cell



## Off-target effects

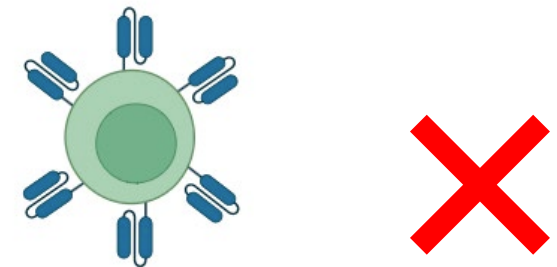


Healthy cell

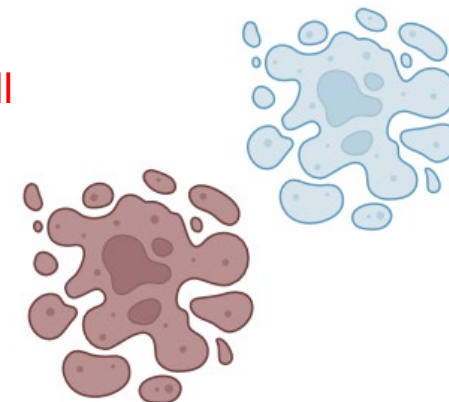


Killing of cells with non-target antigen

## On-target off-tumor effects



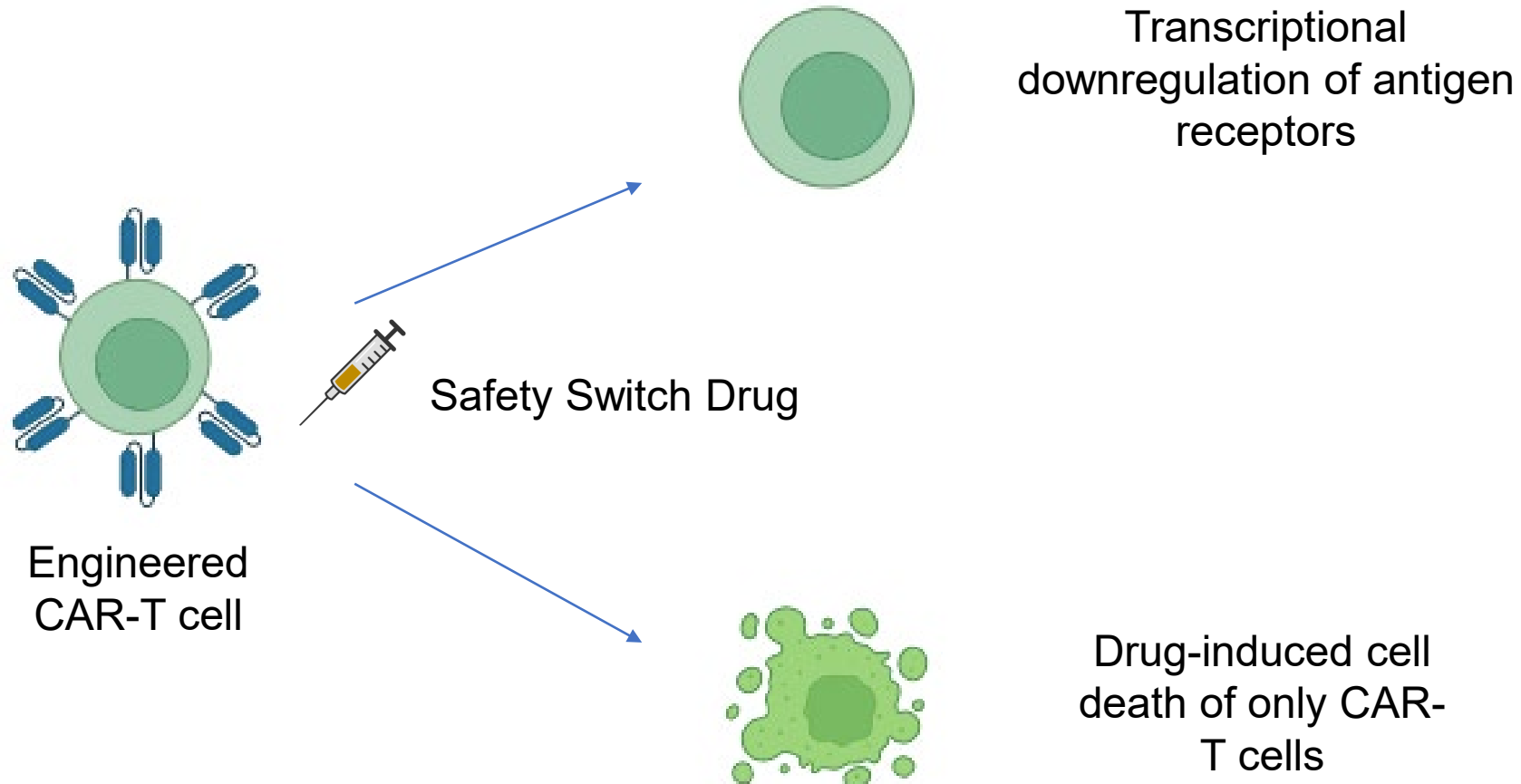
Healthy cell



Recognition of target antigen on healthy cells

# The CAR-T Safety Switch

- Once infused, CAR-T cells are difficult to modulate compared to traditional oral and IV cancer drugs, where dosage can be changed to mitigate toxicity
- Currently used in investigational clinical trials



# Requiring Safety Switches in CAR-T Cell Products

**Regulatory Science Solution:** With adequate data from preclinical trials, the FDA should move towards requiring CAR-T cell manufacturers to incorporate a safety switch mechanism in these therapies

## Benefits

- Efficient review - speed up regulatory processes
  - Accelerate risk mitigation and clinical risk monitoring processes
- Improved safety and effectiveness
  - Benefit/risk profile
- Advancing the safety of CAR-T cell therapies

## Potential Limitations

- May be difficult to require all manufacturers to incorporate this into their products
  - There are multiple methods of producing Safety Switches for CAR-T cells
- If the manufacturer can show there are no off-target effects, this requirement could be waived

# Conclusion

Incorporation of safety switches into CAR-T cell products will allow for an efficient method for increased regulatory capacity and safety

# Acknowledgements

FDA Advisors – Center for Biologics Evaluation and Research

Sakshi Tomar, PhD

Maitreyi Chattopadhyay, PhD

University of Rochester CTSI

Joan Adamo, PhD

