

Anne Eichmann.
Ensign Professor (Cardiology).
Professor of Cellular and Molecular Physiology
Yale University Medical School
Yale innovator awardee 2022

Drug Delivery across the Blood Brain Barrier



D²B Team

Vascular and CNS - Entrepreneur -
Global Authority Science



Anne Eichmann, PhD.
Ensign Professor of Medicine
(Cardiology)
Professor of Cellular
and Molecular Physiology



Kevin Boye, PhD
Research Scientist
Entrepreneur

Entrepreneur -
Science

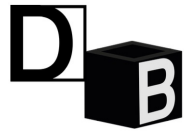
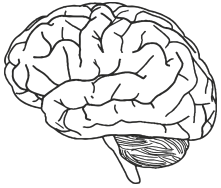


Luiz Geraldo, MD, PhD
Resident
Entrepreneur

Business -
Science

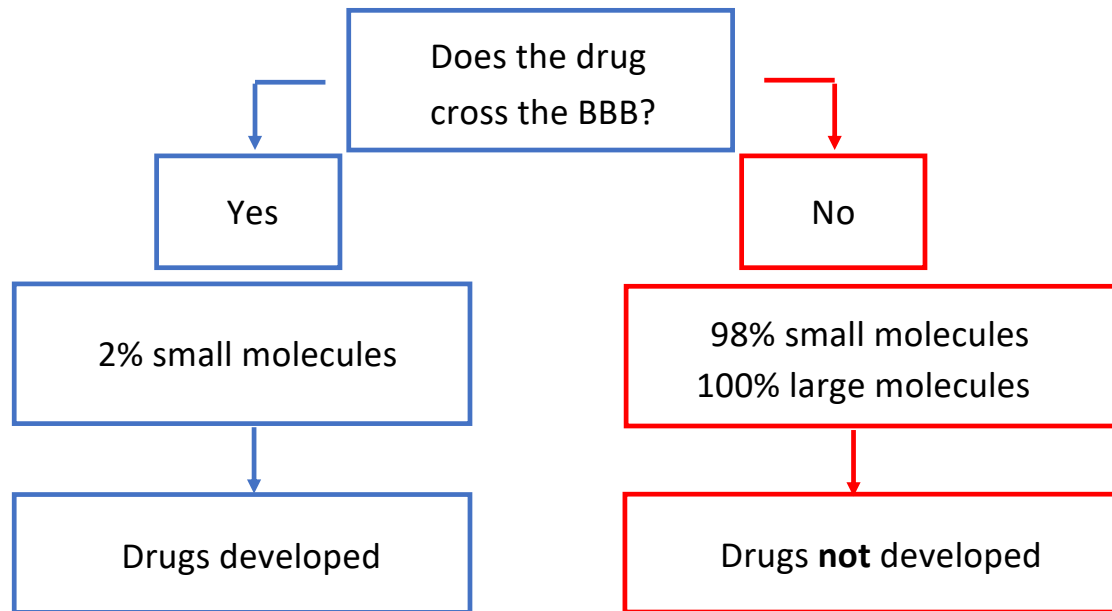


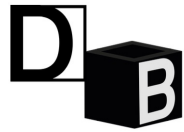
Morag Grassie, PhD
Associate director of business
development
Yale OCR



Product: Patented Monoclonal antibodies that transiently open the BBB

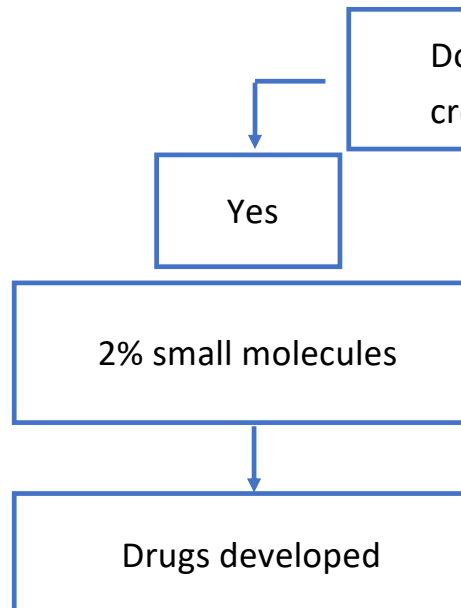
Most drugs do not cross the BBB. Therefore, most brain diseases remain incurable. **This is a major unmet medical need.**

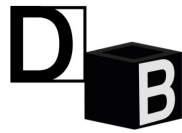
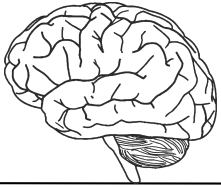




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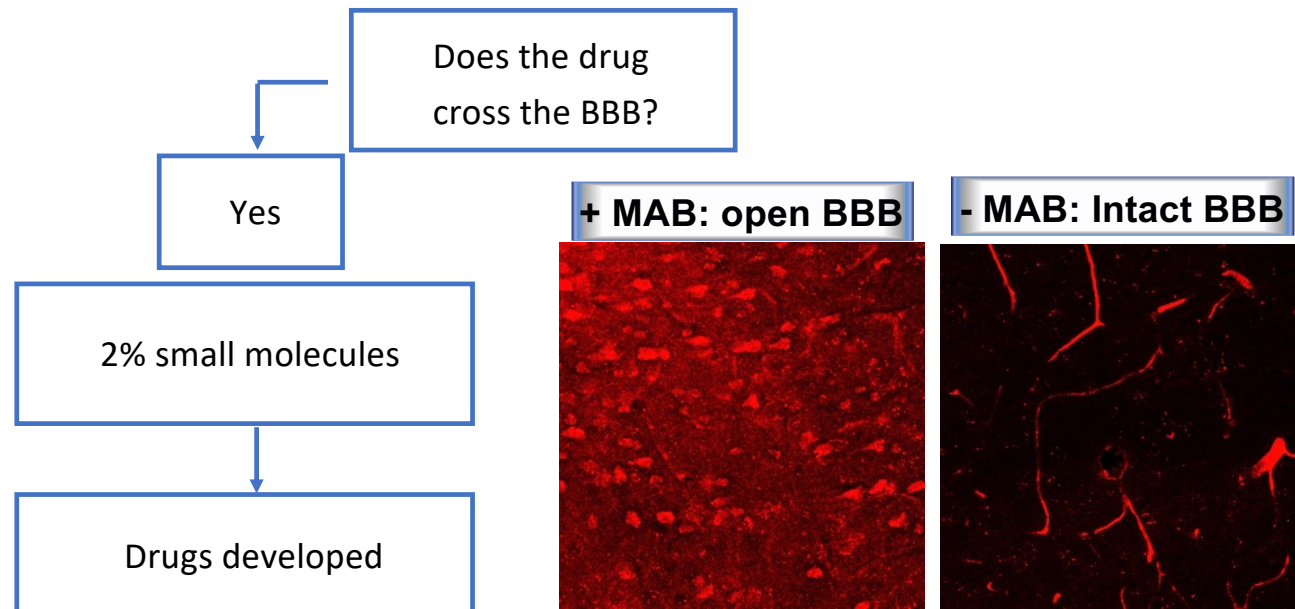
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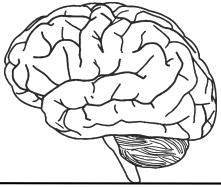




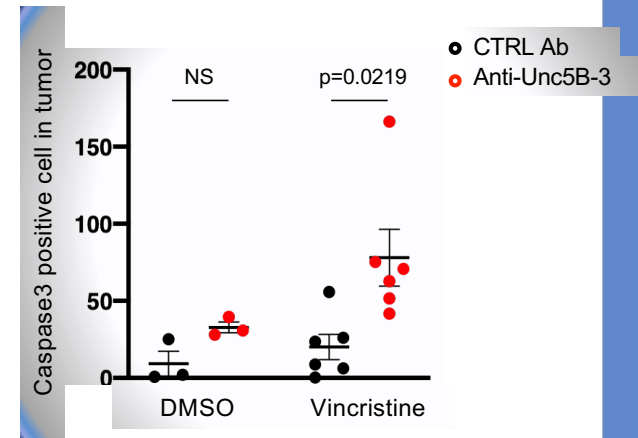
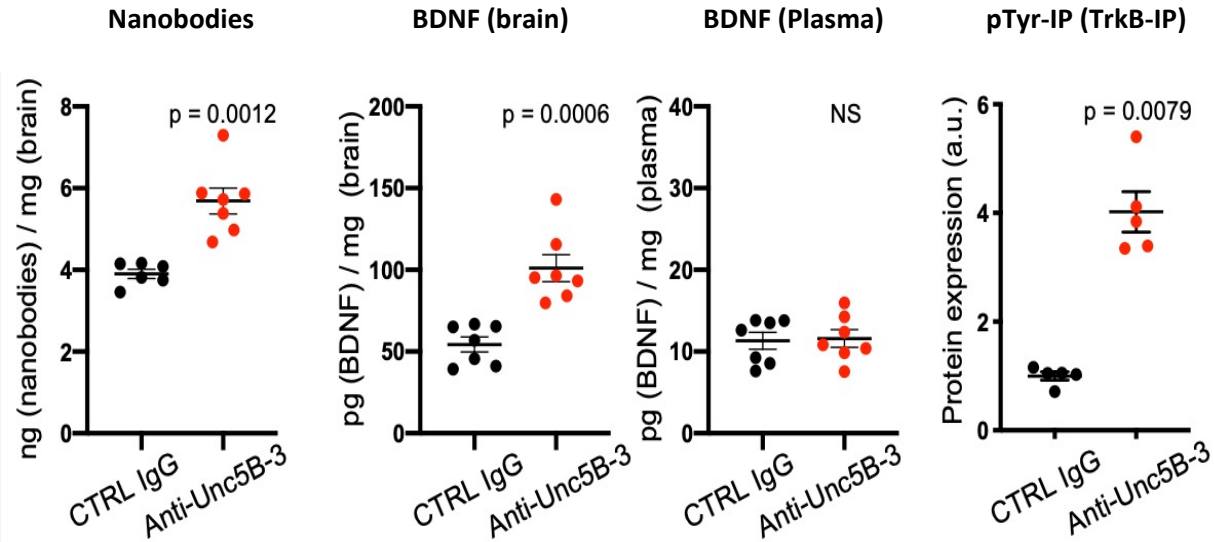
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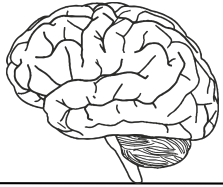
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DB Therapeutic Utility: Delivery of bioactive molecules <70kDa





D³B Market Potential

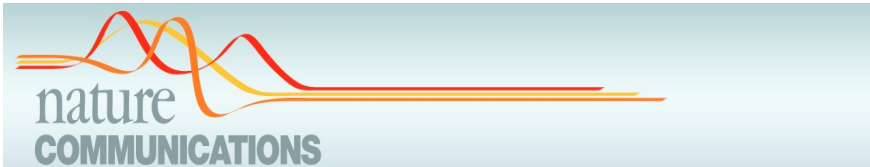
brain cancer, brain metastasis, neurological diseases, infections

Global CNS drug market size **USD \$130 billion** in 2022 (200 billion in 2030)

Ref: Precedence research press release Jan 2023

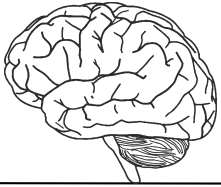
We outperform the Competition

	D³B	MRI-guided focused ultrasound with micro-bubbles	Receptor-Mediated-Transcytosis	Mannitol
Known BBB maintenance mechanism	✓	✗	✗	✗
Reversible Non damaging	✓	✗	✓	✗
Brain-wide	✓	✗	✓	✓
Delivery of various drugs	✓	✓	✗	✓
IV Injection	✓	✓	✓	✗

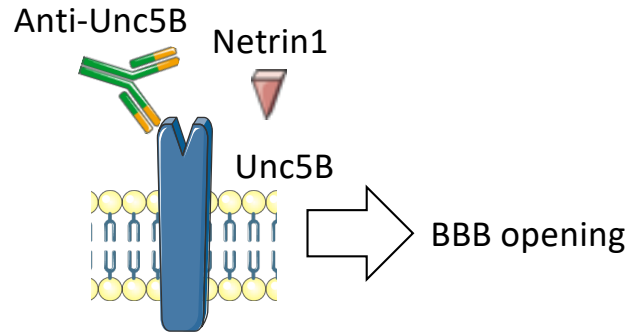


Endothelial Unc5B controls blood-brain barrier integrity

Kevin Boyé¹, Luiz Henrique Geraldo^{1,2}, Jessica Furtado¹, Laurence Pibouin-Fragner², Mathilde Poulet^{1,2}, Doyeun Kim³, Bryce Nelson⁴, Yunling Xu², Laurent Jacob², Nawal Maissa², Dritan Agalliu⁵, Lena Claesson-Welsh⁶, Susan L. Ackerman⁷ & Anne Eichmann^{1,2,8✉}



DB The Science



10 Human monoclonal ABs

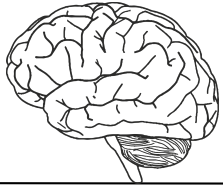
MAB target : Endothelial transmembrane receptor Unc5B
Guardian of BBB integrity

Discovered pathway function

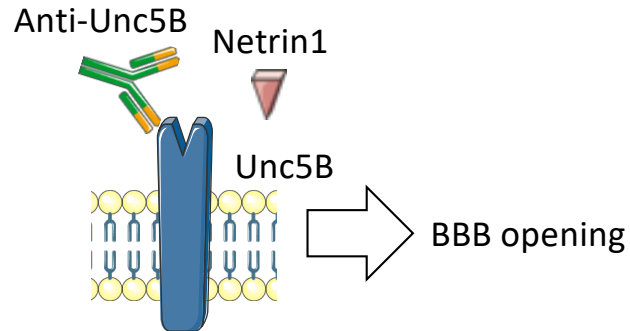
World-authority in Neurovascular Research (> 150 publications,
> 20.000 citations)

Selected publications:

Nature 2004; 432: 179-86
Genes Dev 2007; 21: 2433-47
Dev Biol. 2008; 318: 172-83
Circ Res. 2009; 104: 428-41
Dev Cell. 2011; 20: 33-46
J Clin Invest. 2014; 124: 3230-40
Nat Commun. 2016; 7:13517
Science 2018; 361:599-603
Nat Commun. 2022; 13: 1169



D_B The Science



Human monoclonal AB

Isolated from synthetic human Fab library F

9 backup hits

CROs produce and test recombinant antibodies

Lead anti-Unc5B-3:

Human Unc5B	Rat Unc5B
KD=1.29nM	KD=1.34nM

Can be applied to humans

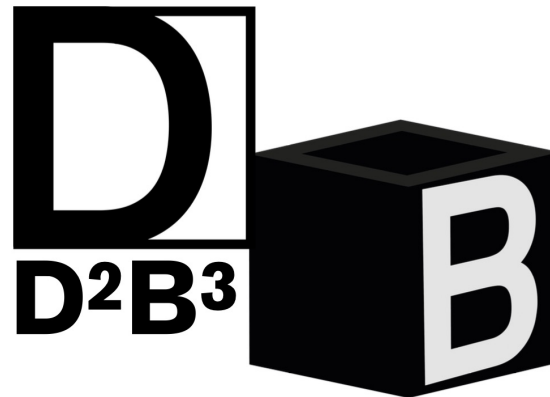
Tested in preclinical rodent models

No significant toxicity expected
(anti-ligand Mabs are Clinically tested)

D_B Milestones and capital plan

Timeline	6/23	1/24	12/24	6/25
Milestones		lead candidate		IND filed
Progress to date (Blavatnik funds \$400K)	CRO reproduced transient BBB opening ✓ Dose-escalation studies underway Backup Abs tested in vivo POC studies			
Activities	Chemotherapeutics delivery ✓ Pre-clinical efficacy in brain cancer ✓	Neoplastic meningitis Brain metastases		Infection Neurological diseases
	Toxicology (in vivo, single and repeat ascending dose)			
		CMC (Formulation)	Stability, standards, scale-up	
			Regulatory advisory	
Capital plan	Lead optimization and IND enabling studies			\$ 5-8 Million

Thank you.



Interested in investing in our technology?

Please contact

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Morag.Grassie@yale.edu