



Holobiome

The answer was inside us
all along.

San Diego, March 30, 2022

Confidential – do not distribute

Holobiome executive summary

- Launched in 2018, Holobiome is a **microbiome sciences company**, Boston-based
- We leverage our **discovery platform** to develop assets for both pharma and consumer markets
- Lead assets are human gut bacteria that target the **gut-brain-axis** for depression and constipation

\$7M+



MULTIPLE
CORPORATE
SUPPORTERS



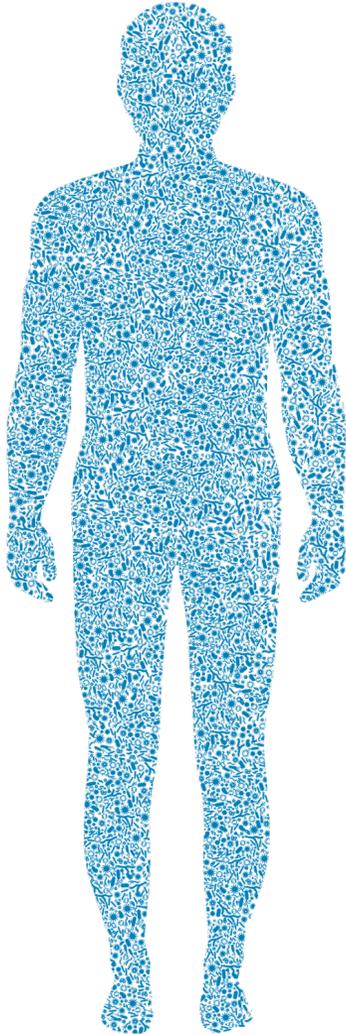
We are not (just) human...



We are **Holobionts**

We have more bacteria in and on us
than there are stars in the Milky Way.

This incredible community is tied to our health



Neurological

Neurodegenerative
Depression
Autism
Neuropathy



Digestive

Inflammatory Bowel Disease
Irritable Bowel Syndrome
GERD
Intestinal motility disorders



Immunological

Rheumatoid Arthritis
Multiple Sclerosis
GVHD
Allergy



Metabolic

Chronic obesity
Diabetes (T1&T2)
Atherosclerosis
Hepatic diseases



Cancer

Immunotherapy efficacy
Melanoma
Colorectal cancer



Infectious Disease

Antibiotic resistant infections
C. difficile infection
COVID-19

Understanding and manipulating the microbiome will change medicine



Holobiome
initial focus



TREATMENTS



OPTIMIZED FOOD



DIAGNOSTICS



PERSONALIZATION

These markets are collectively valued at **hundreds of billions** of dollars

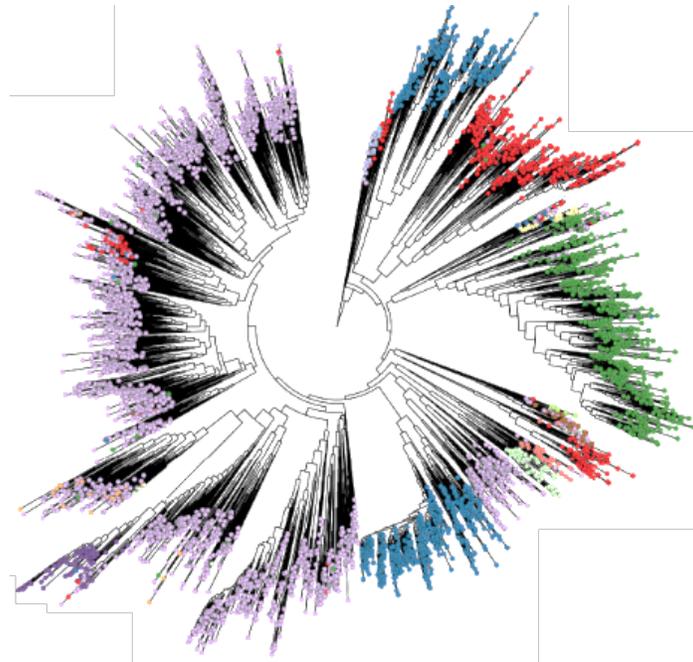
But existing interventions are not the answer

Existing probiotics do not represent our gut microbiome.

They use 30 recycled species, mostly from dairy and soil.



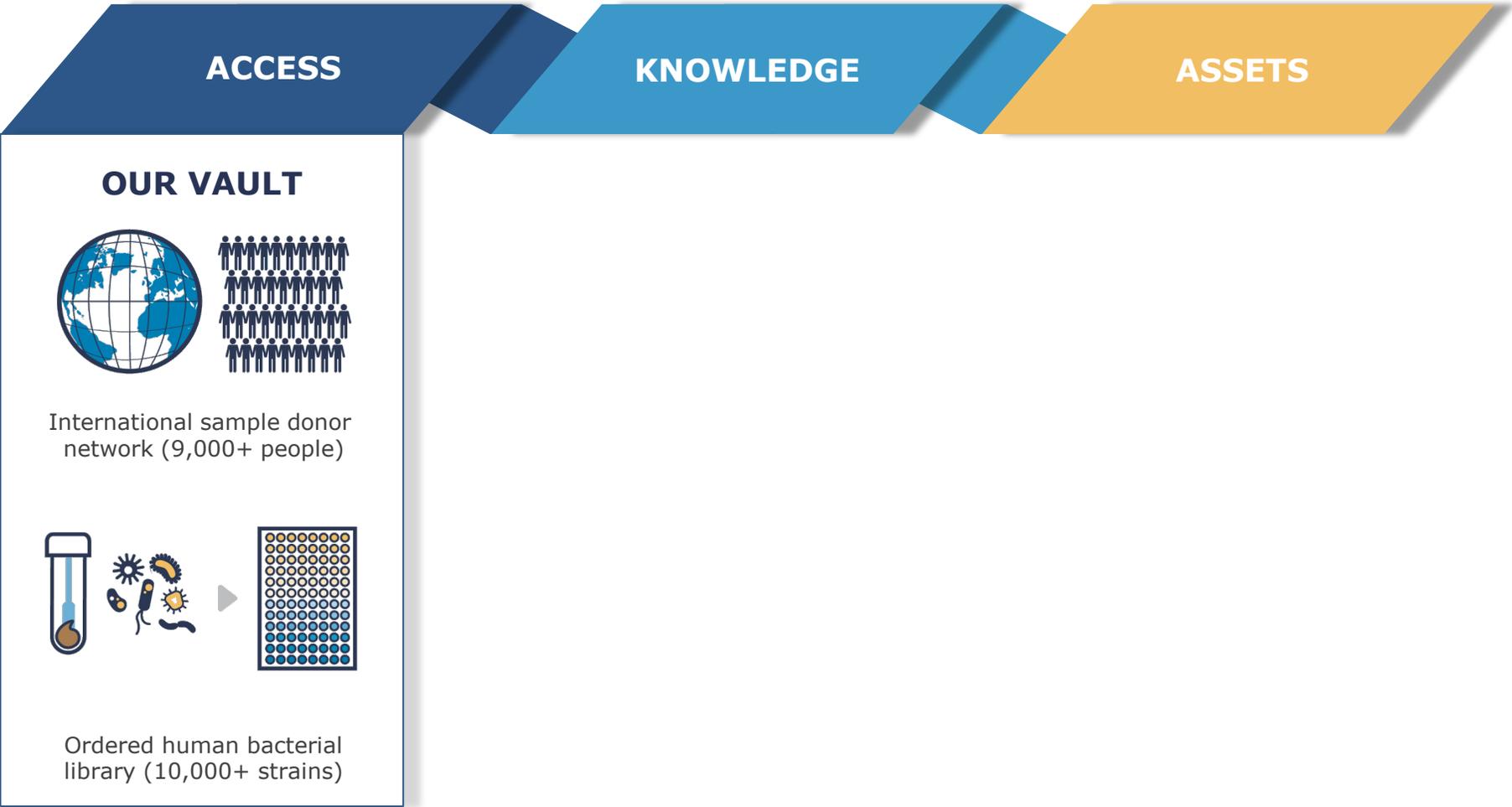
The human gut microbiome is 4,500+ species.



Fecal transplant is crude, not scalable, and variable.



Holobiome is built upon three pillars, giving us a long-term advantage



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Our process yielded two lead assets, with discovery efforts for more

PROGRAMS	DEVELOPMENT STAGE			
	DISCOVERY	PRECLINICAL	MANUFACTURING	HUMAN TESTING
  Asset still owned by Holobiome	HOLO-1 (Depression)			Q3 2022 Q2 2023
  Asset still owned by Holobiome	HOLO-2 (Constipation)			Q4 2022 Q3 2023
	DISCOVERY (Pain)			
	DISCOVERY (Indication 4)			

Targets for all programs are **major biological targets** = ability to expand in other indications

What if the solution to depression lies within us?

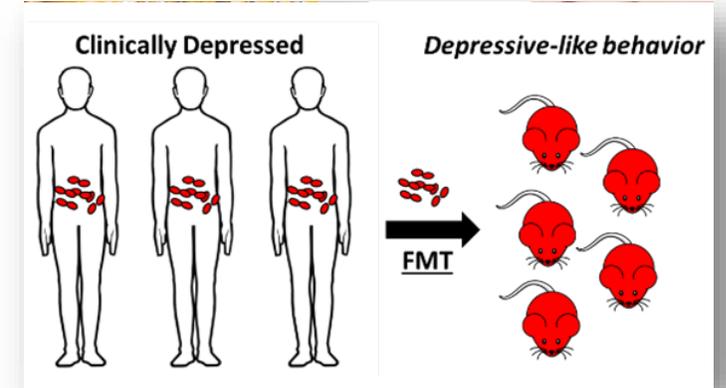
Decades of research suggest the **gut microbiome is connected to depression**
But to do something about this we **need mechanisms to target**



As many as 75% of people with depression report gut issues^{1,2}



Antibiotic use and poor diet increase the risk of developing depression^{3,4}



Depression can be transferred from humans to rodents, via microbiome transplant (FMT)^{5,6}

References: ¹Aguado, 2019, ²Zhang, 2016, ³Lurie, 2015, ⁴Lassale, 2019, ⁵Kelly, 2016, ⁶Zheng, 2016

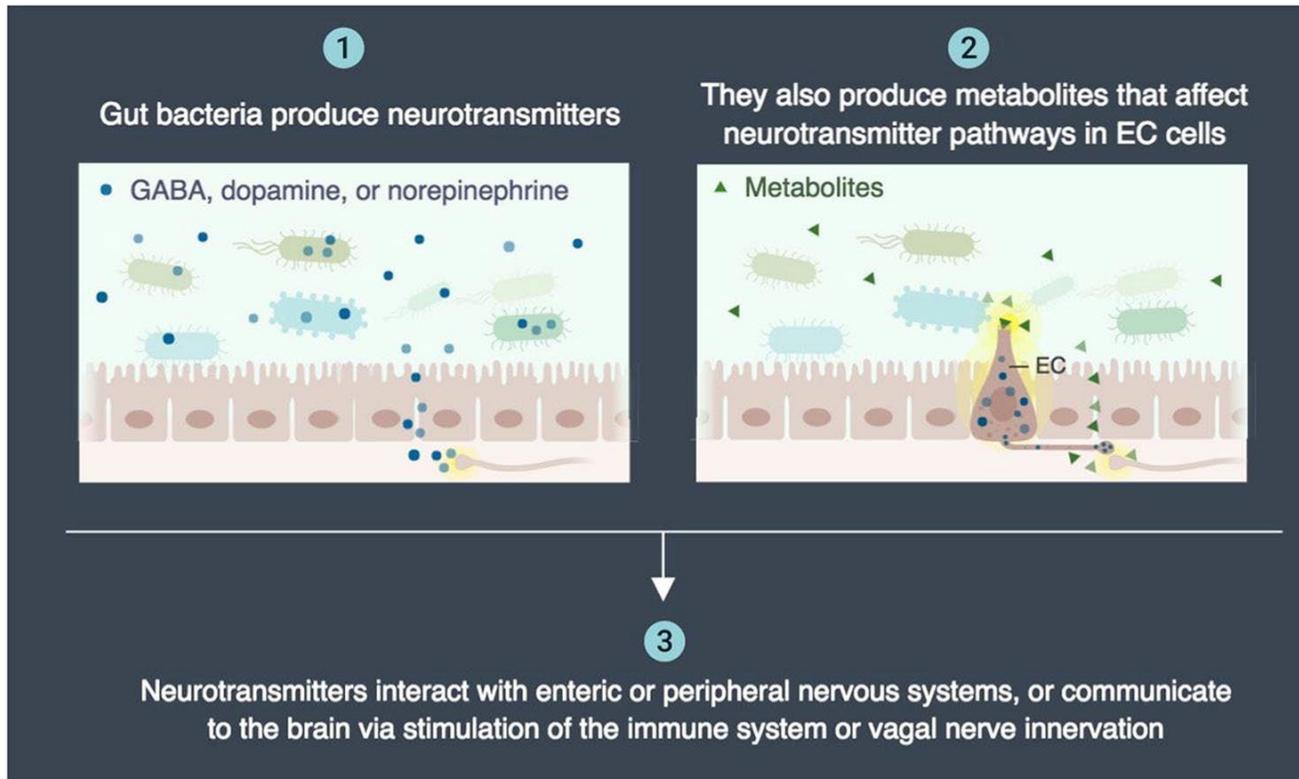
Microbes interact with human neural pathways



Brain Research
Volume 1693, Part B, 15 August 2018, Pages 128-133

Review
Neurotransmitter modulation by the gut
microbiota

Philip Strandwitz



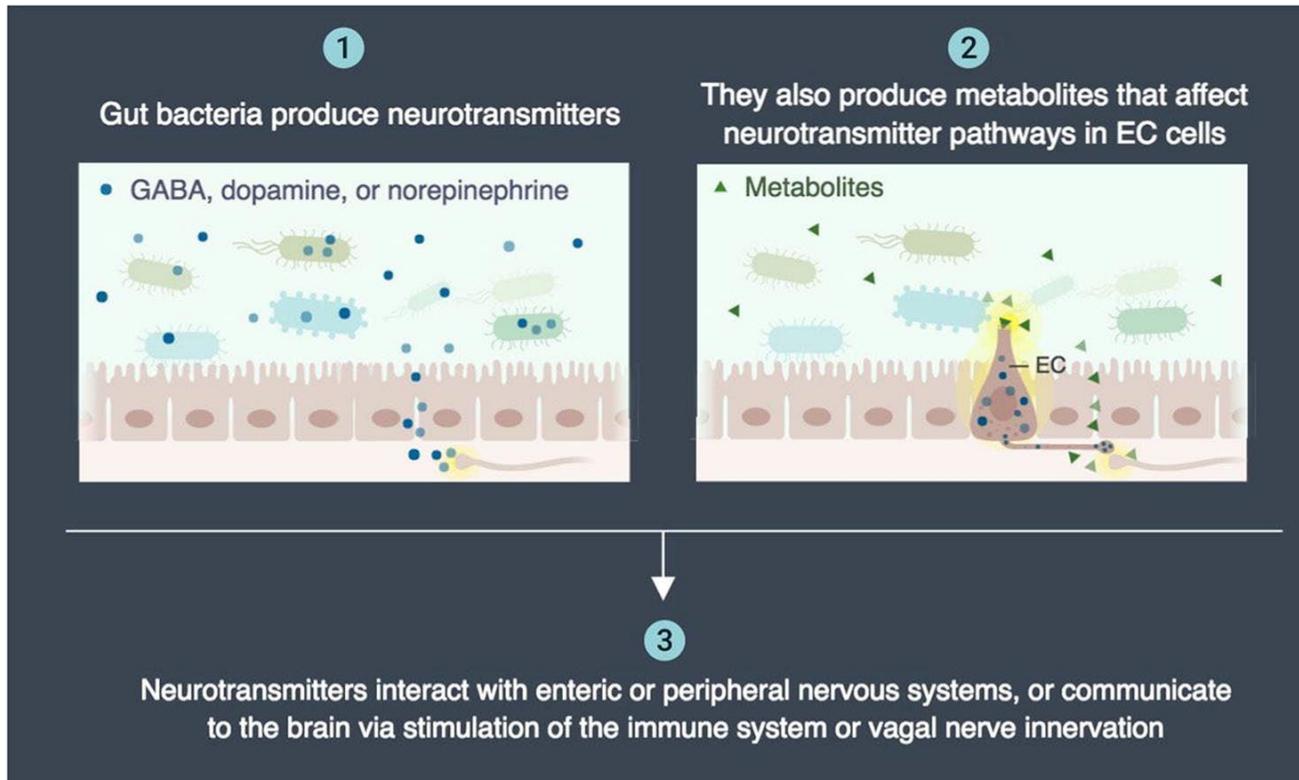
Microbes produce varying levels of specific neurotransmitters



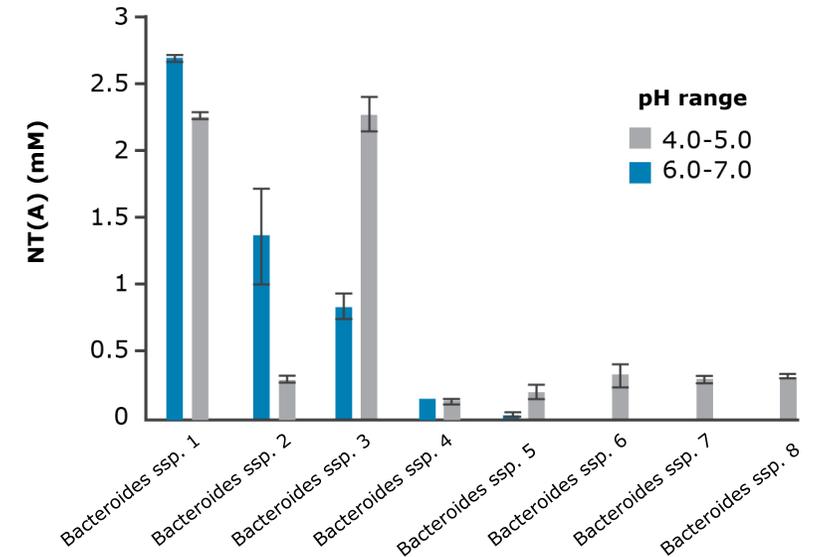
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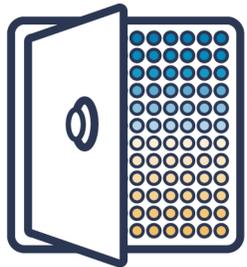
Holobiome found human-derived *Bacteroides* produce **high quantities of neurotransmitter A**



...and low fecal *Bacteroides* are associated with **brain signature of depression** in people

Initial screening allowed us to narrow our focus

We used our platform to go from 31 NT(A) producing species to **14 strains worth advancing**

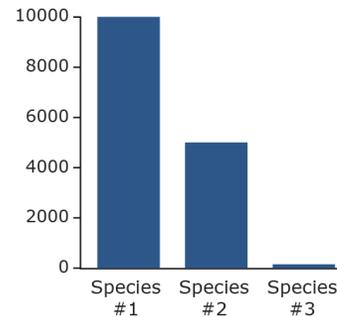


The Holobiome Vault



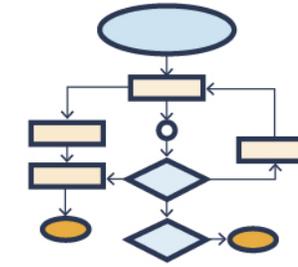
31 potential NT(A) producing species

Selection informed by proprietary co-culture assay and genetics



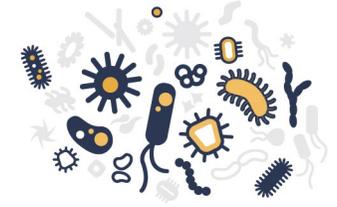
Validated NT(A) production in various conditions

Further supported via human microbiome transcriptomics



Internal strain selection algorithm

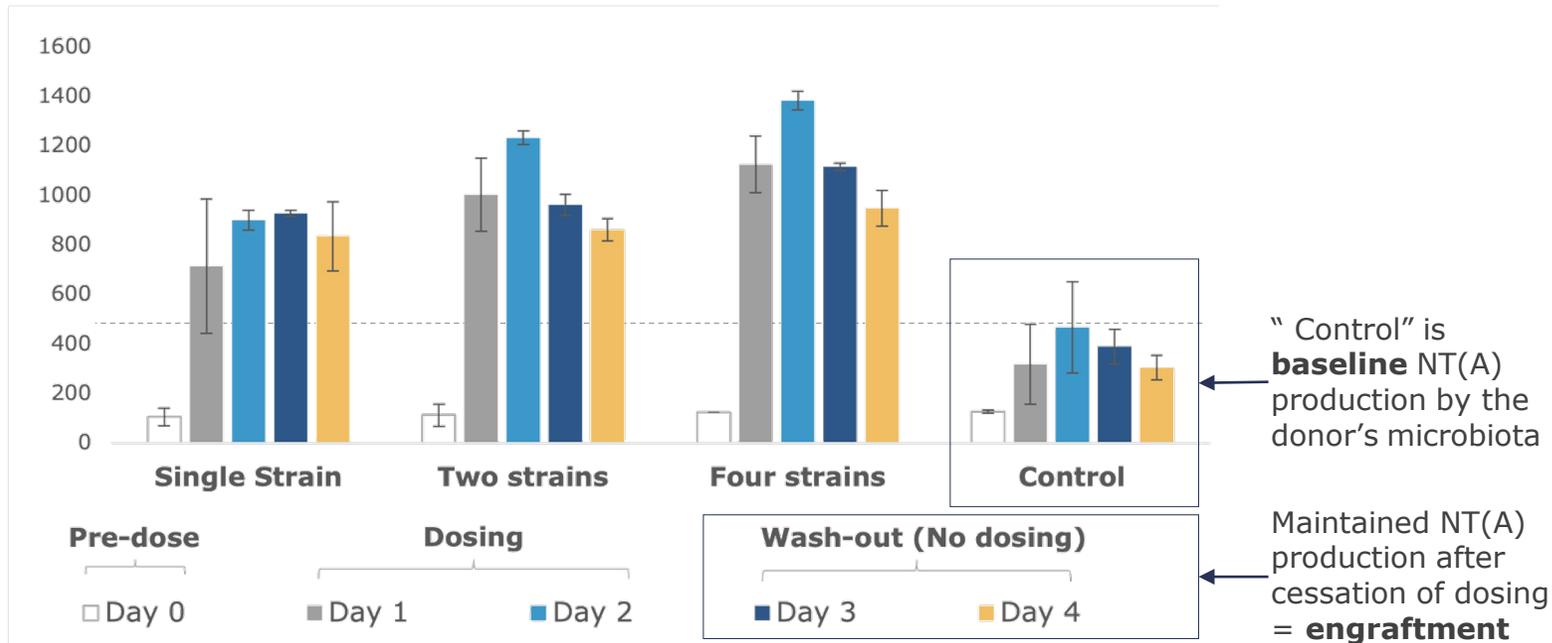
Multiple key considerations, such as manufacturability and safety



14 strains for further testing

Results of one *in vitro* experimentation model

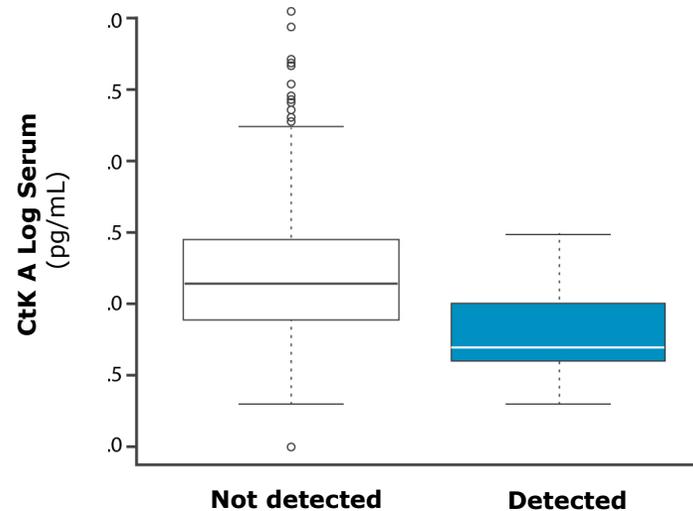
- Holobiome has its own in-house **human gut simulator**
- We used it to confirm our bacteria can **elevate NT(A)** in a complex microbial ecology



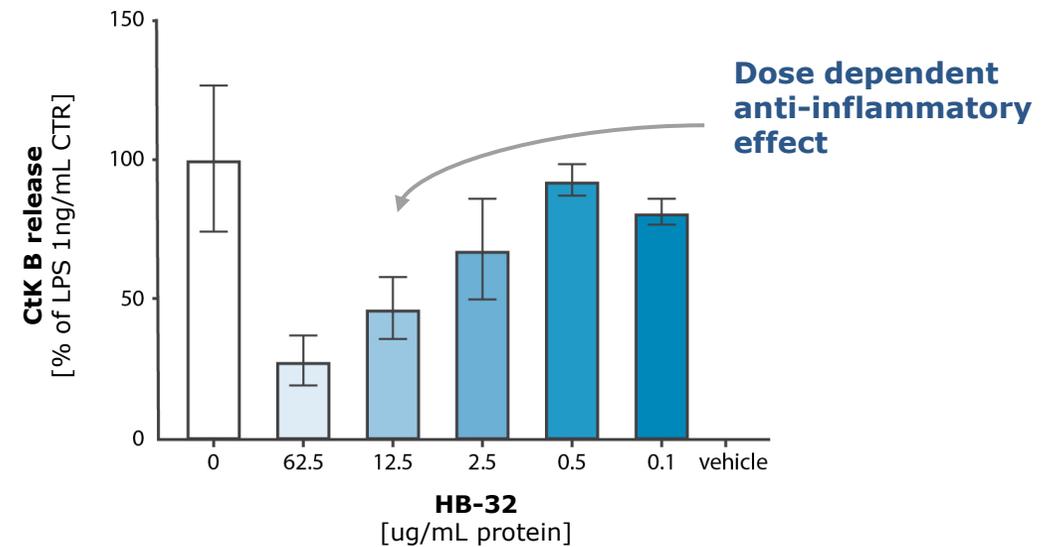
Human data review and cell experimentation

- We profiled these strains for the ability to reduce inflammation, **a second mechanism** for treating depression
- We found one strain, **HB-32**, is anti-inflammatory

The presence of HB-32 is associated with **lower inflammation** in a cohort of 500 people ($p=0.00817$)



HB-32 has an **anti-inflammatory effect** on human immune cells

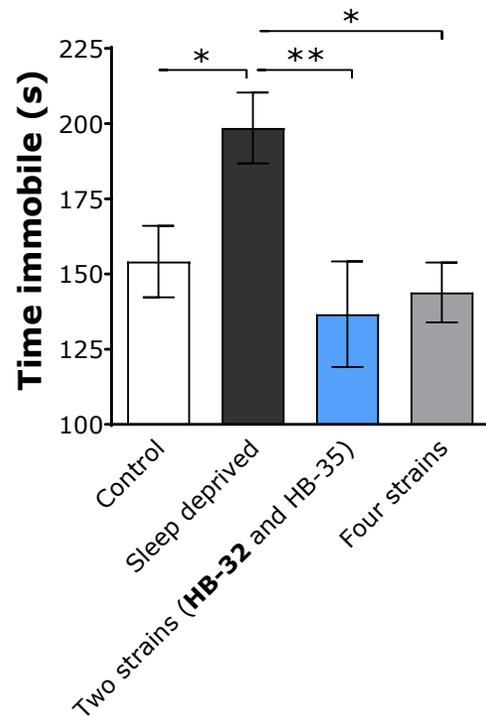


HB-32 PBMC assay

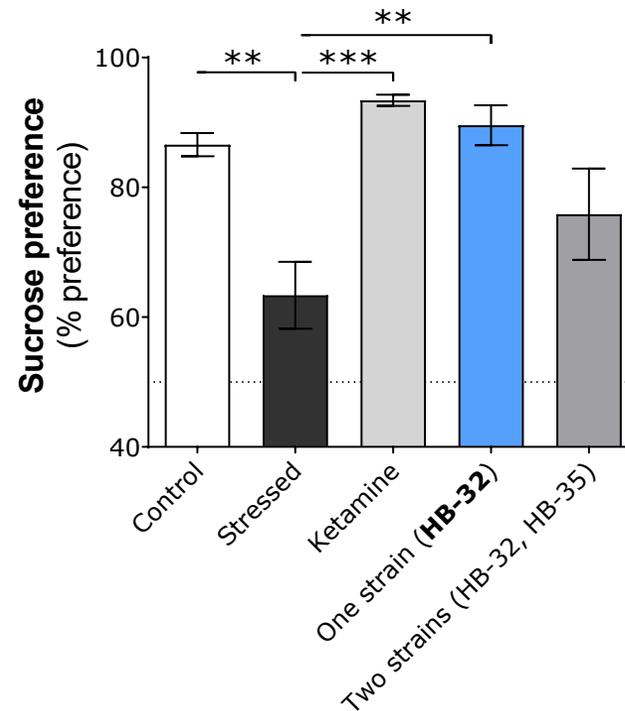
Animal model experiment results

In two models of depression-like symptoms, our strains exhibited protective effects, including **modulation nearly equal to ketamine**

MODEL #1
Sleep deprivation-induced



MODEL #2
Social defeat-induced



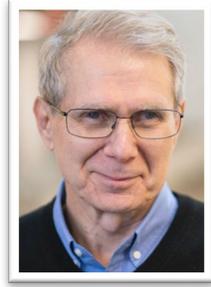
We now seek to advance **HB-32 (HOLO-1)** into CMC and human testing

Our foundations are built upon decades of expertise in microbiology



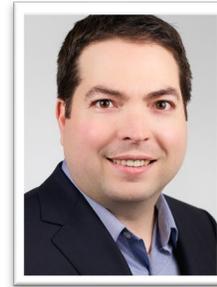
Philip Strandwitz, PhD
CEO + Co-Founder, Director

- Microbial ecologist, entrepreneur
- Inventor of core technology
- Henri Termeer Fellow



Kim Lewis, PhD
Co-Founder, Director

- Professor Northeastern University
- World leader in microbiology
- 200+ publications, \$50M+ grants



Michael LaFleur, PhD
President + Co-Founder, Director

- Decades of microbiology experience
- 10+ years of CEO leadership
- \$30M+ in non-dilutive grants



Katya Gavrish, PhD
First Employee

- Curator of the Holobiome Vault
- Microbial ecologist
- Bacterial cultivation specialist



Jonathan Krive, MBA
Chief Business Officer

- 10+ yrs corp. development
- Microbiome entrepreneur



Mariaelena Caboni, PhD
Principal Scientist

- Immunology, microbiology
- Ex: Novartis and GSK



Stephen Skolnick, BS
Innovation Associate

- Neuroscience, microbiome
- Entrepreneur, inventor



Cameron Friedman, BS
Research Associate

- Microbiology
- Assay development



Bridget O'Connor, BS
Research Associate

- Microbiology, cell culture
- Microbe whisperer



Madeleine Morrisette, PhD
Scientist - Micro

- Microbiome research
- Microbiome analytical

We are strengthened by world leaders in microbiome research and R&D

AstraZeneca 



Iain Chessell, PhD
Board Member

- Head of Neuroscience at AstraZeneca, VP
- Ex-GSK; pain leader

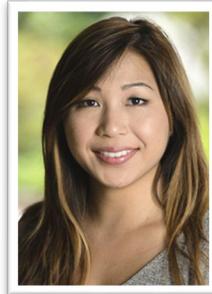
UC San Diego



Jack Gilbert, PhD
Scientific Advisor

- Professor at UCSD
- Leader in microbiome analysis; 250+ papers

Ucla



Elaine Hsiao, PhD
Scientific Advisor

- Professor at UCLA
- Gut-brain-axis leader
- Licensor to Holobiome

 **HARVARD**
MEDICAL SCHOOL



George Church, PhD
Scientific Advisor

- Professor at HMS
- Genetics & synbio pioneer and leader



Abigail Koppes, PhD
Collaborator

- Professor at NEU
- Enteric biology
- Neuron-on-a-chip



Felica Jacka, PhD
Collaborator

- Professor at Deakin University (Australia)
- Behavior + nutrition

UC San Diego

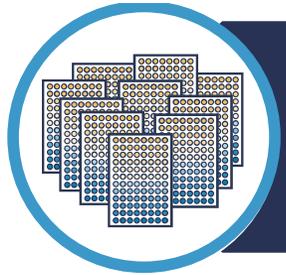


Tony Yaksh, PhD
Collaborator

- Professor at UCSD
- Leader in pain and neurology research

 = Active academic collaboration

We are now ready to scale



Expand the Holobiome Vault 10x
Profile the Vault for **high priority targets**



Automate our laboratory and processes



Build out **machine learning** and
artificial intelligence capabilities

**MASSIVE
THROUGHPUT**



Holobiome

The answer was inside us
all along.