

Richard A Flavell, PhD, FRS

Treating Cancer by Blocking Calcium Entry

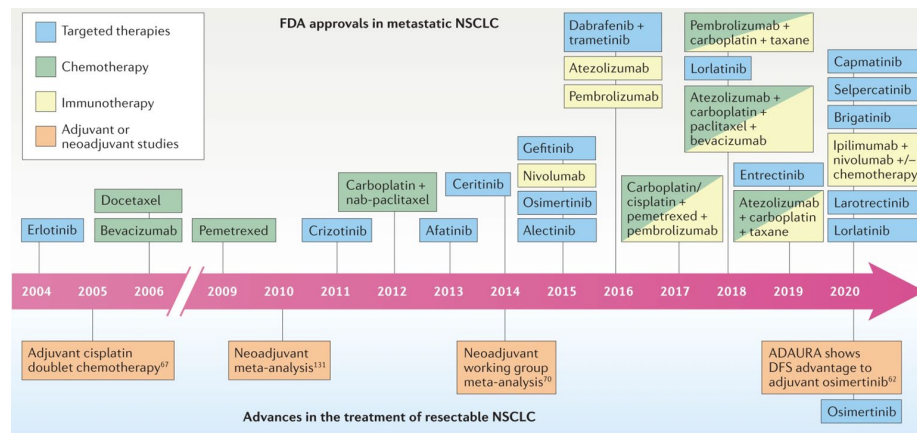


Yale

SCHOOL OF MEDICINE

Problem: Calcium signaling drives all cancer development, yet we have no safe way of targeting it without negatively affecting healthy cells

- 1 Lack of specificity
- 2 High toxicity
- 3 Functional redundancy
- 4 No drug-able target



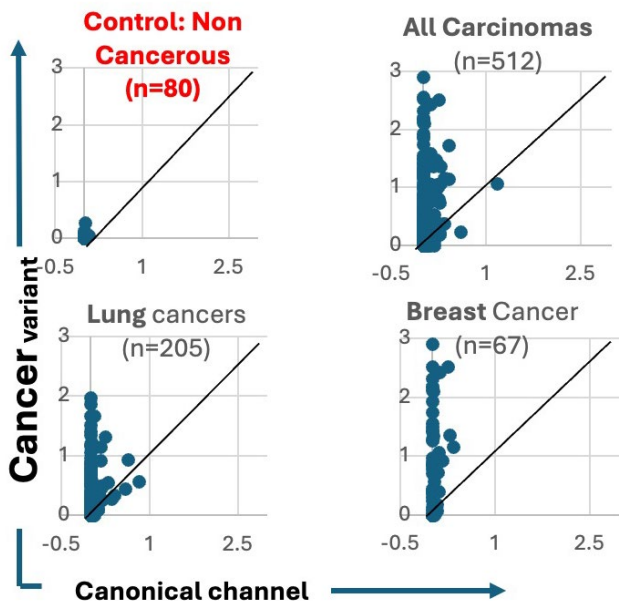
Large moat: no FDA-approved therapies targeting calcium channels for cancer in over 20 years

Solution: Antibodies against a novel calcium channel variant expressed by almost all cancers, but not by healthy cells

1 Lack of specificity

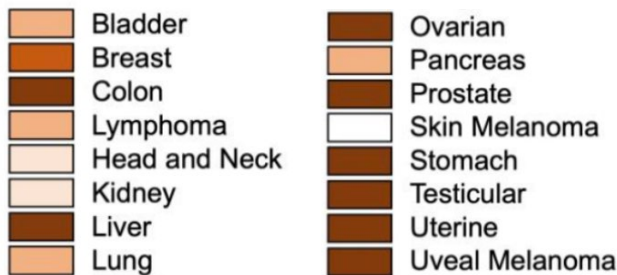
We discovered a **cancer-specific calcium channel isoform** not expressed by healthy cells

mRNA

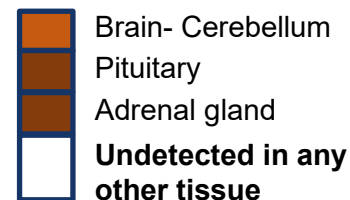


Protein

(A) Cancer patient samples:



(B) Healthy tissues:



Pan-cancer expression:
e.g., Lung, breast, prostate, urethral, colon, glioblastoma, endometrial, leukemia

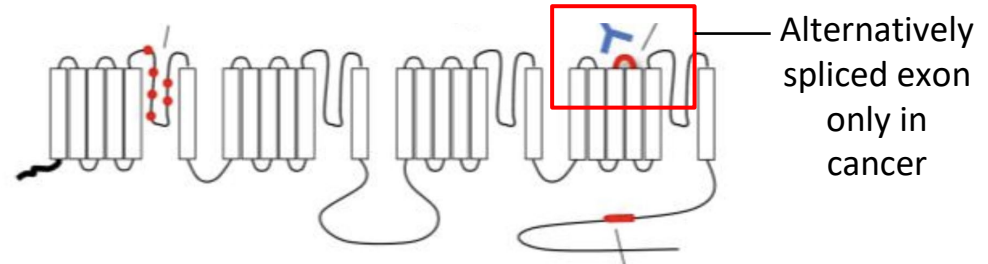
Healthy cells untouched:
Few healthy cells express normal un-spliced channel; **but none express cancer-specific variant**

Solution: Antibodies against a novel calcium channel variant expressed by almost all cancers, but not by healthy cells

2 High toxicity

Non-Small Cell Lung Cancer (NSCLC) patient biopsies:

- High channel expression in tumors
- **Not expressed in marginal healthy lung tissue**



Cancer variant is formed by **alternative splicing event only used by cancer cells** to increase calcium uptake

Epitope 100% conserved across species (Mouse, Rat and Monkey)

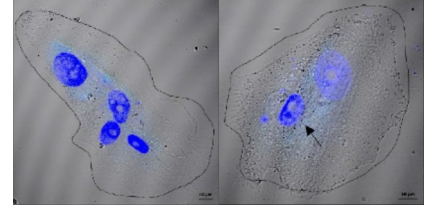
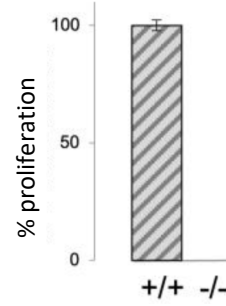
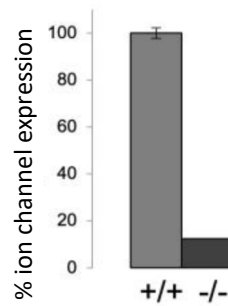
Solution: Antibodies against a novel calcium channel variant expressed by almost all cancers, but not by healthy cells.

1 Lack of specificity

2 High toxicity

3 Functional redundancy

4 No drug-able target



CRISPR K/O → All cancer cultures died in a few days → Syncytial nuclei indicative of failure to divide

The **cancer Ca^{2+} channel** isn't a mutation cells can escape
Once blocked, **no compensating isoforms** for Ca^{2+} uptake

Solution: Antibodies against a novel calcium channel variant expressed by almost all cancers, but not by healthy cells.

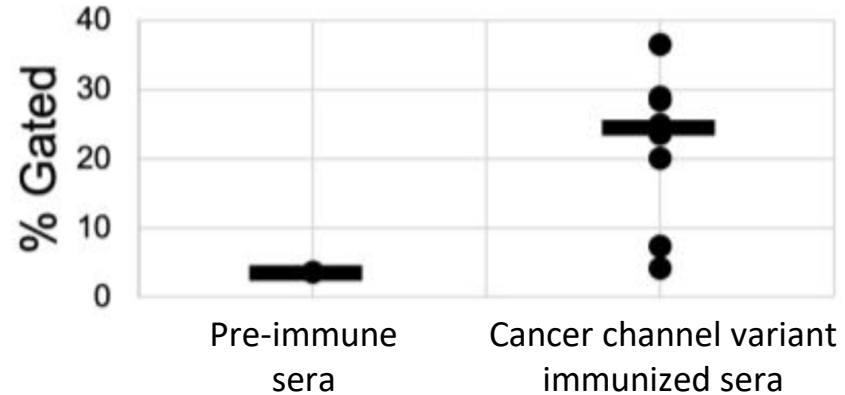
1 Lack of specificity

2 High toxicity

3 Functional redundancy

4 **No drug-able target**

Flow cytometry: **Antibodies against our target bind specifically to human A549 NSCLC cancer cells**



We have **produced human antibodies** that bind the **cancer-specific calcium channel and kill cancer cells.**

Product: World's first cancer-specific calcium blocking antibodies for cancer

1. Fully novel drug class

First-in-class biologic killing cancer via calcium starvation



No competition

2. Synergy with existing therapies

Calcium inhibition reduces standard-of-care drug resistance, boosting effectiveness



Incentive for adoption

3. Applicable to all patients

Target is conserved across nearly all (thousands) of cancers



Expansive market

1st target: Non-small cell lung cancer (NSCLC)

215k

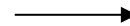
Annual diagnoses

\$19bn

Total addressable market (TAM)

20%

5-year survival rate



Application to many more cancers:









\$225bn

Total addressable market (TAM)

The US **leading cause of cancer deaths**. Our drug has great potential to improve current standard-of-care.

Market is virtually all cancer patients, worldwide.

Competitor Analysis: We lead the field with the best target

	Cancer-specific target?	Pan-cancer applicability?	Drug modality?	target	Clinical trial results?
		 Glioblastoma	Small molecule	Wrong channel	Failed Phase I
		 Neuroblastoma	Small molecule	Ca ²⁺ signal	Failed Phase I
Our Drug		 Virtually all cancers	Antibodies	Cancer specific Ca ²⁺ channel	

Our approach

1. Minimal off-target effects, **much safer**

2. **Much larger market**, targeting nearly all cancers

3. **Faster time to market, greater specificity**

4. Cancer has no compensating mechanisms, **more effective**

5. Precedent: Proves **efficacy of Ca²⁺ inhibition for cancer**

Barriers to Success



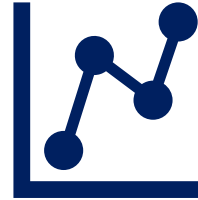
Intellectual Property

Composition of matter patent(s) upon optimization of lead(s).



Far into Pipeline

Fully characterized channel, **already produced humanized antibodies.**



Expertise & Data

Built on **20+ years of our Yale research** on calcium channels in cancer.



Breakthrough Discovery

Only known calcium channel isoform both cancer specific and functionally non-redundant.

Why now?

It's time for a new approach to kill cancer by calcium starvation



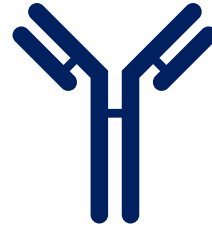
**Huge Interest,
Unmet Need**

Accumulated work that Ca^{2+} inhibition is **critical to killing cancer cells**.



**Breakthrough
Discovery**

First cancer-specific calcium channel target in oncology history.



**Maturation of
Antibody Technology**

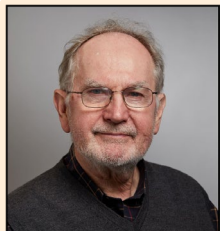
Antibody design allowing **amino-acid level precision**.



**Strong
FDA Support**

Quadrupling in antibody-based drug approvals in 2024.

A Therapeutic Calcium Channel Blocking Antibody for Cancer



Richard A. Flavell
PhD, FRS

**Co-Founder of
Ciedon**

Sterling Professor of Immunobiology,
Yale School of Medicine

HHMI Investigator,
Howard Hughes Medical Institute

Co-Founder, [Alexion Therapeutics](#)

Founding CSO, [Biogen](#)



Terrence Town, PhD
Co-founder of [Ciedon](#), CEO

Former Postdoctoral Researcher
Yale University School of
Medicine: Flavell Lab

**25+ year veteran of translational drug
development**

**Professor of Physiology & Biophysics, USC Keck
School of Medicine (former)**



Didi Matza, PhD
Co-founder of [Ciedon](#), CSO

Former Postdoctoral Researcher
Yale University School of
Medicine: Flavell Lab

**Calcium channel expert, discoverer of the
technology.**

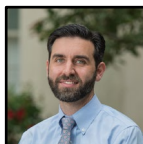
**Senior Lecturer, Open University of Israel
(former)**

**New IP will belong to Yale and to be exclusively licensed to
[Ciedon](#), a [Yale spin-out](#) founded by Flavell and two former Flavell
lab members**

Yale Collaborators



Mario Sznol, MD
**Clinical Advisor/ World Expert in
Immunotherapy**
Professor of Medical Oncology



**Michael Chiorazzi,
MD, PhD [Oncologist](#)**
Assistant Professor of
Medical Oncology



Hong Peng, PhD, MBA
[IP & Business Advisor](#)
Director of Business
Development



Jonathan Alderman, MS, RLATG
[Flavell Lab Manager](#)

Research and Development Plan

Yale CANCER CENTER Funding

