CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

THE UNIVERSITY OF TEXAS AT AUSTIN

Cancer Protein Therapeutics Discovery & Development: A Roadmap for Transitioning from Academia to the Clinic

George Georgiou
Depts. of Chemical Engineering, Biomedical Engineering & Molecular Biosciences
University of Texas at Austin

Research Support from

CPRIT CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

NIH National Institutes of Health

Clayton Biotechnologies

DEFENSE THREAT REDUCTION AGENCY · UNITED STATES OF AMERICA

aeglea BIOTHERAPEUTICS

SANOFI

abcam® discover more

leidos

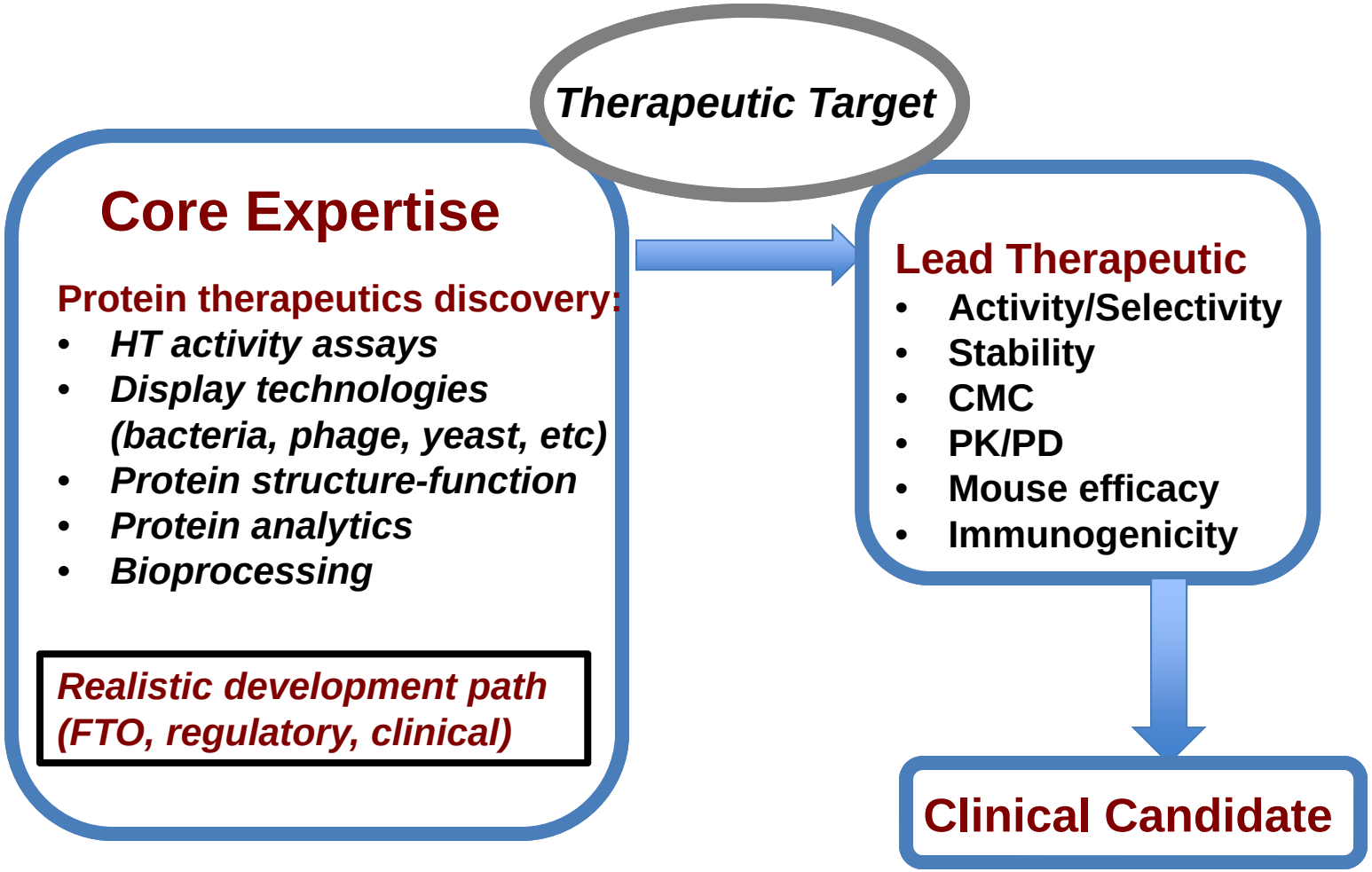
COI Declaration: The presenter is a founder and holds equity in GMA LLC, Aeglea Biotherapeutics and Kyn Therapeutics LLC

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

THE UNIVERSITY OF TEXAS AT AUSTIN

The Georgiou Laboratory

Discovery & development of protein therapeutics (biologics)



- *2 biologics in clinical development: Anthim (Elusys), AEB1102 (Aeglea Biotherapeutics)*
- *2 additional protein therapeutics on path to IND*

CPRIT GRANTS & RESEARCH TRANSLATION OUTCOMES

Award/ Year	Title	Type of Grant	*Technology*	Translation Status
DP150061 2015	"Preclinical Development of a Therapeutic Enzyme for Checkpoint Inhibition in Cancer"	Product Development	Developing the first enzyme for cancer immunotherapy	***Kyn Therapeutics (2015)***
RP140664 2014	"Development of Therapeutic Antibodies Having both Fc_{γ} and Fc_{α} Functions"	HIHR	A new class of highly cytotoxic Ab therapeutics	***In Development***
RP120314 2012	"Engineering and Preliminary Evaluation of a Fully Human, Non-immunogenic Asparaginase…"	HIHR	Developing a less toxic version of a widely used therapeutic	***In Development***
RP100890 2010	"Advanced (Pre-IND) Preclinical Development of a Novel, Highly Promising, Human Therapeutic Enzyme…"	Individual	Engineered Arginase for the Treatment of L-Arg requiring tumors	**Aeglea Biotherapeutics/AE Rase Inc Phase I**
RP100612 2010	"Molecular Engineering l Evaluation of High Potency Therapeutic antibodies For Cancer	HIHR	**Cancer antibodies Displaying greatly improved ADCC**	**Licensing negotiations with several pharma/biotech**

Constraints in Biomedical Translational Research in Central Texas

- **Limited access to experienced, nationally recognized, business development and C-level executives in Texas**
- **Not trivial to engage top VCs and biotech investors (very small local VC community)**
- **Small local network of advisors with experience and connections in biotech**

Advantages

- **UT Austin more open and helpful in working with industry relative to other institutions (Office of Technology Transfer; Office of Research Support)**
- **Austin attractive as a relocation destination**
- **Strong science pool; much less competition for talent than biotech hubs**

Our Model for Translating New Therapeutics

1. **Advance technology in the lab through grant support**
   - **Address early on the key issues for translation:**

   - IP and freedom to operate

   - Are there glaring regulatory or reimbursement roadblocks?

   - Appropriate preclinical validation models

   - Chemistry, control, manufacturing (CMC)

   - Pharmacology

2. **Partner and leverage UT Austin's strength and our lab's expertise to advance *discovery* and mechanistic validation studies**

   - Large lab (32-26 FTEs) with expertise in protein engineering, immunology, biochemistry, pharmacology, downstream processing

Our Model for Translating New Therapeutics (cont.)

3. **Negotiate license to holding company from UT Austin with seed funding from friends & family:**

Rationale:

- VCs and high quality investors reluctant to engage with Universities outside Boston and Bay area

- Inventors need to articulate the scientific rationale and plan

- Need to commit resources for international patent prosecution; difficult for Universities to do in the absence of a license because of costs

- Need to engage advisors and high level legal business development

4. Raise Series A or equivalent funding from high quality investors

- **"Socialize" the technology" though publications and presentations**
- **Exploit scientific founders' network**
- **Establish connections with VCs**

Our Model for Translating New Therapeutics (cont.)

5. Post Series A financing:

1. **Scientific Founder should engage as a Director**

2. **Leverage the academic lab though sponsored research agreements**

3. **Research collaborations, joint publications**

Complete Transparency and Respect of UT Austin COI Policies

Research must advance knowledge and be disseminated through publications

- ***No trade secrets***
- ***No development work that is not aligned to hypothesis-driven research or does not advance students' careers***

Opportunities for students to be engaged as consultants or part time employees of NewCo

- ***In accordance with COI and student policies overseen by the Provost the VP for Research***
- ***Consulting activities must be clearly separated from University obligations and not involve University resources***

Students benefit from gaining industrial experience, are exposed to real world problems, enhance their skill set, financial rewards

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

aeglea BIOTHERAPEUTICS

THE UNIVERSITY OF TEXAS AT AUSTIN

Founders:
Drs. Everett Stone, Res. Asst. Prof. & Dr. Georgiou, UT Austin
Dr. David Lowe, CEO (formerly Skyline Ventures Palo Alto)

- **Based in Austin, TX**
- **Currently 22 full time employees**
- **$19.6 million CPRIT grant to AERase Inc/Aeglea Biotheraputics (2014)**
- **Drug Development company, no wet lab**
- **First phase I study has commenced, second Phase I in 1 Qt 2016**
- **Deep pipeline, all in-licensed from UT Austin**

- ***$750,000/yr SRA between Aeglea Biotherapeutics and UT Austin to pursue discovery, engineering and early development of protein therapeutics***

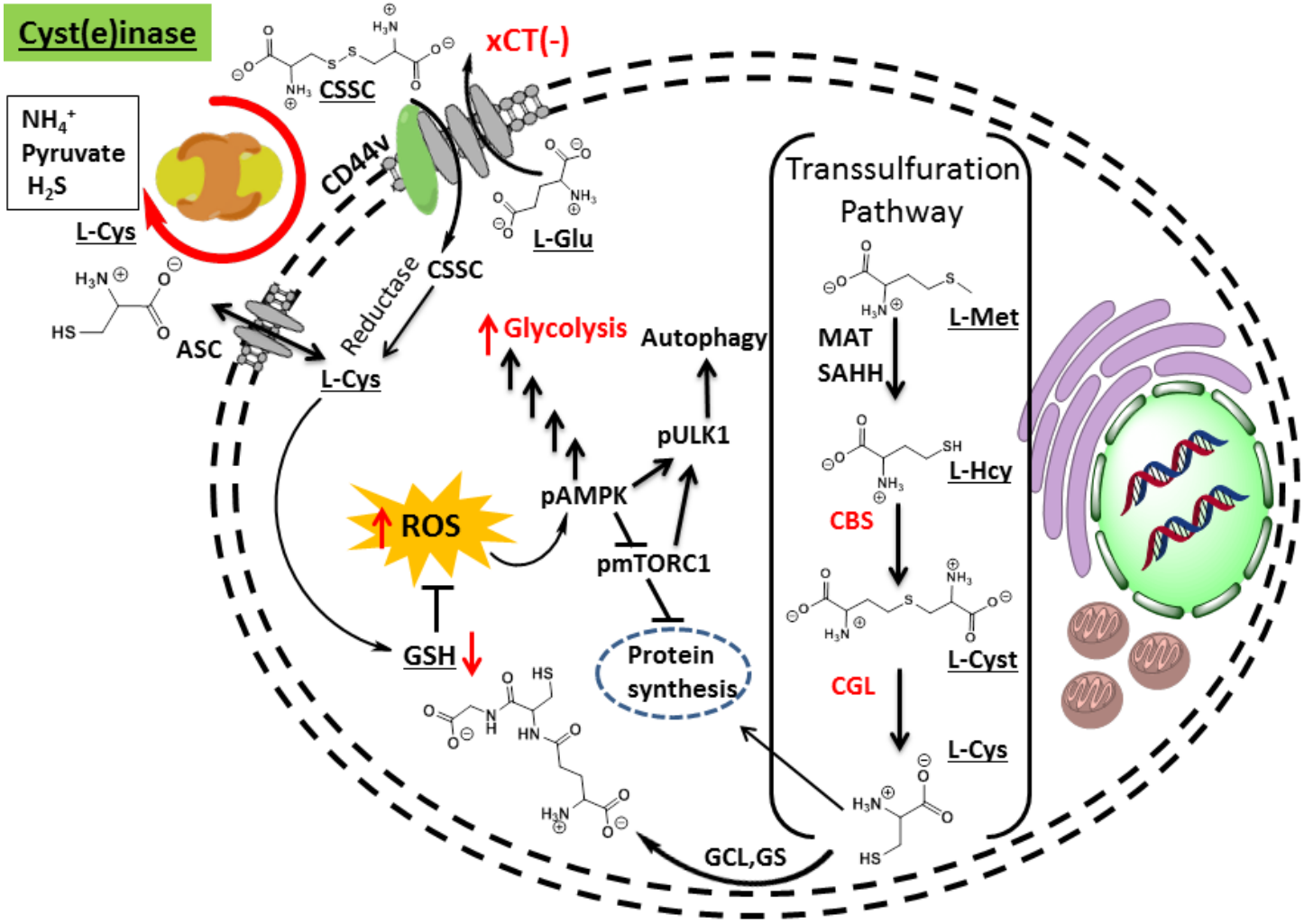
- ***Students engaged as consultants or part time employees***

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

aeglea BIOTHERAPEUTICS

THE UNIVERSITY OF TEXAS AT AUSTIN

AEB3103: A Human Engineered Enzyme for Potent Tumor Ablation via the Systemic Depletion of Serum Cystine/Cysteine

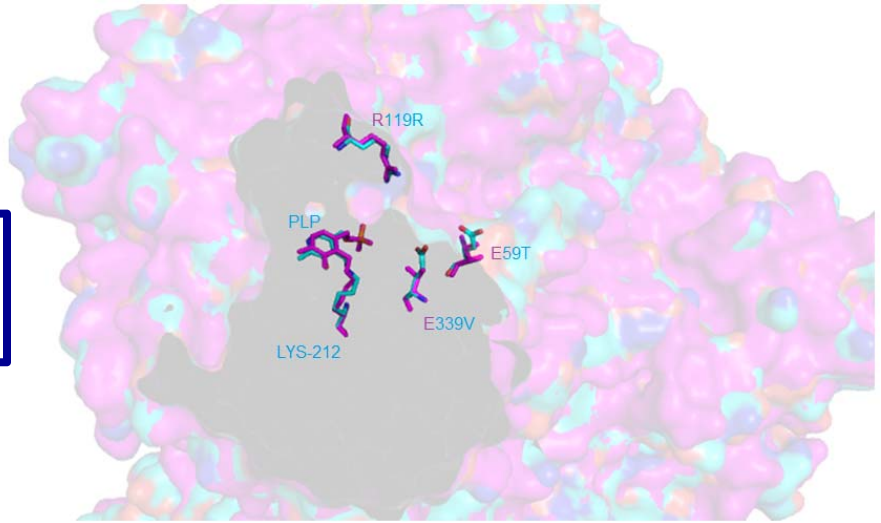


CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

aeglea BIOTHERAPEUTICS

THE UNIVERSITY OF TEXAS AT AUSTIN

AEB3103: A Human Engineered Cyste(i)nase for Cancer Therapy



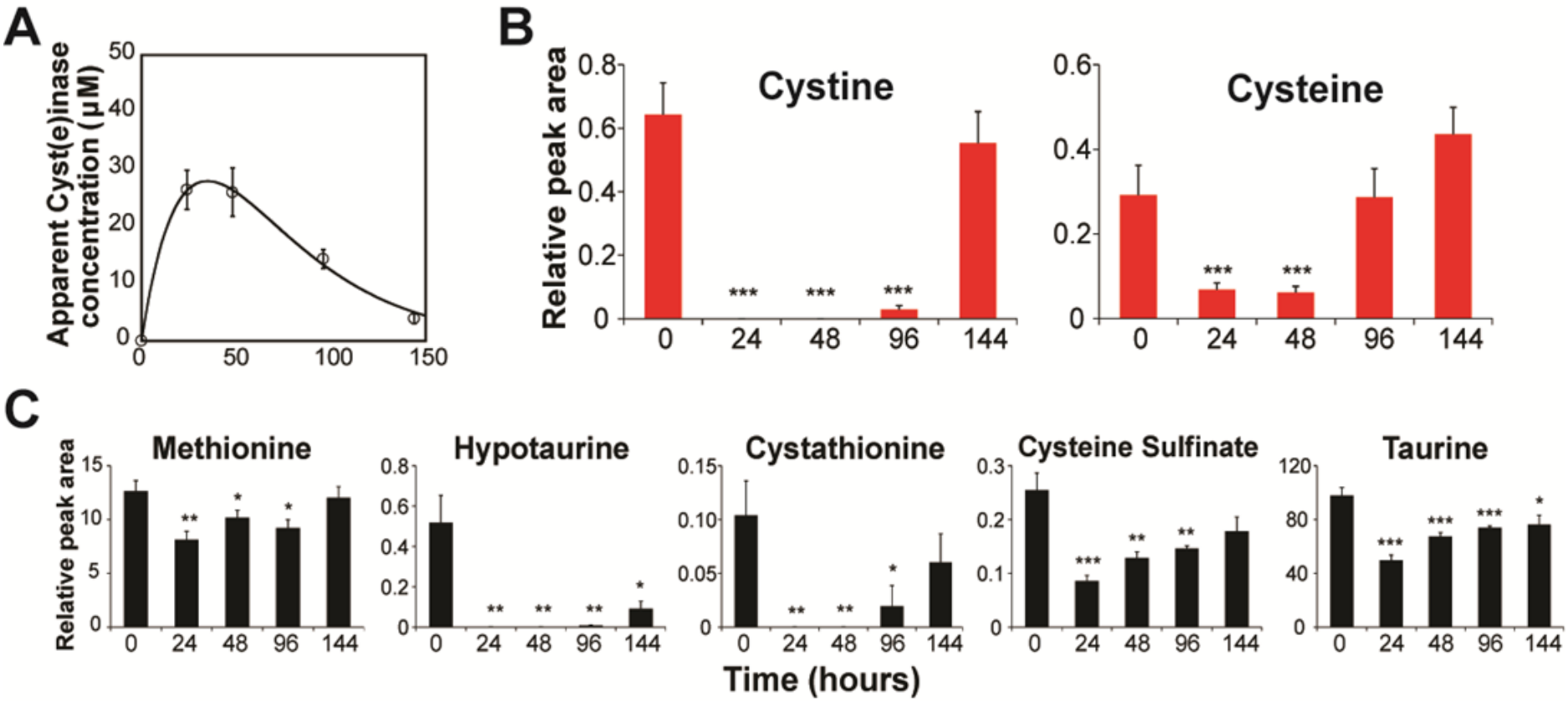
- ***In vitro AEB3013 selectively kills cancer cells via induction of excessive oxidative stress leading to cell cycle arrest and apoptosis***
- **Well tolerated with no change in appetite or weight loss**
- **Favorable pharmacokinetics in non-human primates**

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

aeglea BIOTHERAPEUTICS

THE UNIVERSITY OF TEXAS AT AUSTIN

Metabolic Effects of AEB3103 (Cysteinase) in Mice

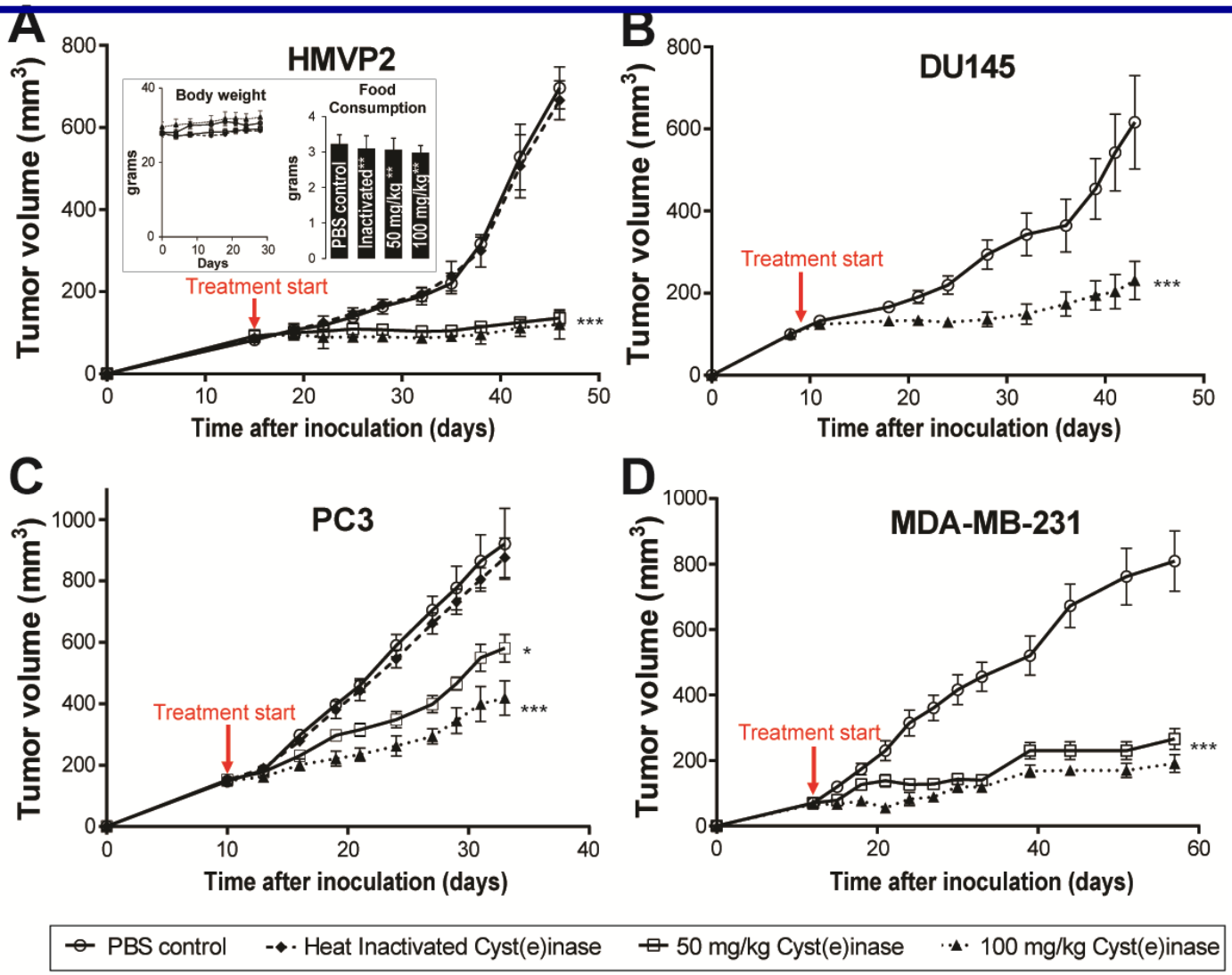


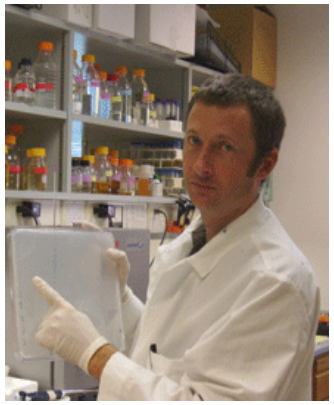
CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

aeglea BIOTHERAPEUTICS

THE UNIVERSITY OF TEXAS AT AUSTIN

AEB3102 Potently Inhibits Tumors (Prostate, Triple Negative Breast Cancer) in Multiple Mouse Models





Shira Cramer
Candice Lamb
Matt Bonem
Kendra Triplett

Dr. David Lowe, CEO
Dr. Scott Rowlinson
Dr. Susan Alters

Prof. Everett Stone

Professor John DiGiovanni & Dr. Achinto Saha,
Pharmacy (Animal models)

Professor Jessie Zhang & Wupeng Yan
Molecular Biosciences (Crystallography)

Professor Stefano Tiziani & Dr. Surendar Tadi,
Nutrition (Metabolomics)