



Methylzyme

# Epigenetic immunotherapy

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Director, Center For Epigenetics & Biomarkers, Pathology

Co-Leader, Genomics, Genetics and Epigenetics Research Program

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Yale Cancer Center and Smilow Cancer Hospital

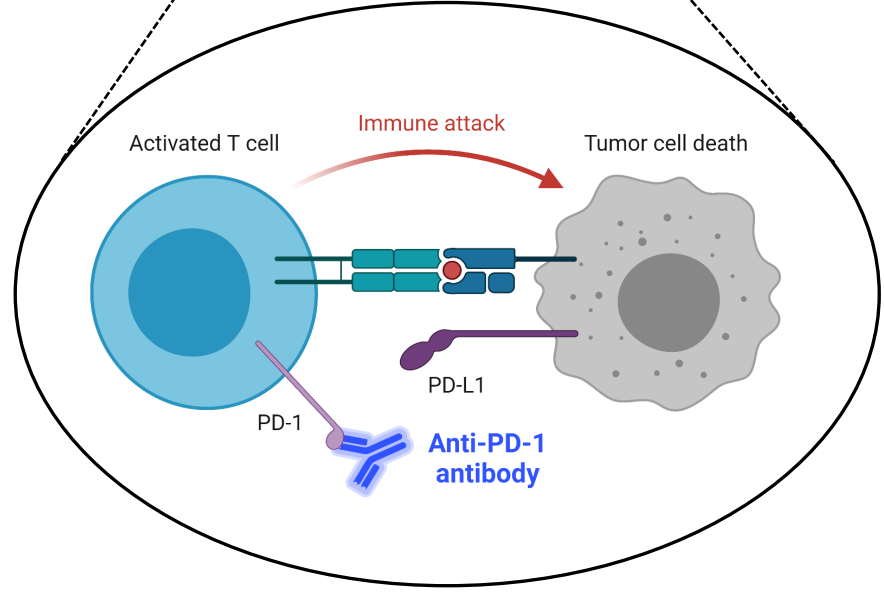
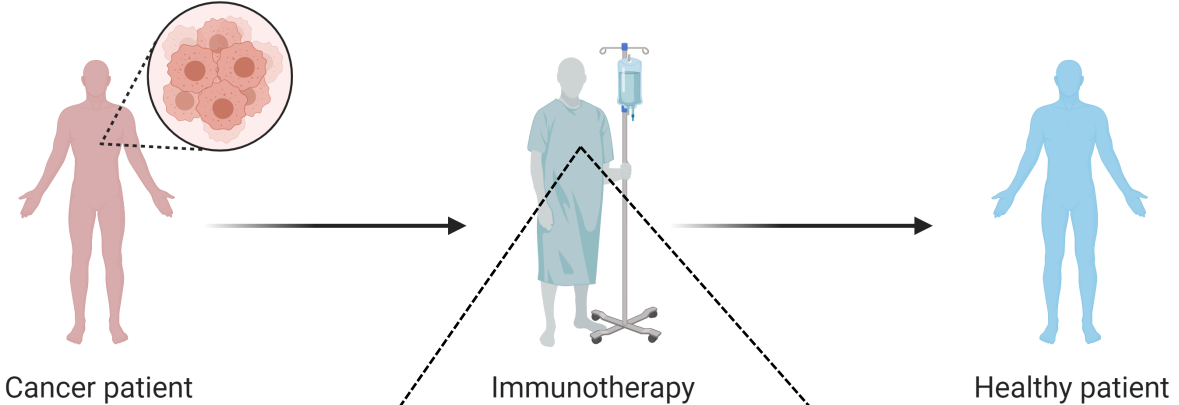
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# Immunotherapy



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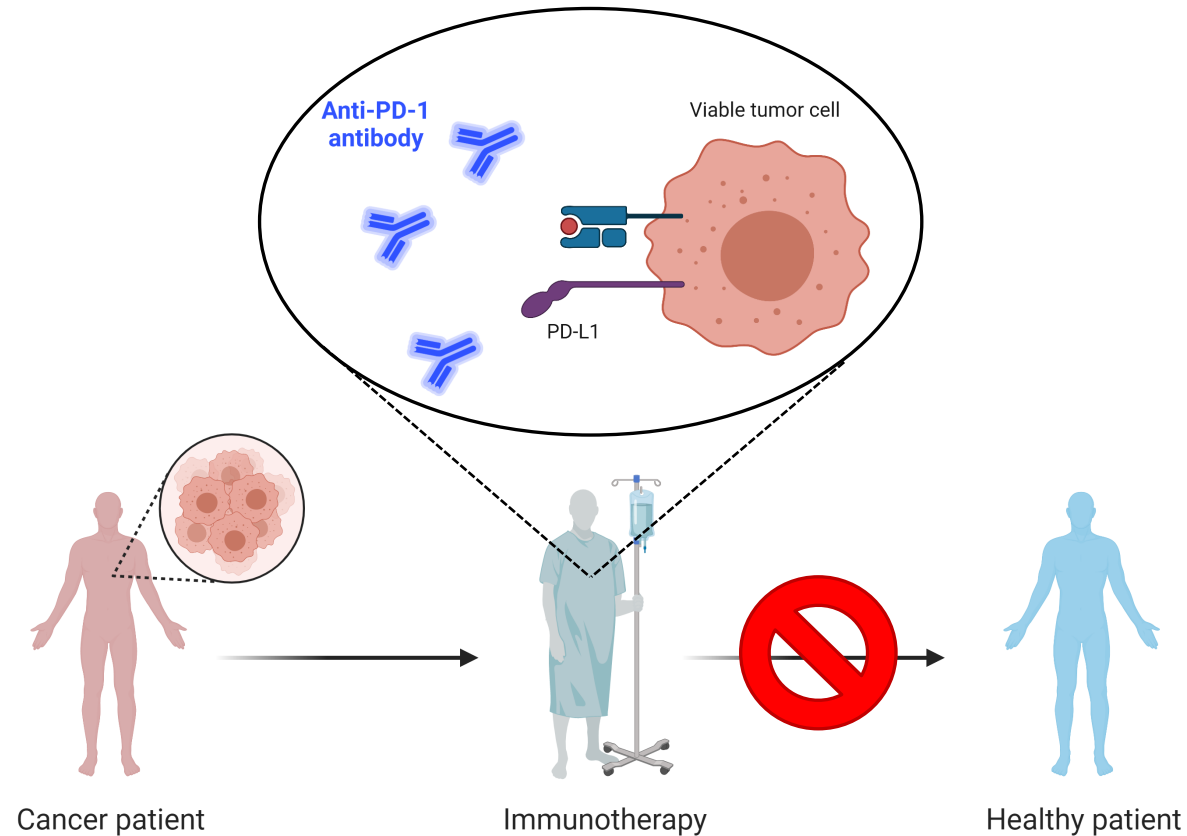




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# Unresolved challenge

– NOT effective in **resistant** tumors (breast, melanoma, prostate...)

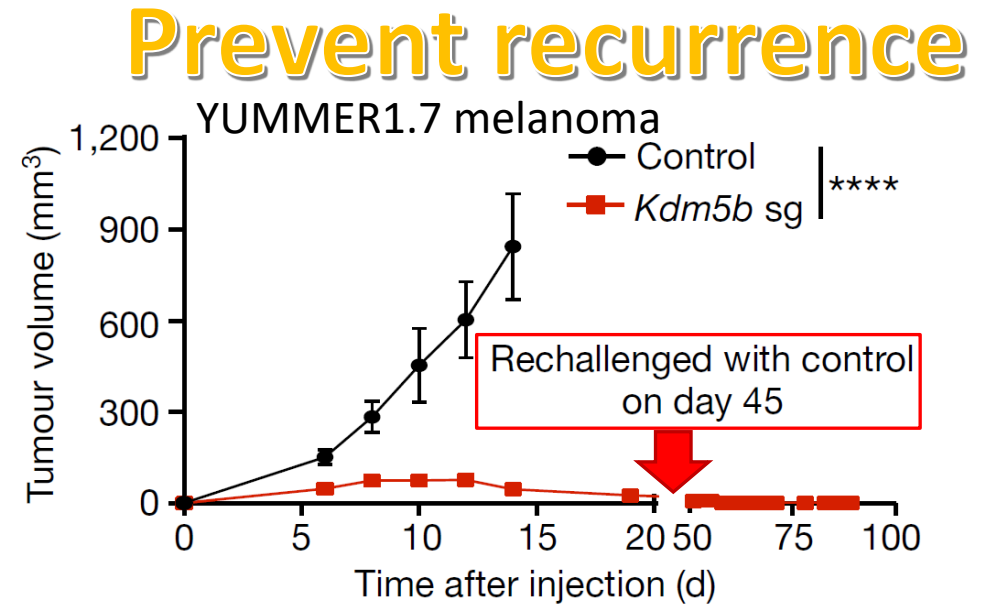
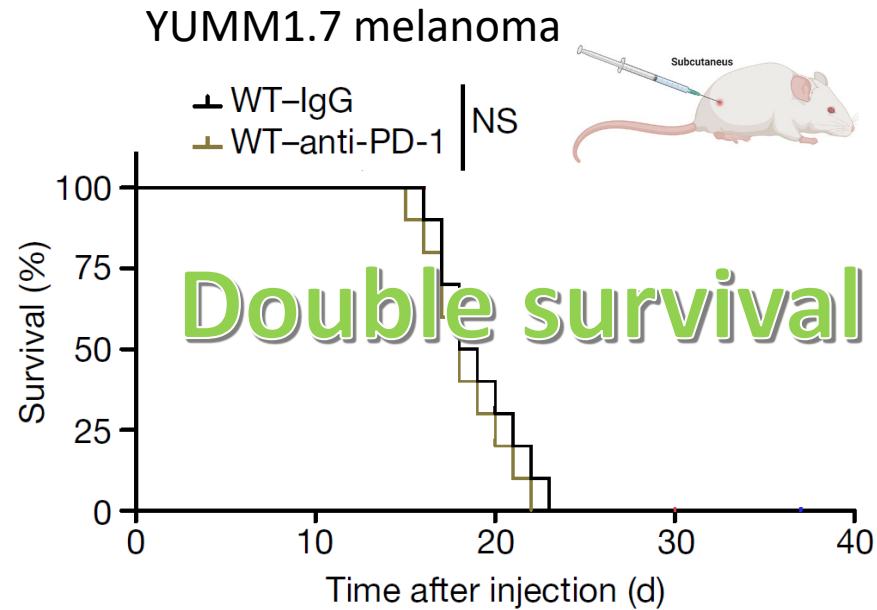


# New opportunity



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## Targeting **KDM5B** to boost antitumor immune responses



Zhang et al *Nature* 2021



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Article

# KDM5B promotes immune evasion by recruiting SETDB1 to silence retroelements

<https://doi.org/10.1038/s41586-021-03994-2>

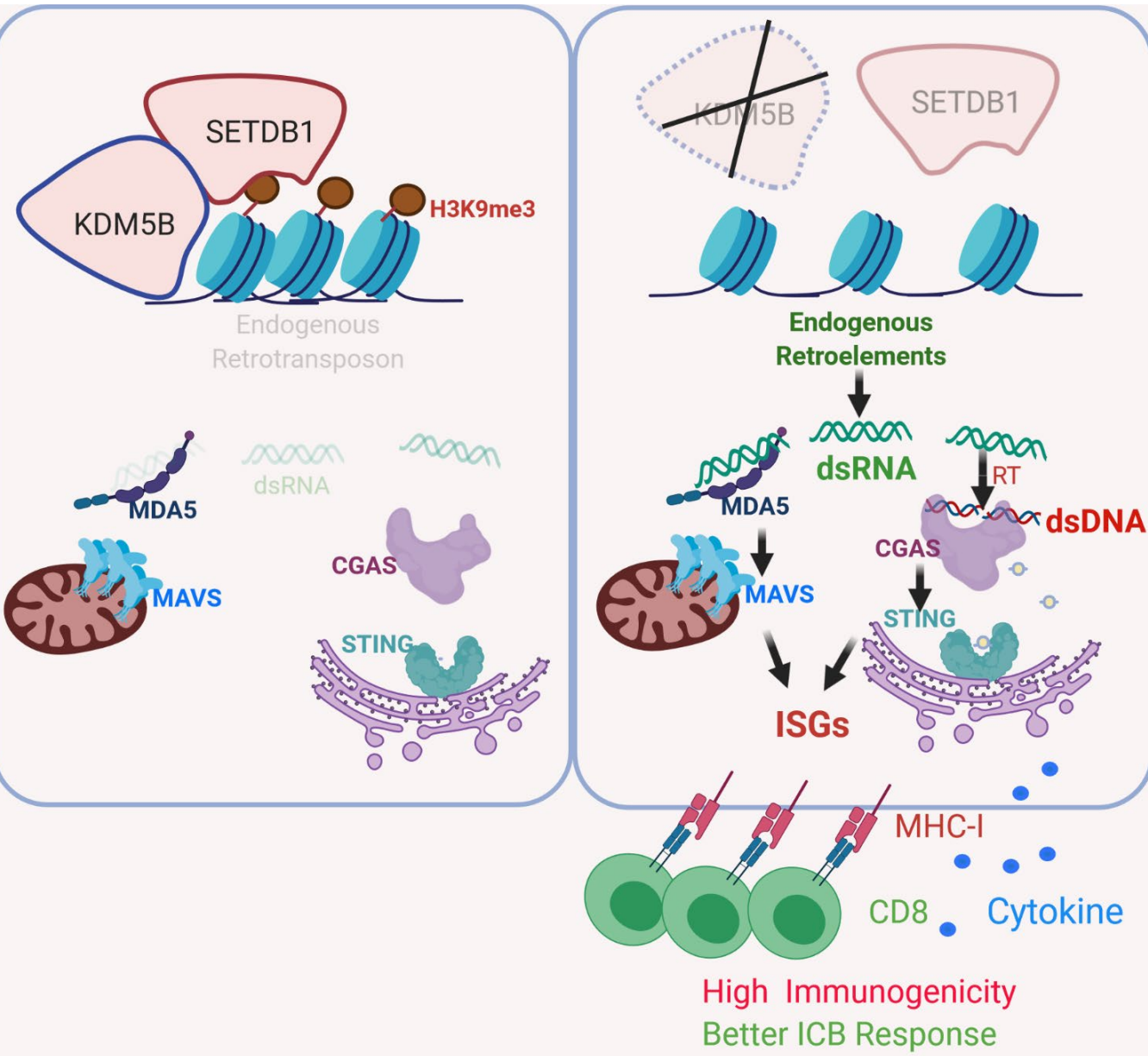
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Shang-Min Zhang<sup>1</sup>, Wesley L. Cai<sup>1,12</sup>, Xiaoni Liu<sup>1,2</sup>, Durga Thakral<sup>2</sup>, Jiesi Luo<sup>3,4</sup>, Lok Hei Chan<sup>1</sup>, Meaghan K. McGeary<sup>1,2</sup>, Eric Song<sup>5</sup>, Kim R. M. Blenman<sup>2,6,7</sup>, Goran Micevic<sup>2</sup>, Shlomit Jessel<sup>6</sup>, Yangyi Zhang<sup>1,8</sup>, Mingzhu Yin<sup>1,8</sup>, Carmen J. Booth<sup>9</sup>, Lucia B. Jilaveanu<sup>6,7</sup>, William Damsky<sup>2,7</sup>, Mario Sznol<sup>2,7</sup>, Harriet M. Kluger<sup>6,7,10</sup>, Akiko Iwasaki<sup>5,7,10,11</sup>, Marcus W. Bosenberg<sup>1,2,4,5,7,10</sup> & Qin Yan<sup>1,4,7,10</sup>✉

## KDM5 inhibitors do not work!

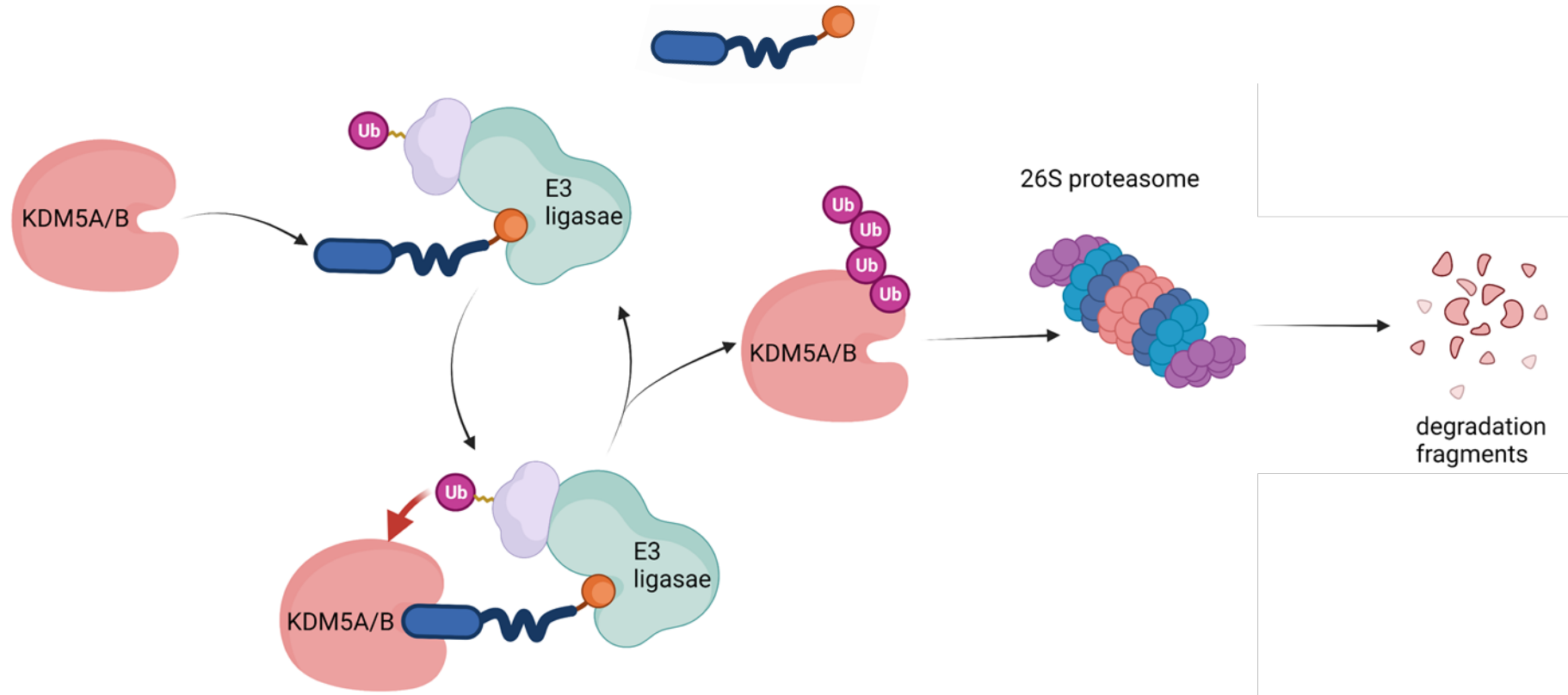


# Our solution



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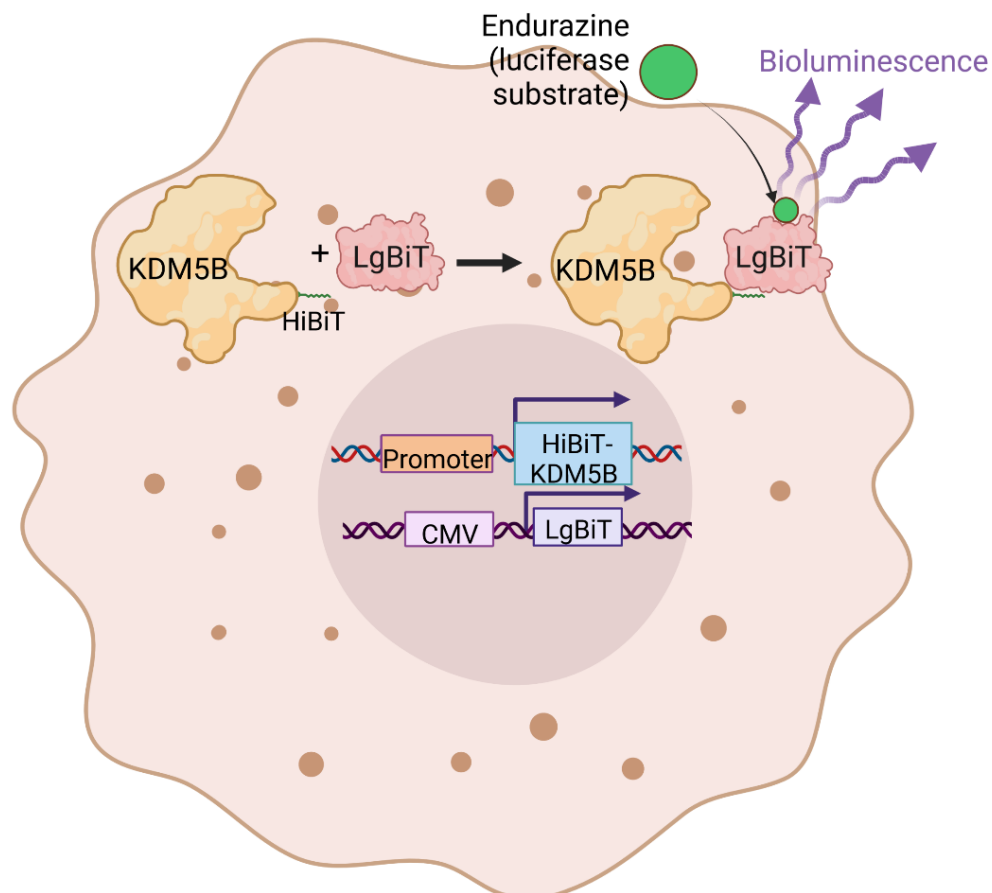
## KDM5 protein degrader



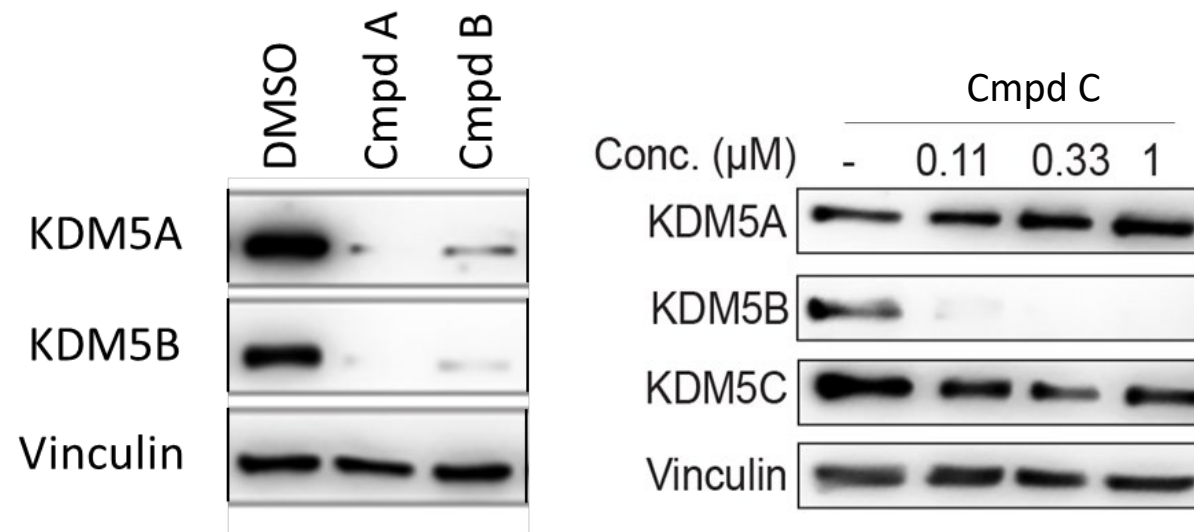
Hijacking cellular protein scavenger machinery

# Our platform and discovery

## HiBiT-tagged reporter



## Representative hits



# Our team



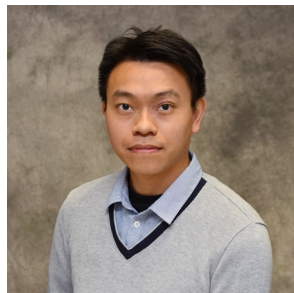
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**Qin Yan, PhD**

Professor of Pathology  
Director, Center For Epigenetics & Biomarkers, Pathology  
Co-Leader, GGE Research Program  
Scientific Co-Director, Center For Breast Cancer, Yale Cancer Center

- **Co-discovered KDM5 demethylases**
- **Led the first HTS for KDM5i**
- **Led KDM5i project supported by NExT**
- **Expert on ubiquitination**



**Lok Hei (Jack) Chan, PhD**

Associate Research Scientist  
Department of Pathology  
Yale School of Medicine

- **Developed the degrader screening platform**



**Jian Jin, PhD**

Mount Sinai Endowed Professor of Therapeutics Discovery  
Dept of Pharmacological Sciences & Oncological Sciences  
Director, Mount Sinai Center for Therapeutics Discovery  
Icahn School of Medicine at Mount Sinai

- **Co-Founder, Cullgen, a top degrader company**
- **Inventor of ~70 issued US patents and published international patent applications**
- **Advanced 5 compounds to clinical trials**
- **An inventor of Daprodustat, approved in US & Japan**

Klose, Yan et al, *Cell* 2007  
Lin, Cao et al, *PNAS* 2011  
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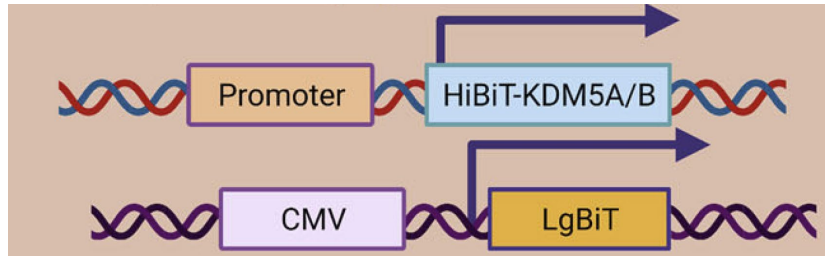


# Why invest in Methylzyme now?



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- Based on recent high impact discoveries from Yale
- HiBiT-tagged **reporter platform** for HTS of cell-permeable degraders



- “**First in class**” KDM5 degraders
- Unique immuno-competent mouse cancer models
- Partnership interests from pharma and ventures
- Supported by a 2022 Blavatnik Award until May 2024
- **Need: \$15 million, to advance several series to IND filing in two years.**