Envivo

Founders

Vlad Senatorov, Ph.D. Candidate in Neuroscience, UC Berkeley
Aaron Friedman, Ph.D. Candidate in Integrative Biology, UC Berkeley

MTI team

Chris Eiben, Ph.D. Candidate in Bioengineering, UC Berkeley/UC San Francisco
Nisreen Hejab, Ph.D. Candidate in Comparative Biochemistry, UC Berkeley
The Problem: Current treatments produce poor patient outcomes

Traditional treatments focus on symptoms not causes

Injury and BBB breakdown → Recovery → Latent period (delayed pathogenesis, inflammatory signaling, neurodegeneration) → Symptoms reported (cognitive impairment, dementia, epilepsy)

Envivo treats casual BBB disease early
1. Diagnose high risk patients
2. Use preventative treatment
The Problem: Untreated blood-brain barrier (BBB) pathology causes neurodegenerative disease.

**Sources of BBB damage**

- Infection
- Stroke
- Trauma
- Aging
- Concussion

**Outcomes**

- Epilepsy
- Neurodegeneration
- Cognitive Impairment
Our Markets: Identifying patients who have BBB pathology that causes disease

2 million people have traumatic brain injuries every year
Our Markets: Identifying patients who have BBB pathology that causes disease

- 2 million people have traumatic brain injuries every year
- 10-40% will develop epilepsy
- Total lifetime medical cost for these patients is $9.2 billion
- Stroke: 1 million people per year
- Brain tumors: 20K per year
The Mechanism: Blood albumin activates the TGFβR pathway causing neuropathologies

When the BBB is disrupted, albumin enters the brain and activates pathological inflammatory TGFβR signaling
Basic Research: Albumin leakage causes disease

Stages of pathology:

Albumin enters the brain activates inflammatory signaling

The signaling cascade causes network reorganization, neural dysfunction, and neurodegeneration

Outcomes include cognitive decline, neurodegeneration, and epilepsy
Our Diagnostics: Imaging BBB pathology directs treatment

Healthy Vessels

Control A  Control B  Control C

Vascular permeability

0.02  0.04  0.06  0.08  0.1
Our Diagnostics: Imaging BBB pathology directs treatment

**JAMA Neurology**

*Imaging Blood-Brain Barrier Dysfunction in Football Players*

Ilan Weissberg, Bmed*, Ronel Veksler, Bmed, BSc†, Lyn Kaminski, MSc†, Rotem Saan-Ashkenazy, MSc‡, Dan Z. Milikovsky, Bmed*, Itai Shefer, MD*; Alon Friedman, MD, PhD‡, §

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Damaged Vessels

Vascular permeability

![Brain imaging with varying levels of vascular permeability](image)
Our Therapeutics: Novel small molecule IPW prevents and reverses pathology with excellent clinical properties.

**IPW properties**
- Potent inhibitor
  - $IC_{50} = 75$ nM
- Long half-life
- Orally bioavailable
Proof of Principle: Treatment prevents epilepsy in a clinical scenario

BBB damaged mice given drug orally

- DOC
-CONTROL (ACSF)
-BBB BREAKDOWN (DOC)

Treatment prevents epileptogenesis

- Graph showing % epileptic and # of seizures over time (days)

Berkeley University of California
Sutardja Center for Entrepreneurship & Technology
The Aging Market: Cognitive decline, mild cognitive impairment (MCI), dementia and Alzheimer’s disease
Our Therapeutics: A new approach for treating cognitive decline in aging

ECoG recordings from aged mice show increase in power of delta and theta bands, similar to dysfunction seen in young mice treated with albumin.

Treating aged mice with IPW improves memory performance. IPW also improves resistance to induced seizures.
Our Timeline

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<td>Dosing Efficacy Toxicology</td>
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$3 Million | $0.5 Million | Millions

We are here
Our Team

Founders
Aaron Friedman and Vlad Senatorov

Scientific Directors
Dr. Daniela Kaufer, PhD, and Dr. Alon Friedman, MD, PhD, PIs and advisors with 10 years research experience developing our new approach.

Clinical Advisors
Dr. Barry Hart, PhD, chemist and drug development.
Dr. Michael Rogawski, MD, clinical trials and neurological therapeutics

Business Advisors
Dr. Robert Knight, MD, and Dr. Andrew Dillin, PhD, research professors with previous success in translational startups

Institutional Support