The Innovation Ecosystem

Don't Go it Alone

Monday, May 1, 2023

bu.edu/research/events

BOSTON UNIVERSITY

Boston University Office of Research

Agenda

- Welcome Remarks
- Presentations
  - Arturo Vegas
  - Daniel Cifuentes
  - Gustavo Mostoslavsky
  - Kamal Sen
  - Larry Ziegler
  - Lou Awad
- Q&A
- Innovator of the Year Award Presentation
- Closing Remarks

ResearchER on Tap

Rana K Gupta

Director, Faculty Entrepreneurship
OTD, Innovate@

Continuing our commercialization theme

People over ideas

Don’t Go It Alone: personal journey, including others

- **Who are you – how do you think of yourself**
- **Where are you in your career**
- **What’s your objective (with this idea)**
- **What’s the need**
- **What’s the idea**
- **Chosen pathway for commercialization and why**
- **Our story begins waaay back in 20XX**
- **Where are you now**
- **Resources used along the way**
- **What’s next, what are your milestones**
- **Top one or two learnings**
- **Top one or two surprises**

Small-molecule Annotation of Cytokines

Arturo Vegas, PhD

Assistant Professor
Department of Chemistry, College of Arts and Sciences

BIOLOGICAL DESIGN CENTER

BU NANO | NANOTECHNOLOGY INNOVATION CENTER

TRB
BU | Translational Research in Biomaterials

CMD

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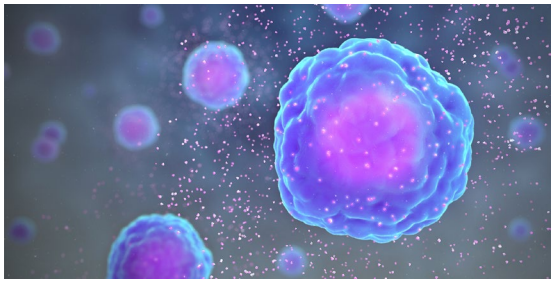
>23M in the US suffer from Immune-Mediated Inflammatory Diseases (IMIDs, non-asthma)

Rheumatoid arthritis

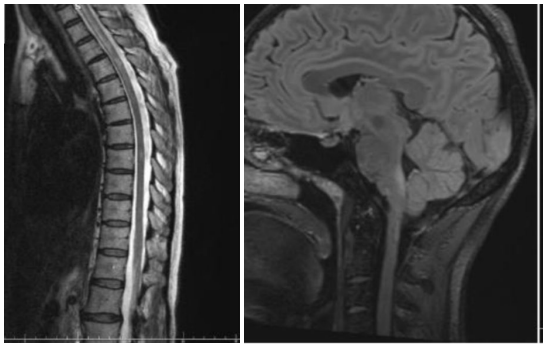
Systemic Lupus

>$200 Bn

Economic cost

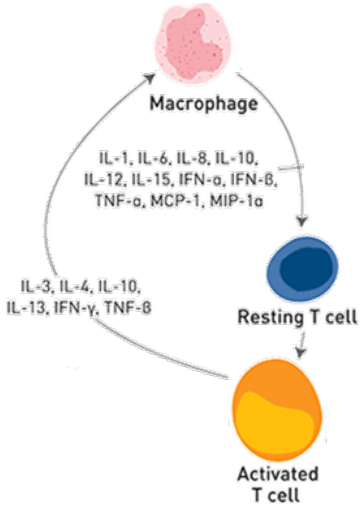


Cytokine storms (infection)

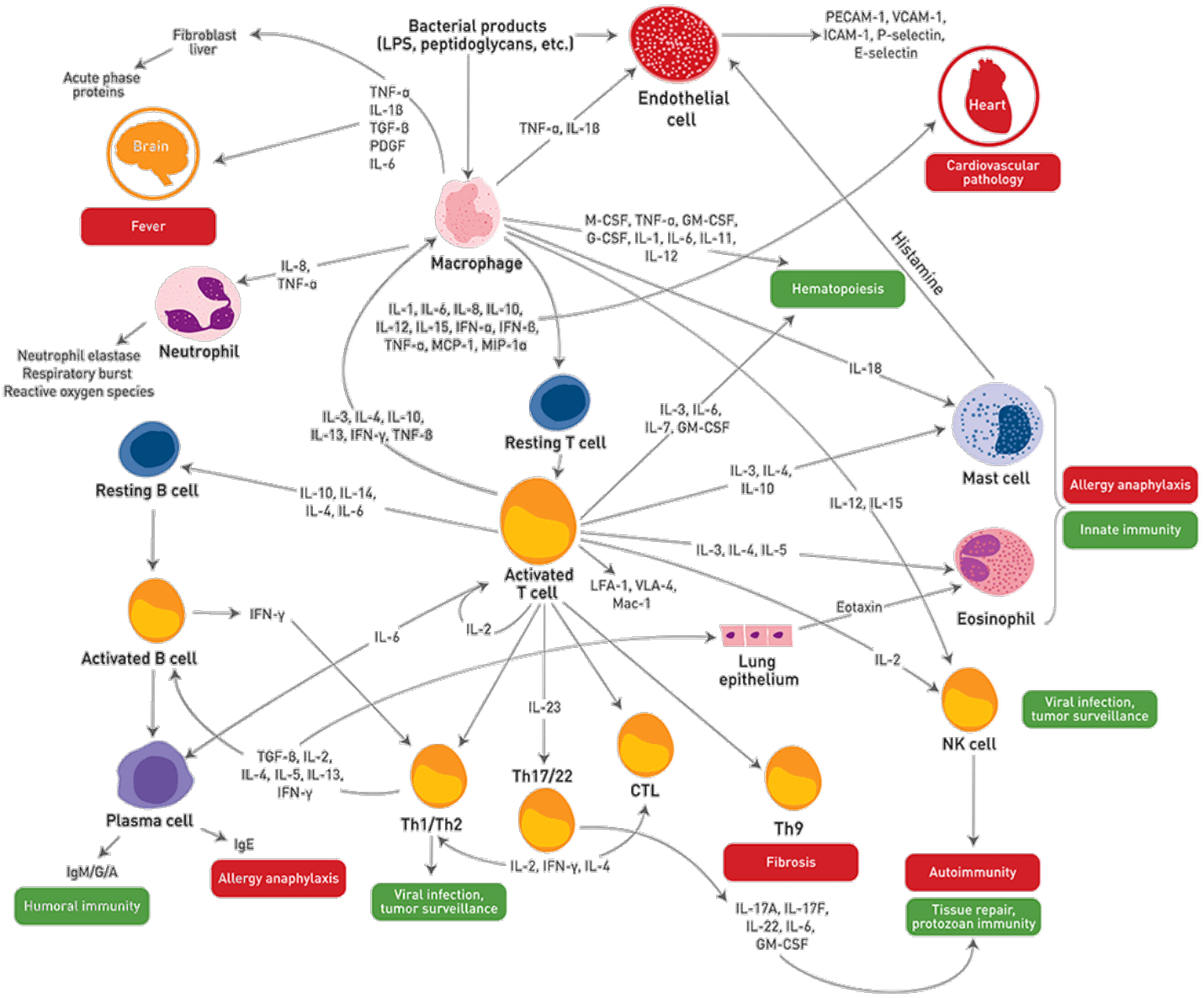


Multiple sclerosis

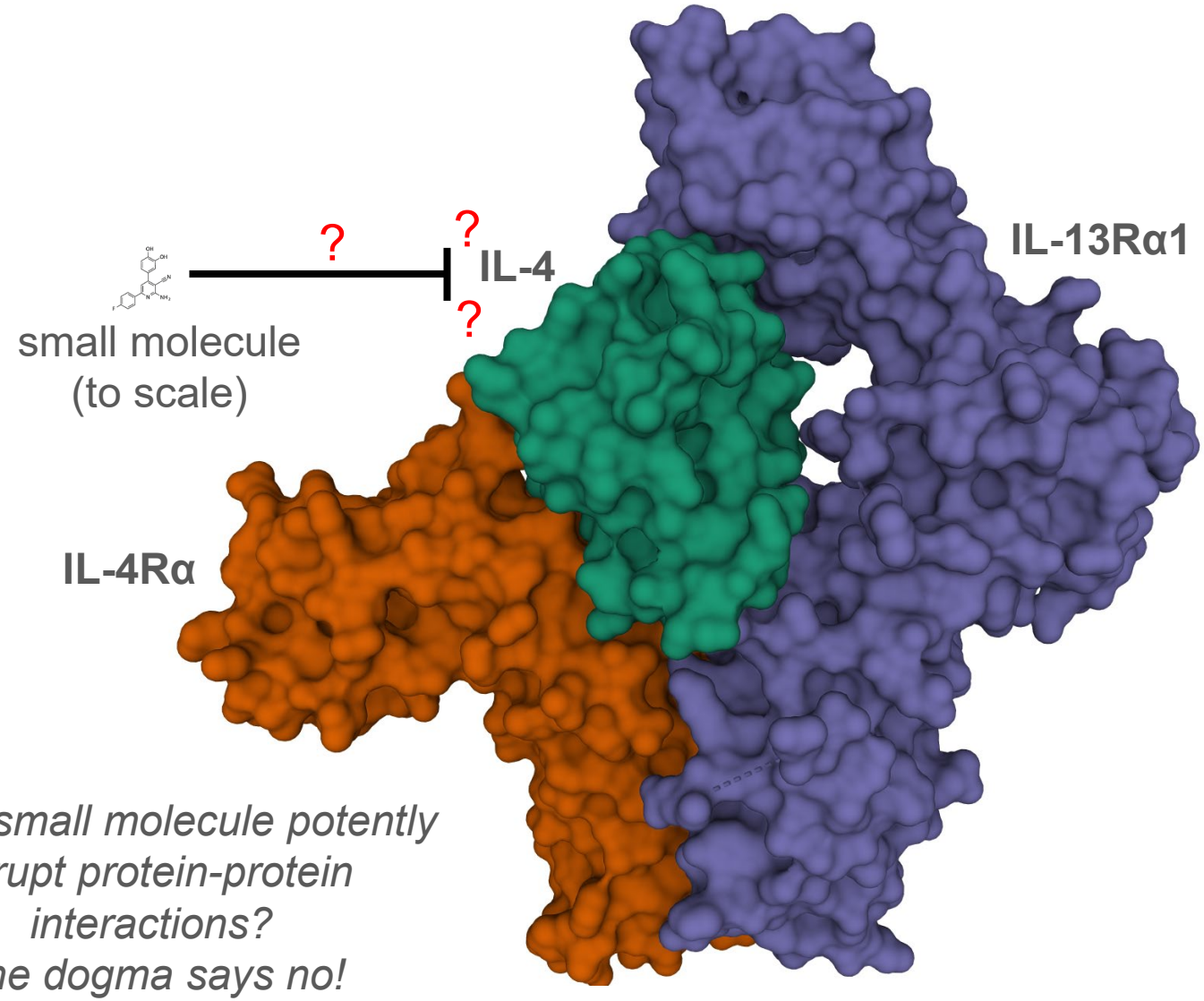
Cytokines drive the full spectrum of immune-mediated disorders



Cytokines drive the full spectrum of immune-mediated disorders



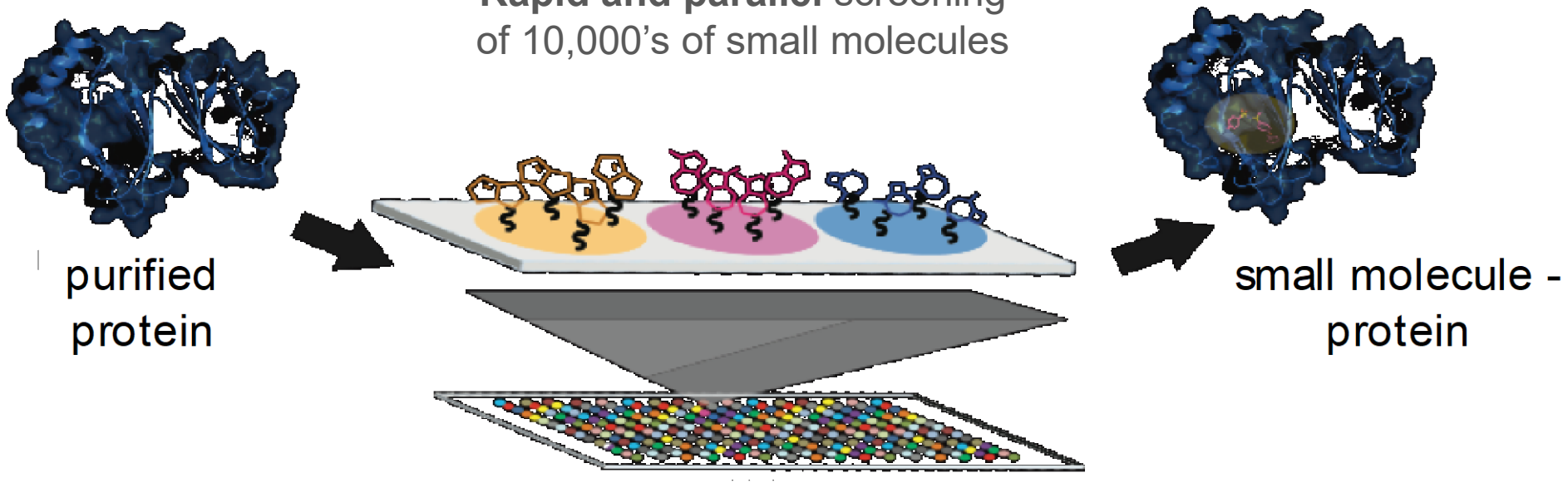
Traditionally it has been challenging for small molecules to interfere with cytokine activity



Can a small molecule potently disrupt protein-protein interactions?
The dogma says no!

Using small-molecule microarrays (SMMs) to discover cytokine inhibitors

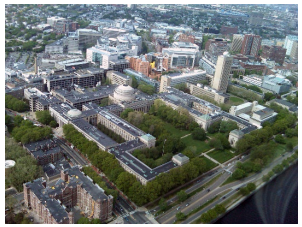
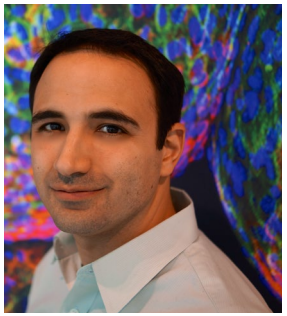
Rapid and parallel screening of 10,000's of small molecules



Cheap and robust assay to identify protein binders

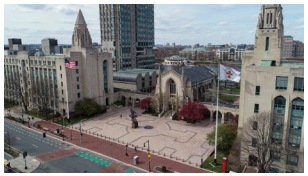
The Path



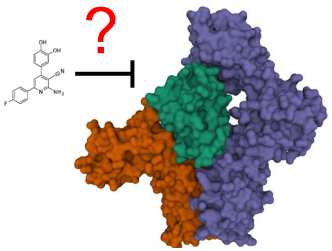




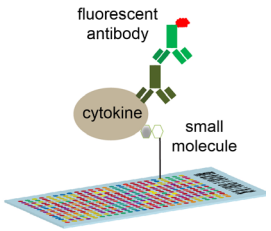
Preceres LLC

sigilon therapeutics — living therapeutics for life™

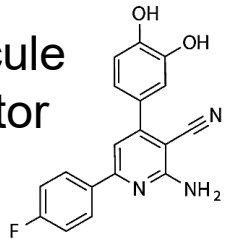


IL-4

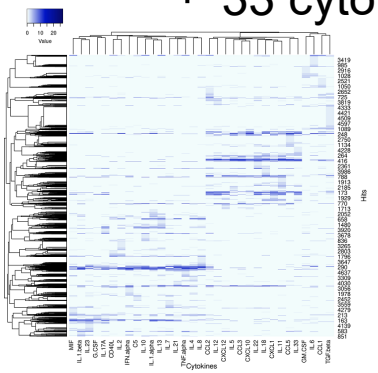


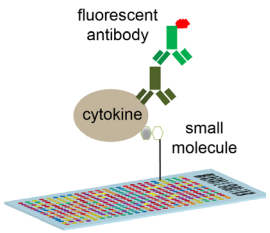


First IL-4 small-molecule (SM) inhibitor



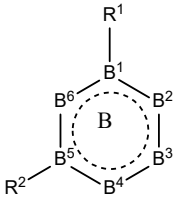
First SM profile map for 33 cytokines





Go big! 33 human cytokines

Defining foundational IP licensing/startup



Google ventures

Johnson & Johnson INNOVATION JLABS

LONGWOOD FUND

FORESITE CAPITAL — Funding the Future of Healthcare

MUBADALA

OMEGA FUNDS

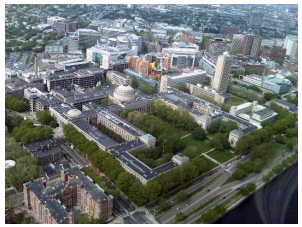
NOVARTIS — NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH

Pfizer

Pledge Therapeutics

Don't Go It Alone

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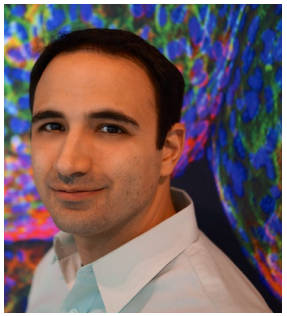
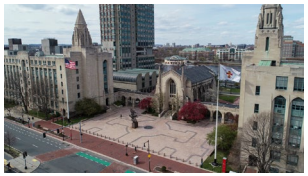

sigilon therapeutics | living therapeutics for life™



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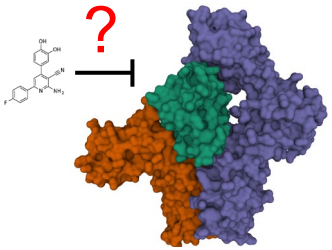

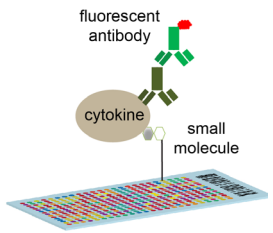

Angela Koehler, MIT

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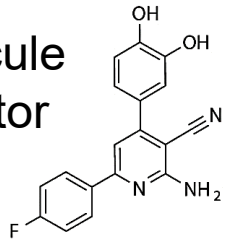

Tom McMurry
BU CTD

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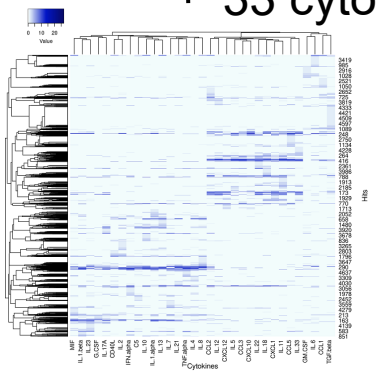
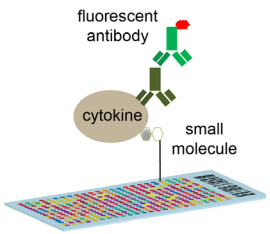


Rana Gupta
BU Ignition



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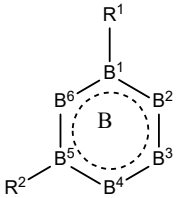

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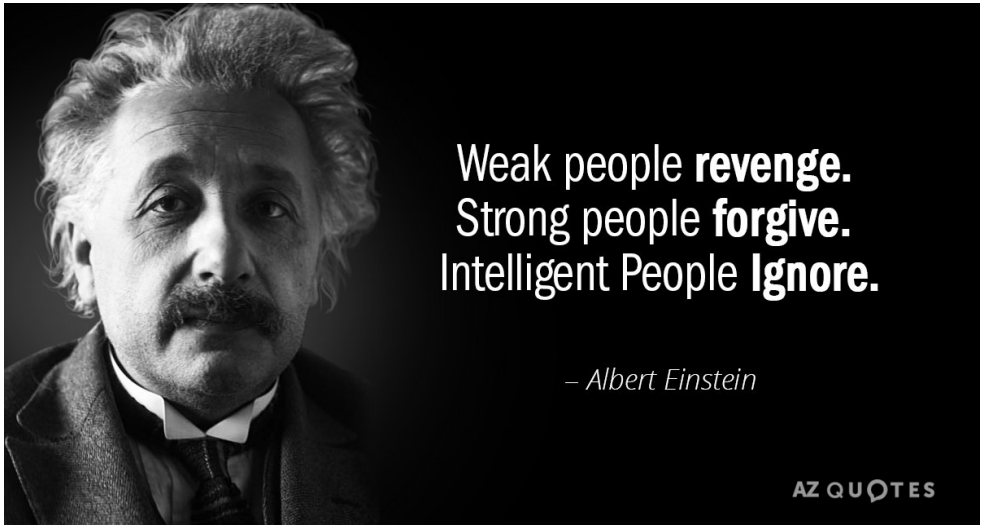
Lesson #1: ***Ignore Dogma***



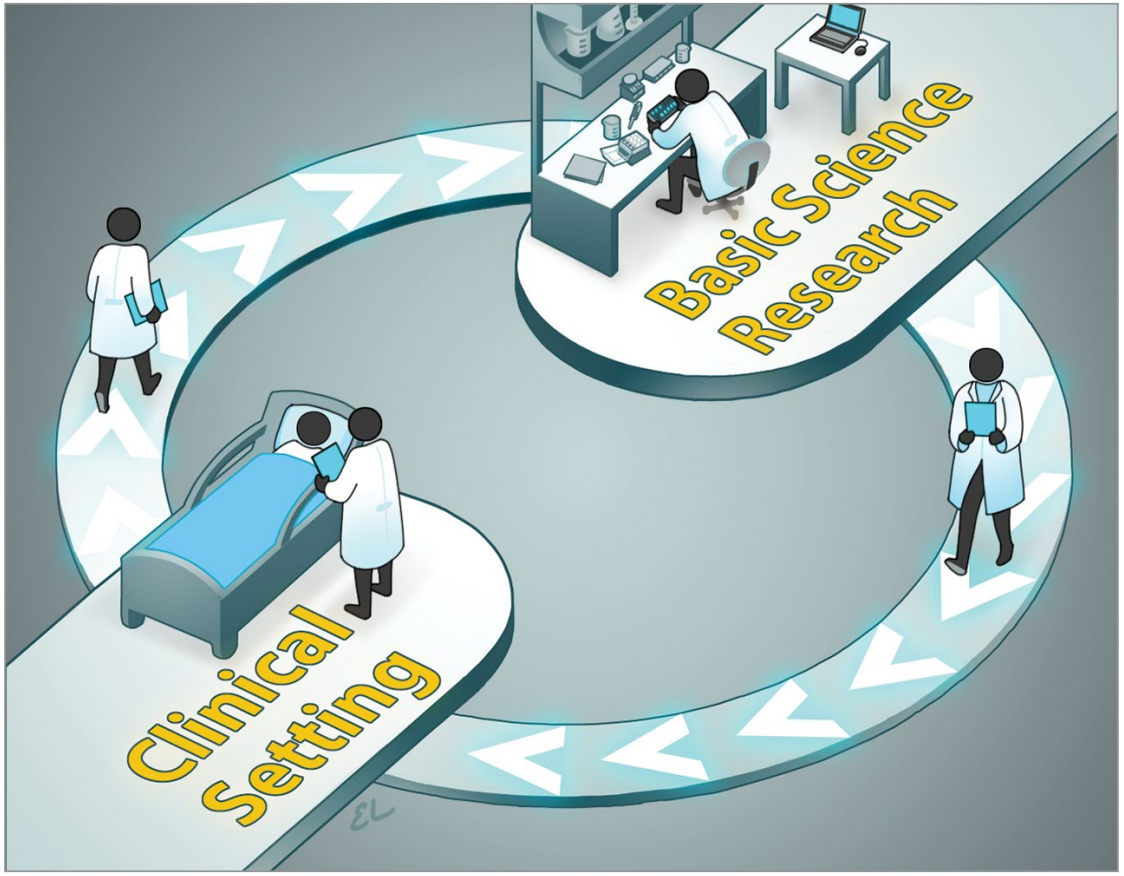
Dogma is a product of our understanding/capabilities of a certain era, it needs to be challenged as we become more capable

Lesson #2: ***Persistence is Rewarded***

"Man, is that salesman persistent."

It can take years to cultivate interest in your inventions

Surprises: ***Bench-side Contributions Matter***



Curiosity… plus a dash of laziness runs the world!

Daniel Cifuentes, Ph.D.
Department of Biochemistry

BOSTON UNIVERSITY

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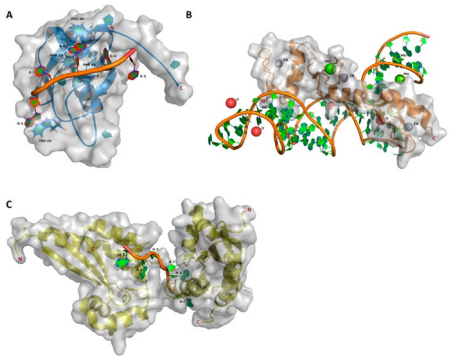
I was born, raised and PhD'ed in Barcelona…

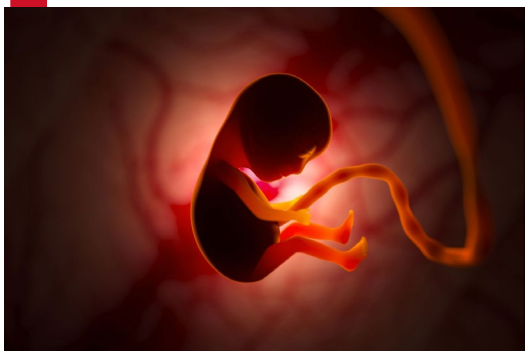
2008 postdoc work:

Revealing all the RNA-binding proteins (RBPs) left me with 2 questions…

> 1500
RNA-binding proteins

1. What is RNA/protein interactions' role?





RNA's role
in regulating embryo blueprint

2.- How we determine and modulate RBPs?

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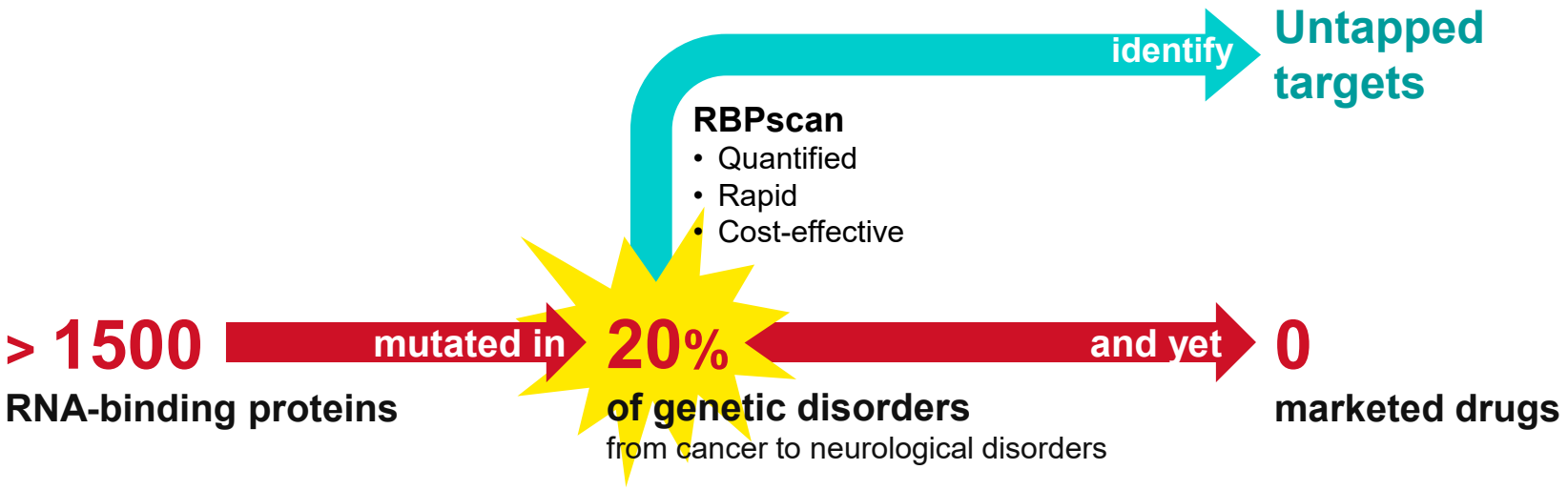
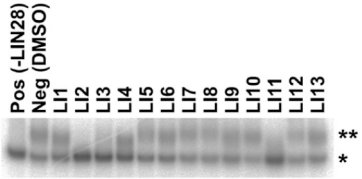


Laziness (+ postdoc Dmitry) move the world!

How can we make this easier???

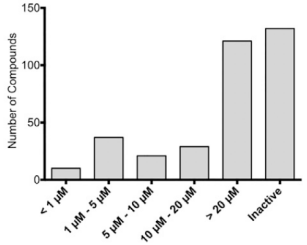
1

Does it not kill cells?



2

Can we validate the results?

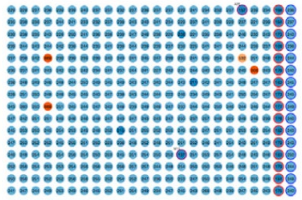


42

Does it disrupt with high affinity?

350

Do any candidates interact with the protein?



101,017

Laziness (+ postdoc Dmitry) move the world!

Untapped targets

1

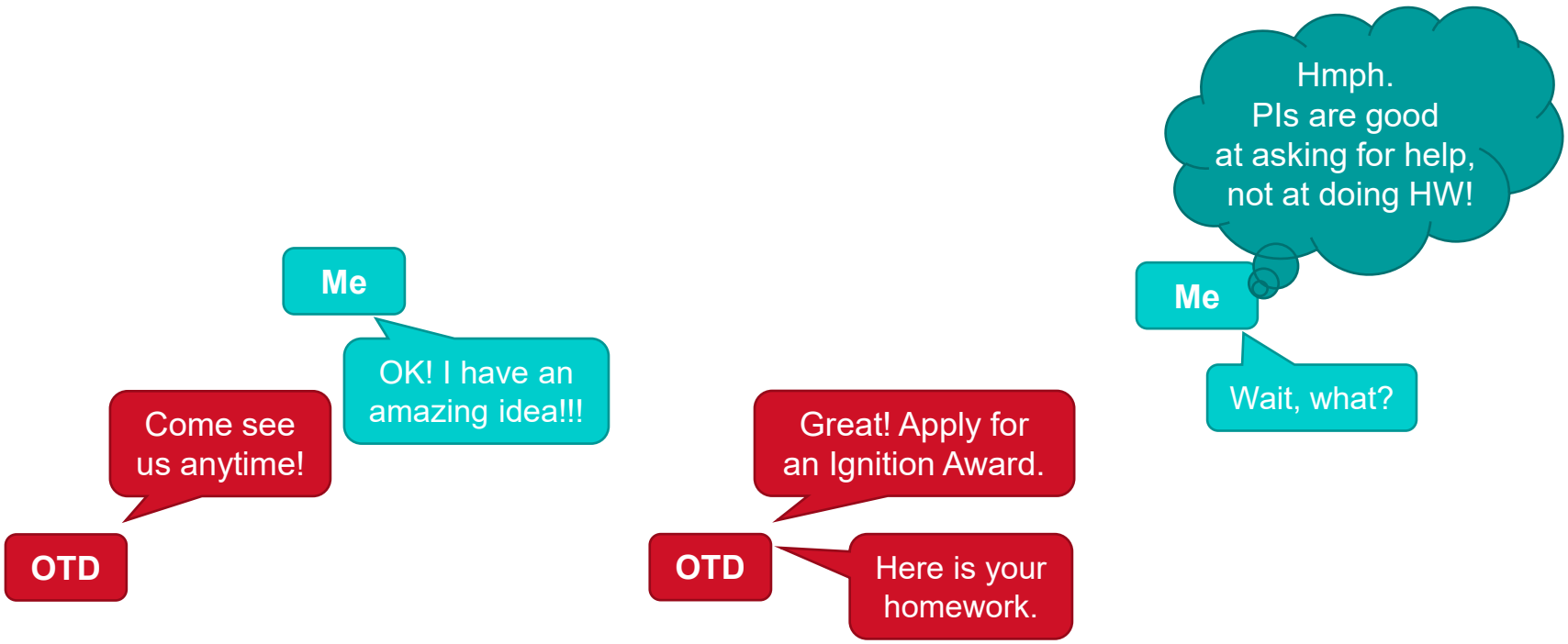
Does it not kill cells?

2

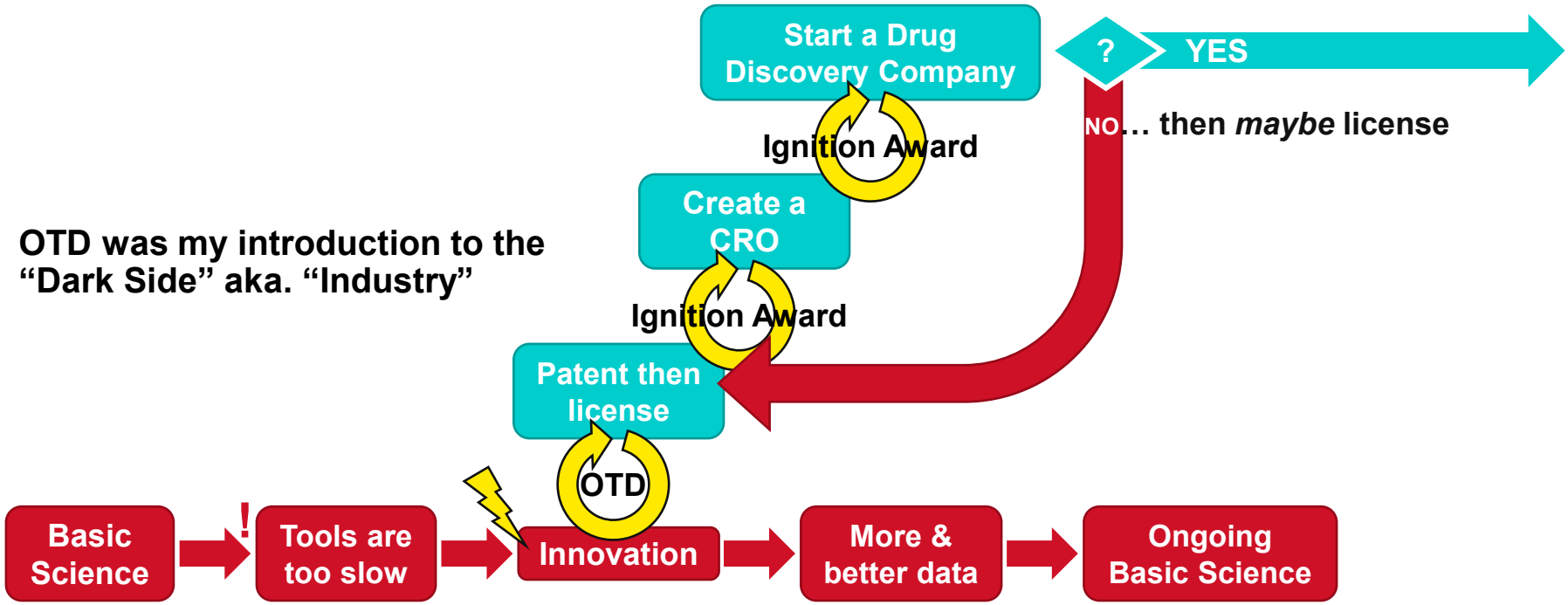
Do any candidates **reliably disrupt** the protein with **high affinity**?

101,017

Our innovation can transform an industry… Time to visit OTD

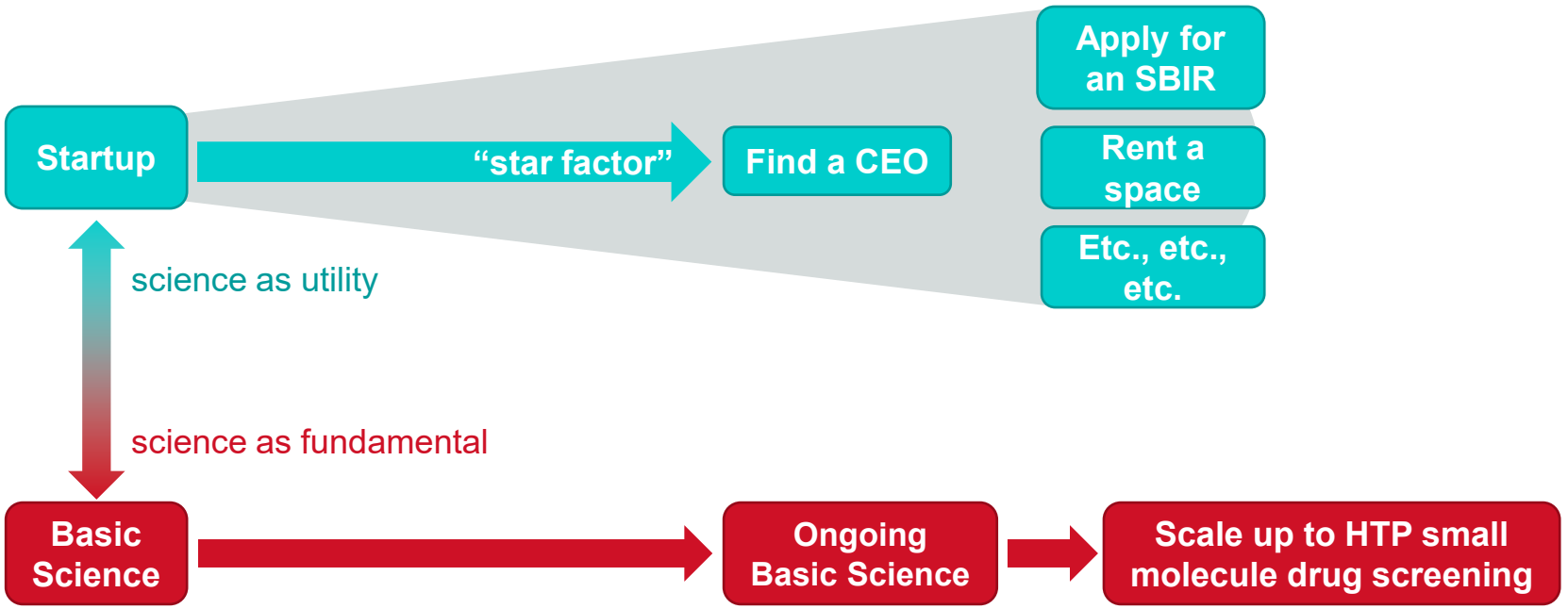


My evolution from researcher to researcher *and* entrepreneur



OTD was my introduction to the "Dark Side" aka. "Industry"

So many more opportunities for surprises



Making conversion of iPSC to T cells a clinical reality

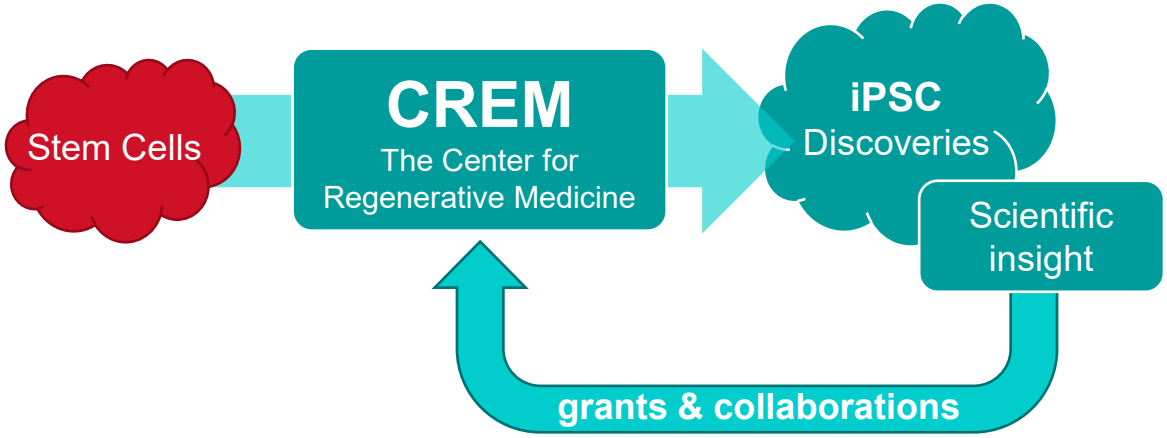
Gustavo Mostoslavsky, Ph.D.
Professor of Medicine and Microbiology
Co-Director and Founder Center for Regenerative Medicine (CReM)
Department of Medicine, BU School of Medicine

BOSTON UNIVERSITY

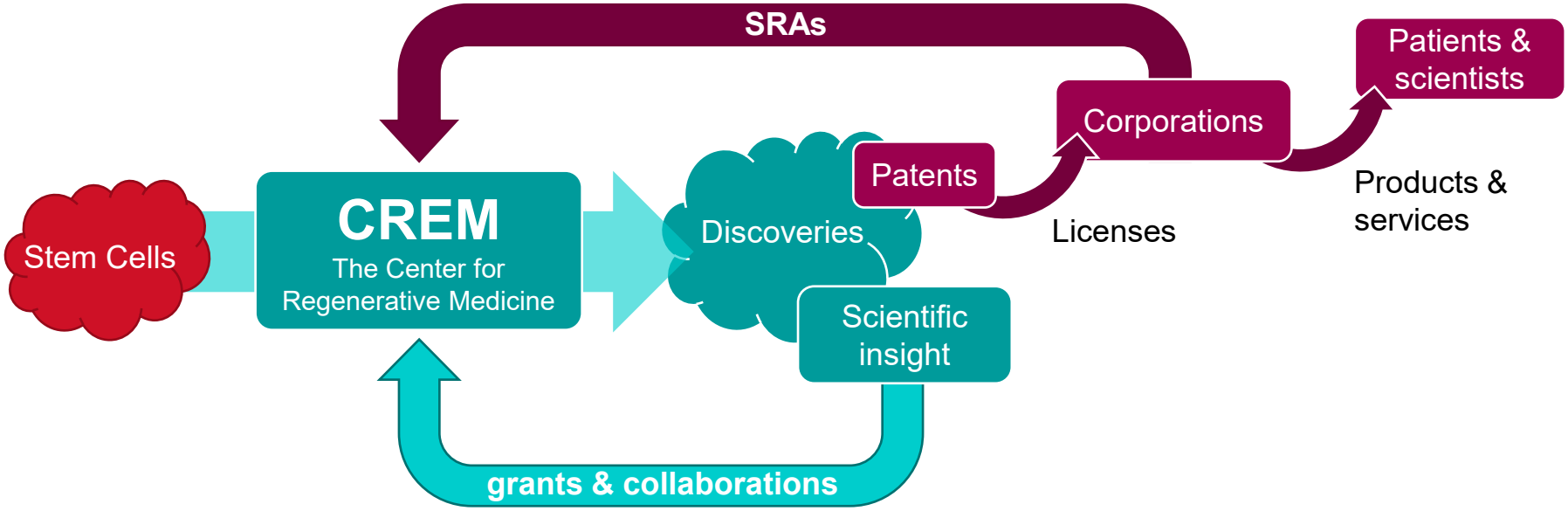
Boston University Office of Research

CAR-T: exciting approach to cancer & autoimmune disease (but expensive & slow)

CREM:
The right tools and the right place for *in-depth studies of how stem cells work*



CREM:
The right tools and the right place for *bringing stem cell discoveries to patients*



A T cell inspired therapeutic dream:
Much cheaper and more broadly applicable CAR-T therapies

Dar Heinze
MD PhD

Develop iPSCs

- Renewable
- Specific
- Safe
- Off-the-shelf
- CARs/ TCRs

Study iT cells

- Model disease
- Produce
  - T cells
  - NK cells

Cancer immunotherapy

- CD8 T cells
- CD4 T cells (some)

Induce tolerance

Reduce autoimmunity

- T regulatory cells

I needed to make a decision: Run my academic lab or start a company?

DID NOT want

- The huge effort to start a company
  - I saw Moderna effort close up
- Have many more resources **BUT** must be focused

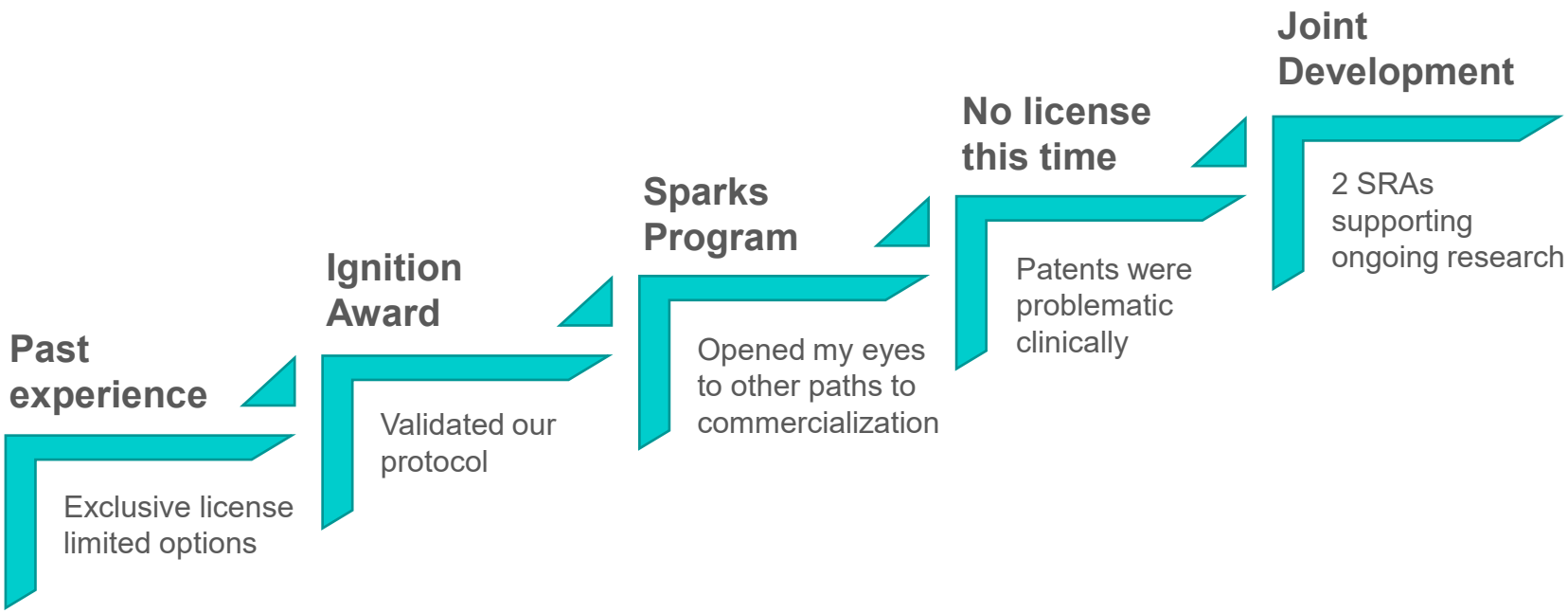
DO want

- To be a professor in academia
- Have limited resources **BUT** freedom to pursue interesting research

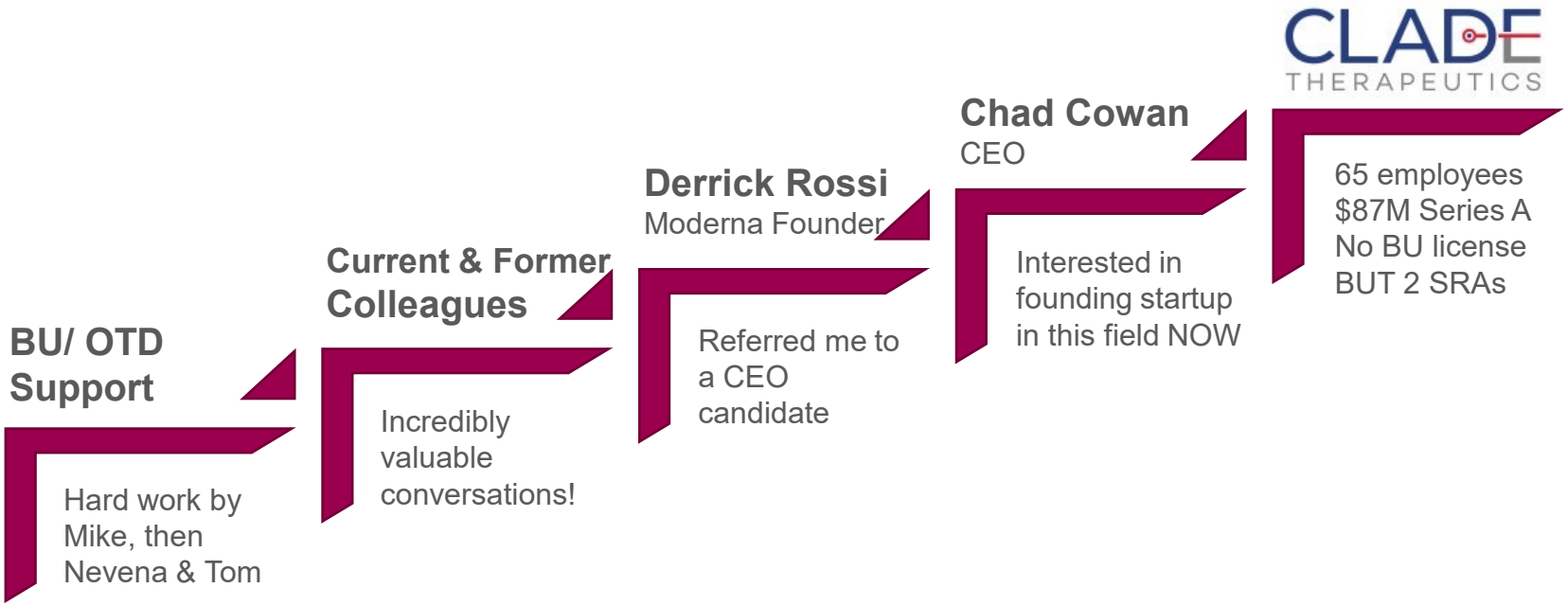
Best of **both** worlds!

Scientific Founder

Scientist ➔ Patent ➔ Company is not the only path!



Get out there: Never be afraid to pick up the phone or send an email



Selective listening in a noisy world

Kamal Sen, Ph.D.
Associate Professor
Department of Biomedical Engineering
College of Engineering

BOSTON UNIVERSITY

Boston University Office of Research

Objective: Transform communication in an increasingly noisy world…

Demand

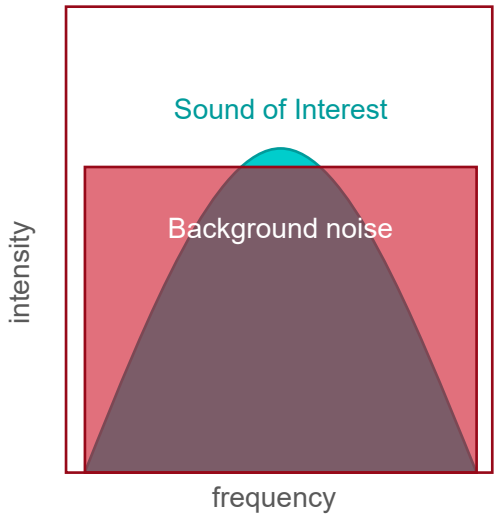
- Hearing impaired
  - Elderly
  - Illness, genetic or injury-triggered loss
- Sound discrimination impaired
  - ADHD
  - Autism spectrum
- Challenging environments
  - Noisy workplaces
  - Noisy social spaces
  - Noisy equipment
  - Faint sounds

Applications

- Listening devices
  - Ear pods
  - Noise-cancelling headphones
  - Smart glasses
  - ~~Hearing aids~~ 

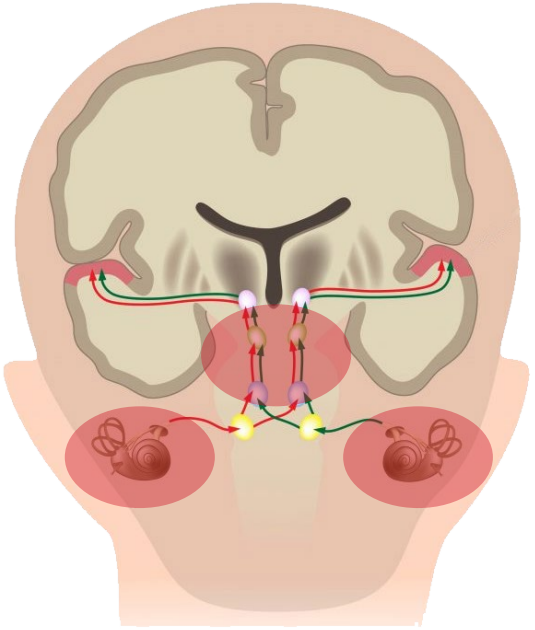
- Human-machine communications
  - Smart speakers
  - Digital assistants

State of the Art: Algorithms focus on processing Sounds in Isolation

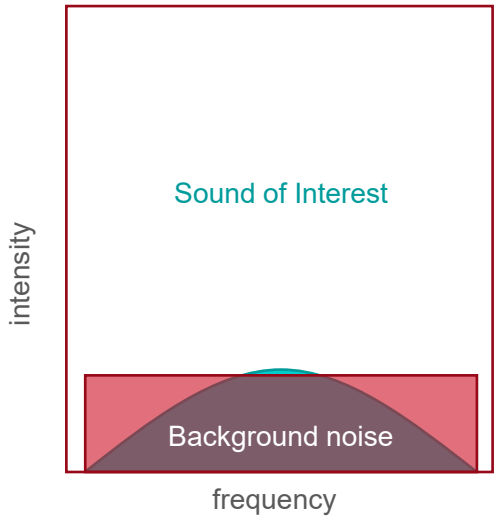


Location Extraction

Frequency Extraction



State of the Art: Noise cancellation without discrimination

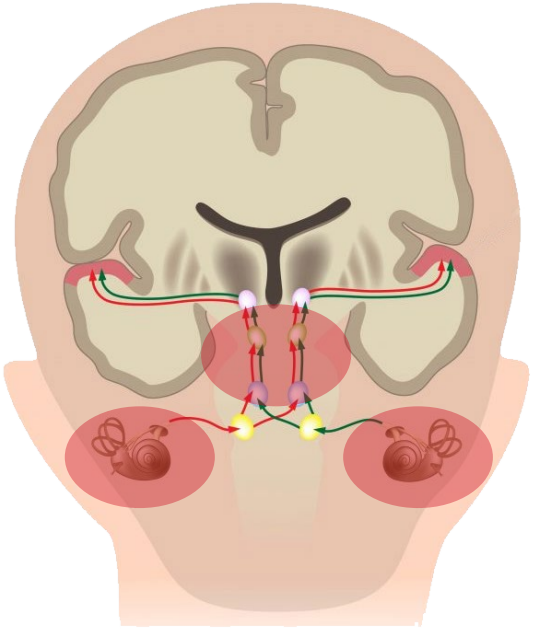


What users get:

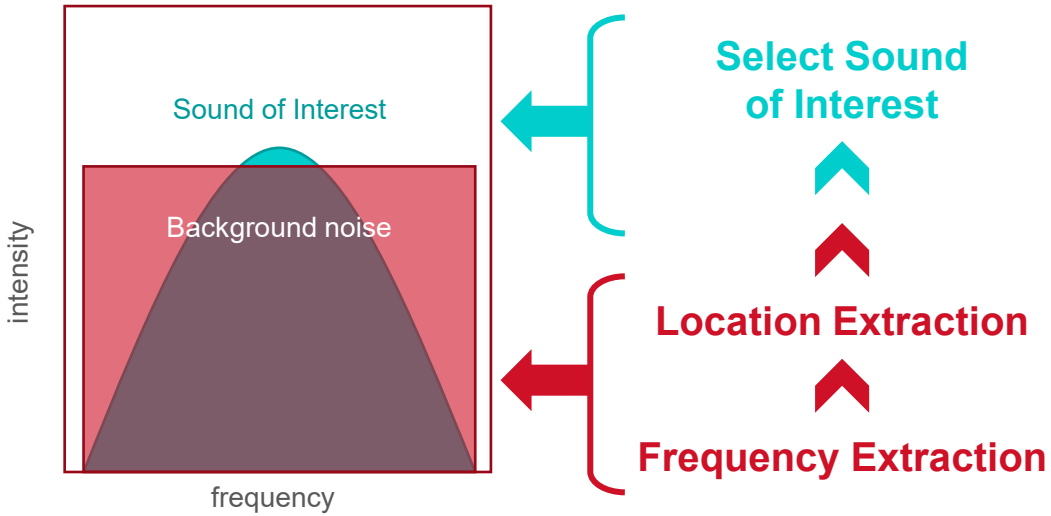
Noise Cancellation BUT Poor Discrimination

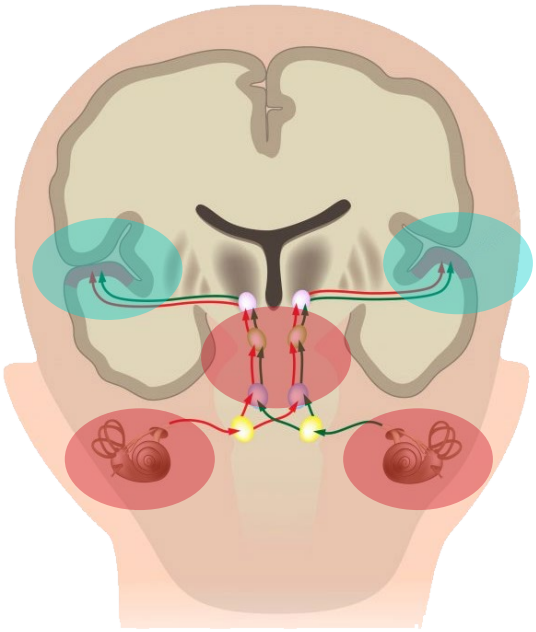
Location Extraction

Frequency Extraction

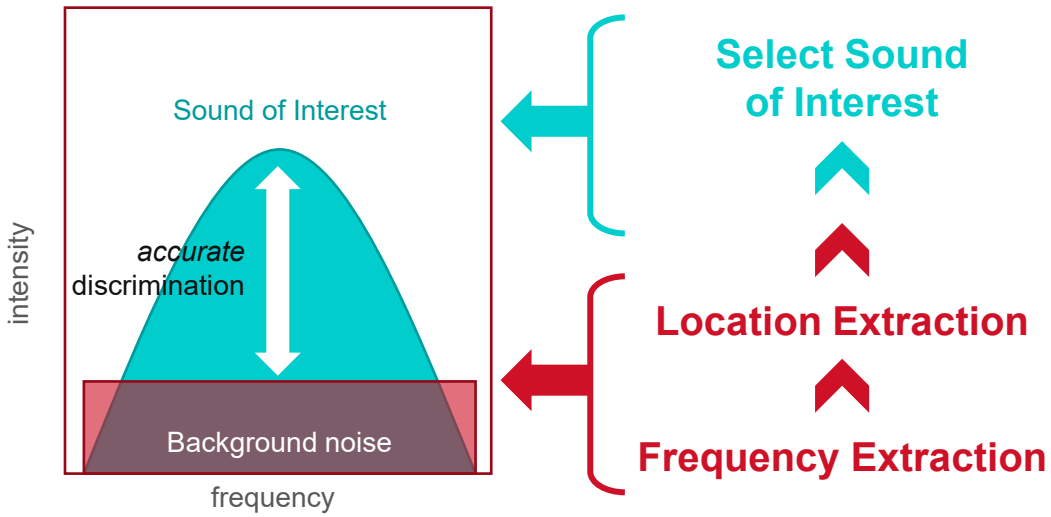


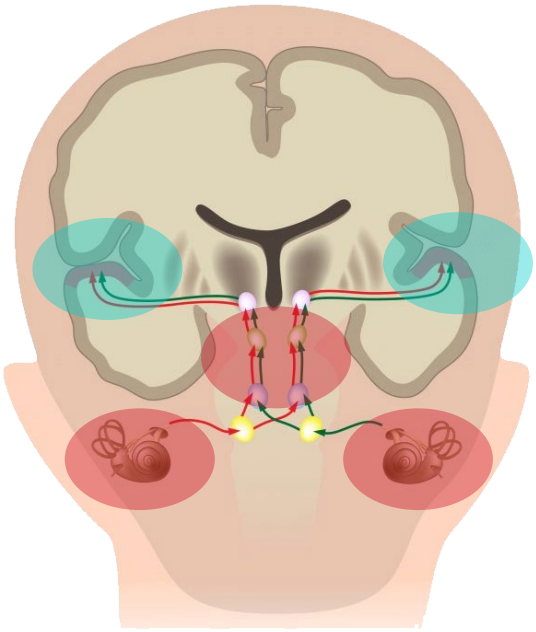
Discovery at BU: Healthy brains excel at Selective Listening





Discovery at BU: Healthy brains excel at Selective Listening





Development at BU: Algorithms that support Selective Listening

What users want:
Accurate Discrimination

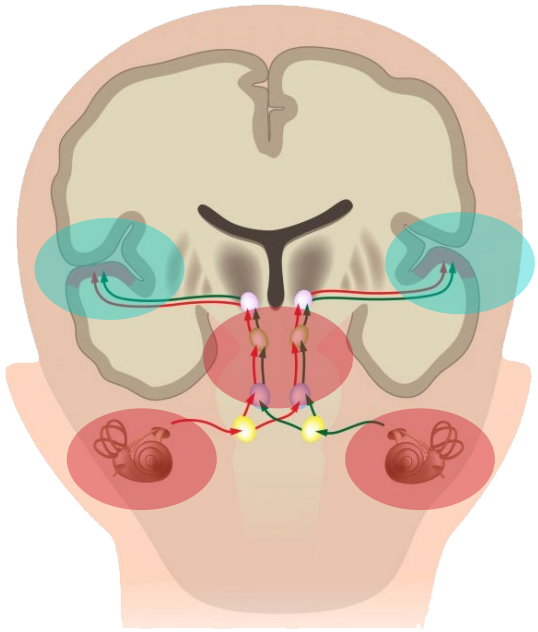
The Natural Sounds & Neural Coding Lab

Select Sound of Interest

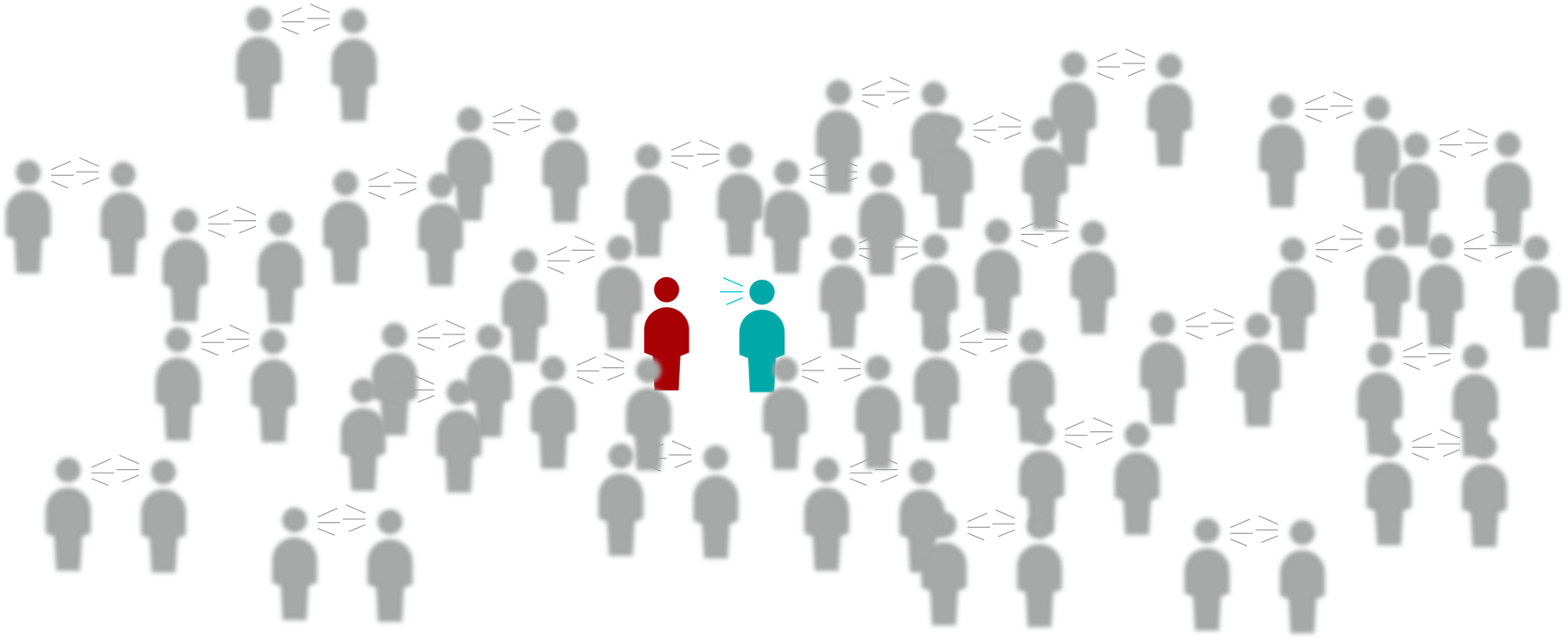
Existing algorithms
(beamformer, neural net)

Location Extraction

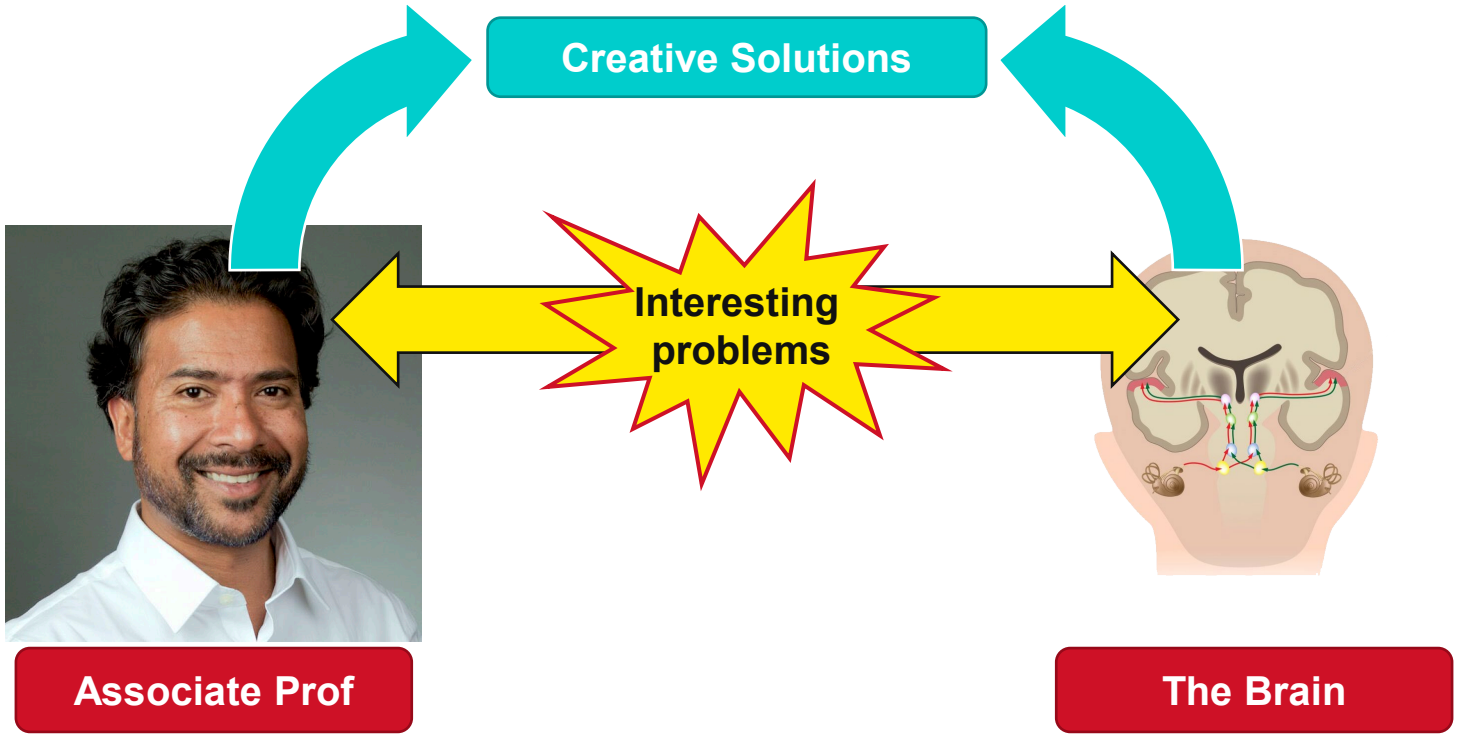
Frequency Extraction



The power of the demo



I love my “day” job: The lab & research are who I am.



Let companies worry about commercialization… but must find right company!

People and programs have been invaluable in acquiring licensee prospects

Collaborators
- Hard work of many graduate students
- Feedback from BU Hearing Research Center

OTD
- Expertise in licensing and IP, biz dev (Rana), pitching (Linda)
- Funding from an Ignition Award

Catalyst
- Revealed that hearing aid companies suffer from NIH
- Generated list of licensee prospects

MAP Program
- Provided additional market research
- Identified new opportunities

Investors
- Invasion of the Equity Investors! (Johannes and Russ)
- “You need a razzle-dazzle demo!”

License strategy is key

1. Collaborating with OTD to structure license agreements
2. Developing a licensing strategy as a pathway to multiple industries (Misty!)
3. Leveraging current understanding to feed into future versions and better technologies

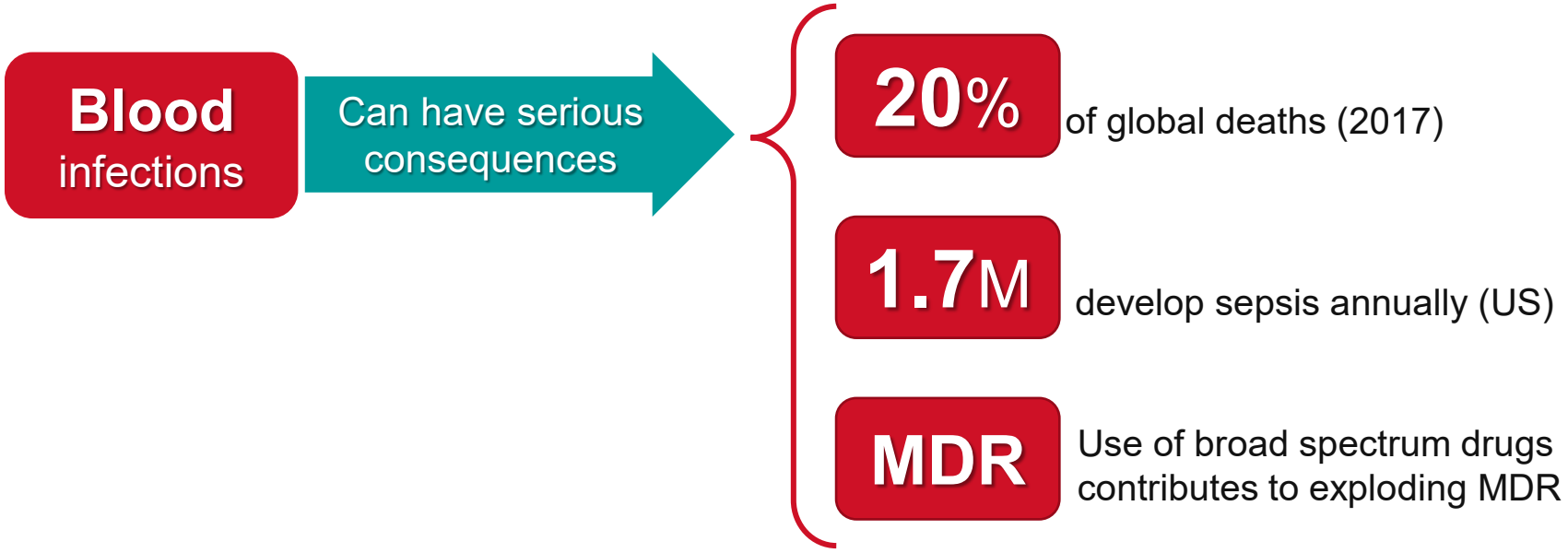
Translating post-9/11 concerns to life-saving rapid selection of impactful antibiotics

Lawrence Ziegler
Professor of Chemistry, CAS
Photonics Center
Boston University

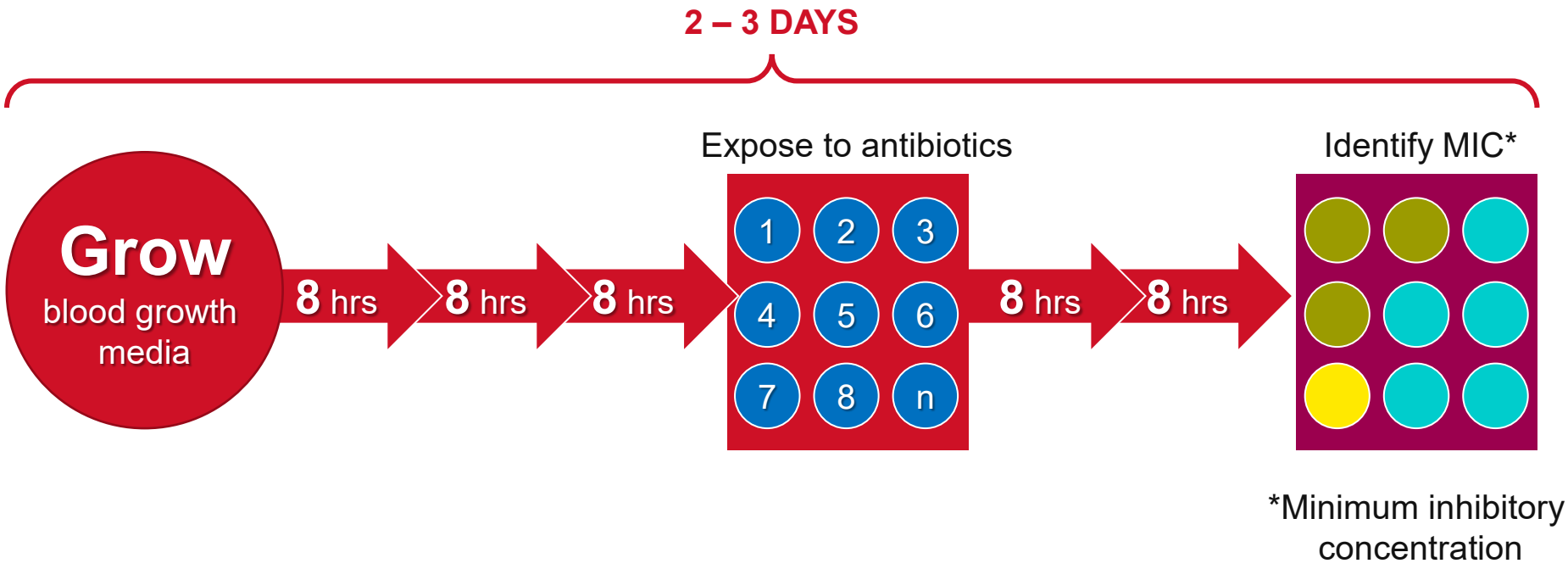
BOSTON UNIVERSITY

Boston University Office of Research

Antibiotic Susceptibility Testing (AST): Identifying the most effective drug



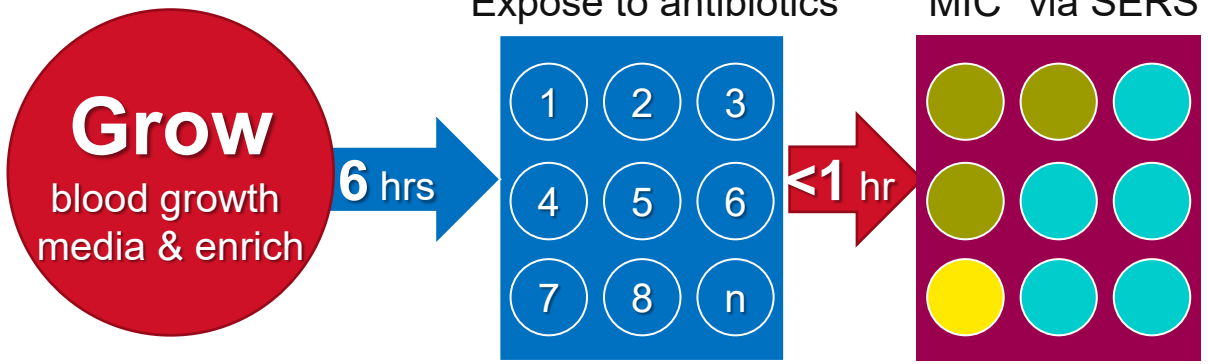
Gold standard AST depends on several stages of bacterial growth (slow).



Our SERS optical technology has (1) extremely high sensitivity to key metabolites, (2) bacterial responses to drugs rapidly alter metabolic rates

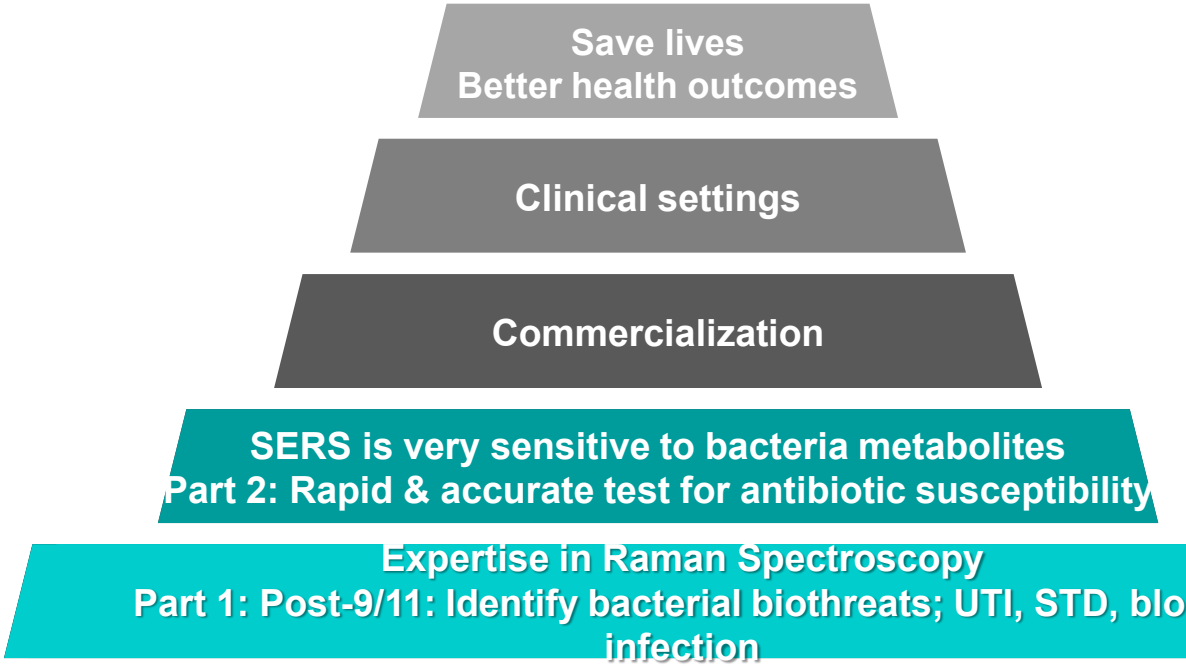
*Surface Enhanced Raman Spectroscopy

< 7 HOURS



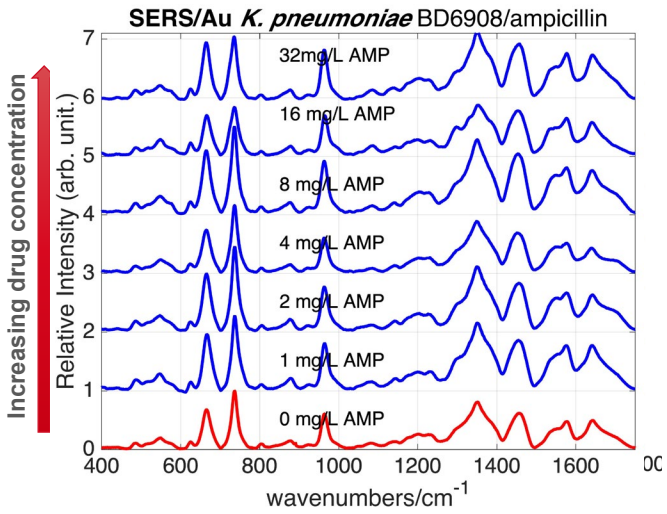
*Minimum inhibitory concentration
Via SERS sensing of rapid bacterial responses

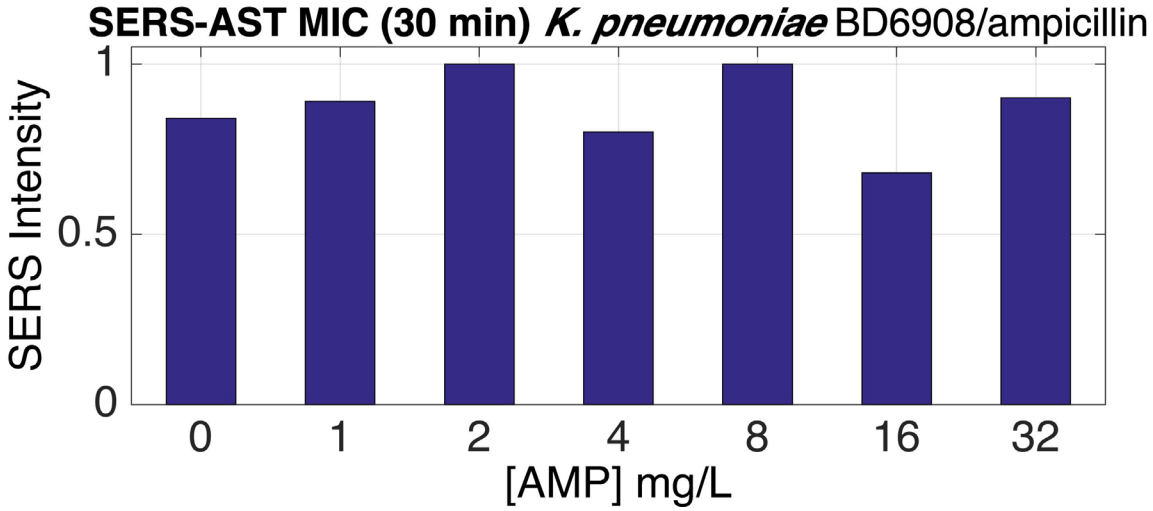
I could never have predicted our innovation from where we started



- NIH
- DOD funding
- NSF, NIH, BD

Ultrafast AST: the most impactful application for this technology



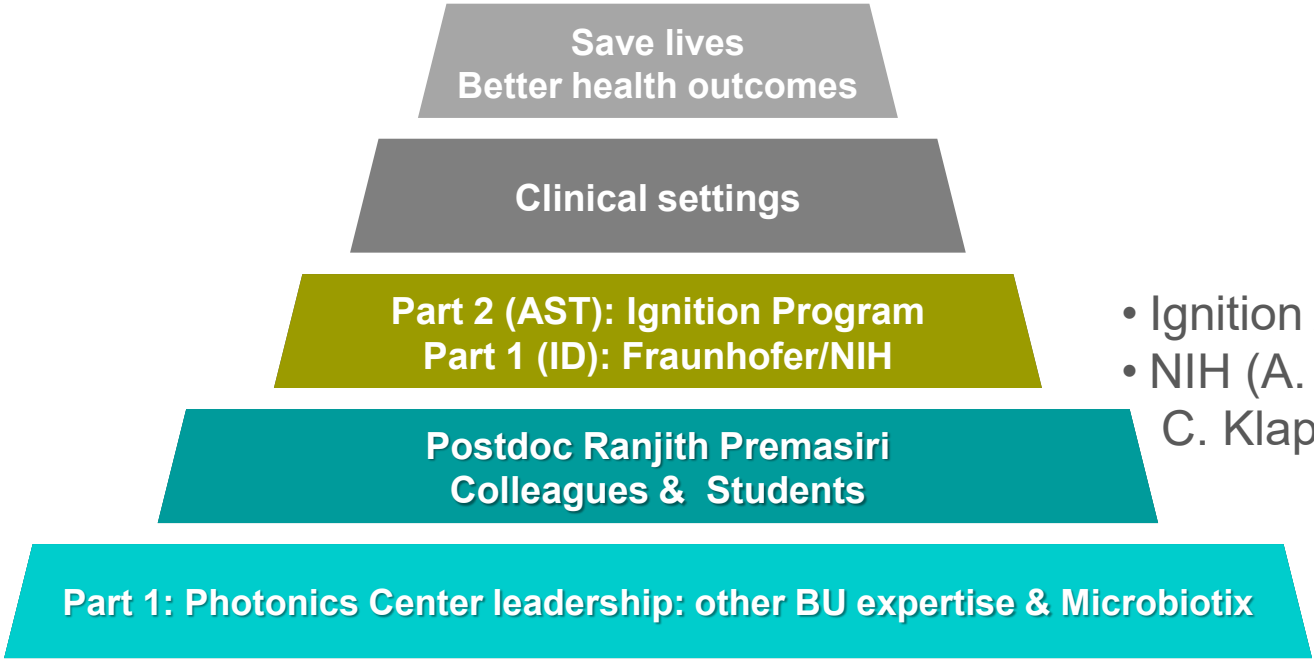


30x faster than growth: Fastest phenotypic AST

Discovery

- The best discoveries are **things I never predicted**
- The talent is in **recognizing the value** in front of you
- **Fundamental understanding** is crucial

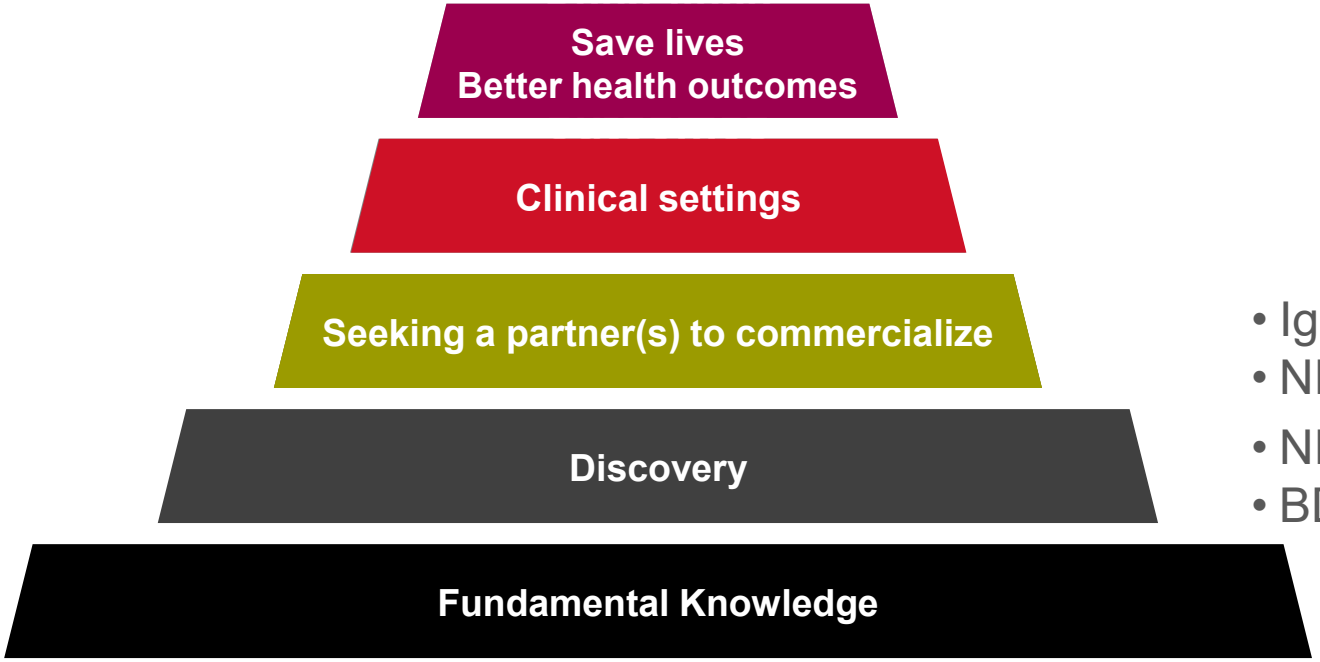
Support from others inside BU and out



- Ignition Award
- NIH (A. Sauer-Budge, C. Klapperich, J. Lee)

- DOD, NIH,
- NSF, BD

Partner or license to get to market quickly



- Ignition Award
- NIH
- NIH, NSF
- BD
- DOD

There has to be more that we can do…

from **son**

to **physical therapist**

to (wannabe) **entrepreneur**

Lou Awad, PT, DPT, PhD
Assistant Professor
Department of Physical Therapy
College of Health and Rehabilitation Sciences: Sargent
Boston University

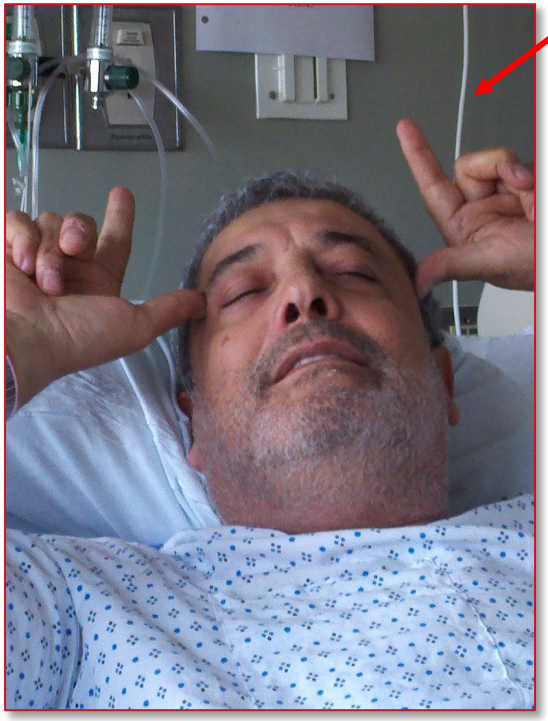
Who are you – how do you think of yourself?

I'm a faculty member at BU where I run a research lab…

I have my priorities straight

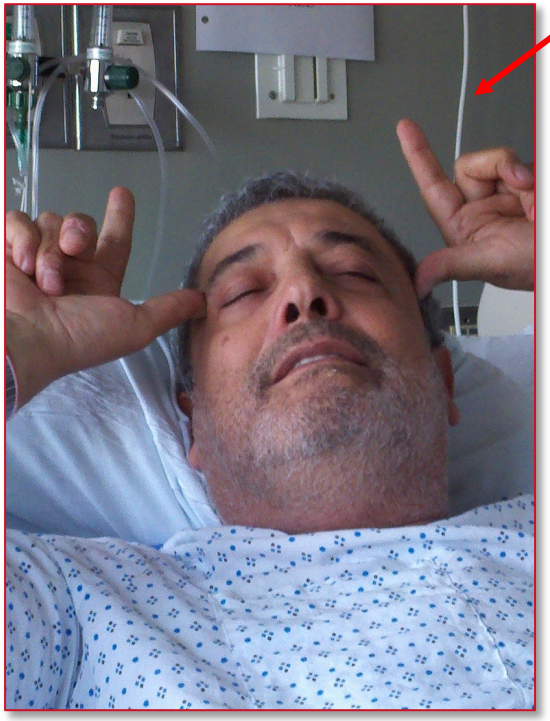
My journey begins with…

Stroke has impacted my family…



There has to be more that we can do…

Stroke has impacted my family…

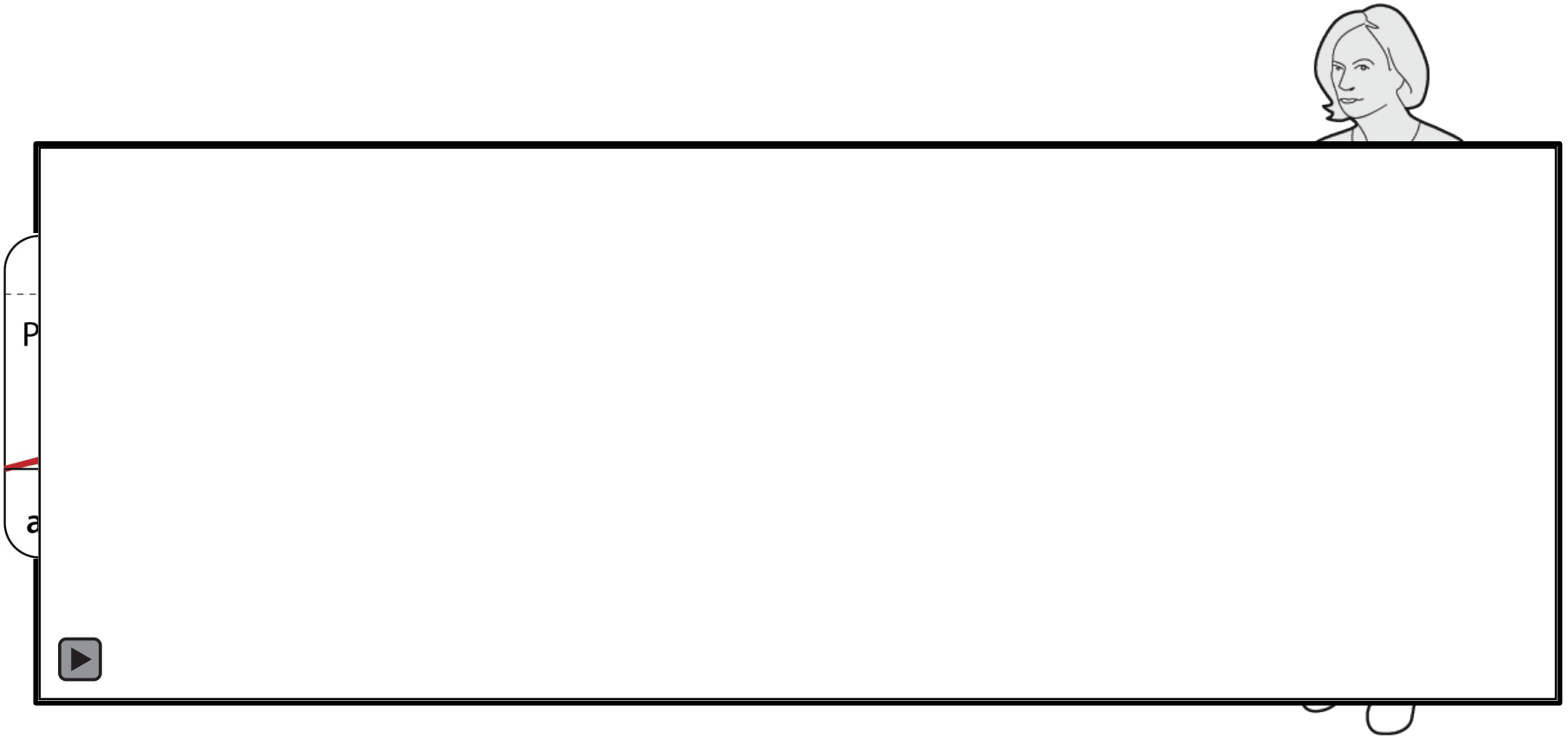


Dad

…10 years later

Uncle

reNeu Neurorecovery Platform will allow us to do more…



Don’t go it alone…lessons from the reNeu journey

FAMILY ⟷ Inspiration & determination

Don’t go it alone…lessons from the reNeu journey

FAMILY ⟷ Inspiration & determination

BUSINESS MENTORS ⟷ Guidance & early funding

Don’t go it alone…lessons from the reNeu journey

FAMILY ⟷ Inspiration & determination

BUSINESS MENTORS ⟷ Guidance & early funding

COLLABORATORS ⟷ New knowledge & skills

Physical Therapy

Engineering

Medicine

Industry

Don’t go it alone…lessons from the reNeu journey

FAMILY ⟷ Inspiration & determination

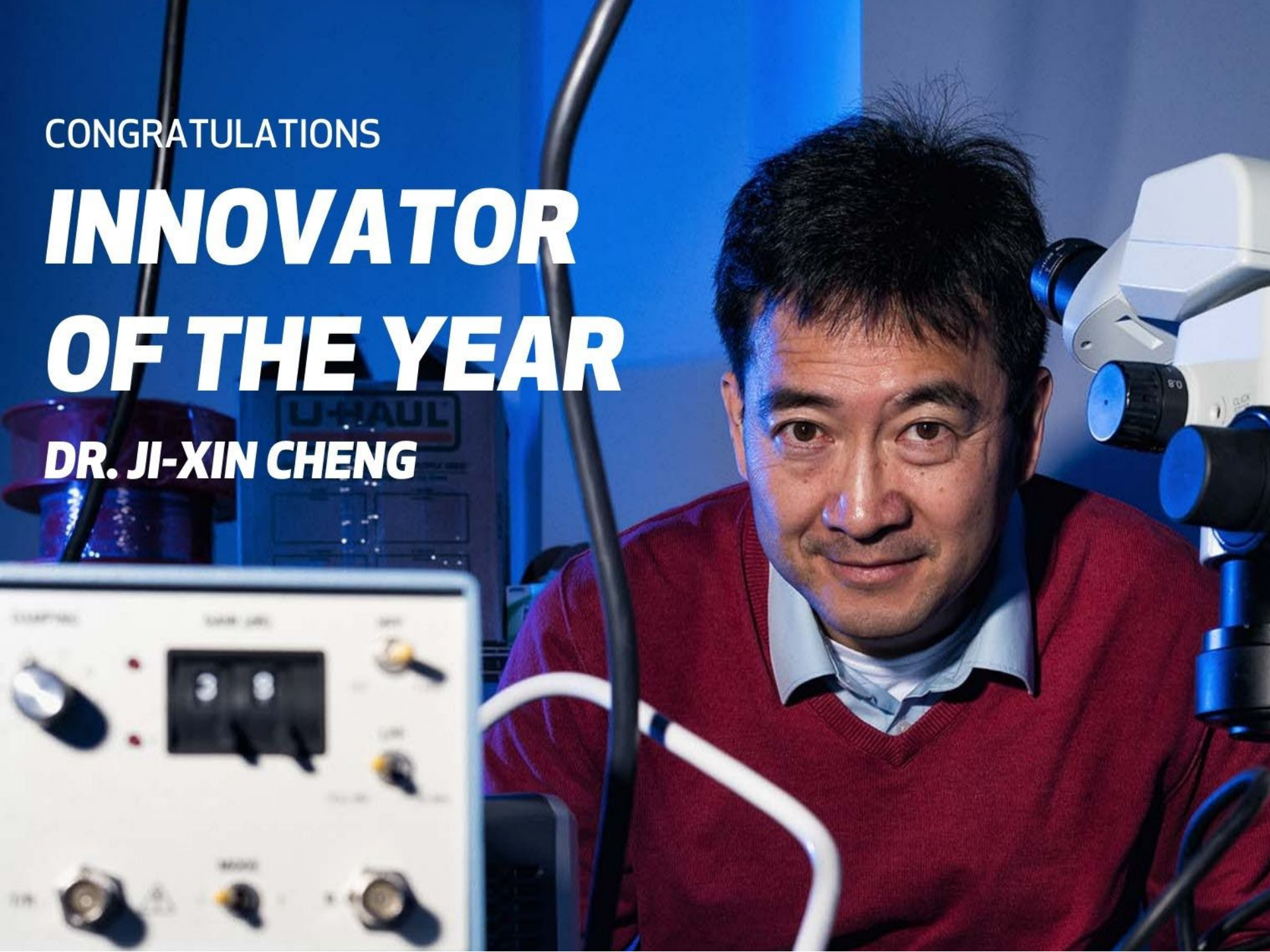
BUSINESS MENTORS ⟷ Guidance & early funding

COLLABORATORS ⟷ Knowledge & skills

TEAMMATES ⟷ Boots on the ground


TELEPHONE
HUDSON
NO 36

Q&A


CONGRATULATIONS
INNOVATOR OF THE YEAR
DR. JI-XIN CHENG

How continuous innovation (继新, ji-xin) happens

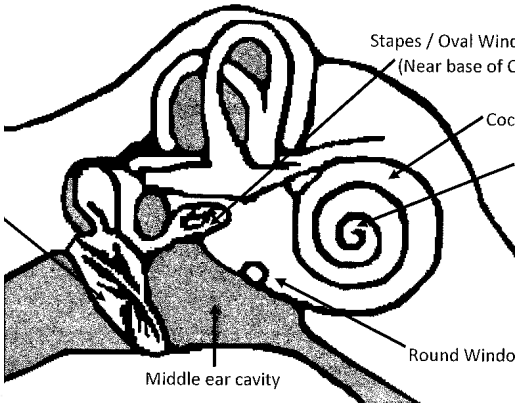
Story 1: Entering a new discipline --- biomedical engineering

"I had no idea what is biomedical engineering. I asked my postdoc advisor at Harvard and he told me that biomedical engineers make artificial bones."

"I started my own career at Purdue. It turns out to be a very good decision, as I was able to bring my spectroscopy expertise to the engineering discipline."

Story 2: Innovation from teaching

RLC model of cochlea



BME305: Lab 9
2011

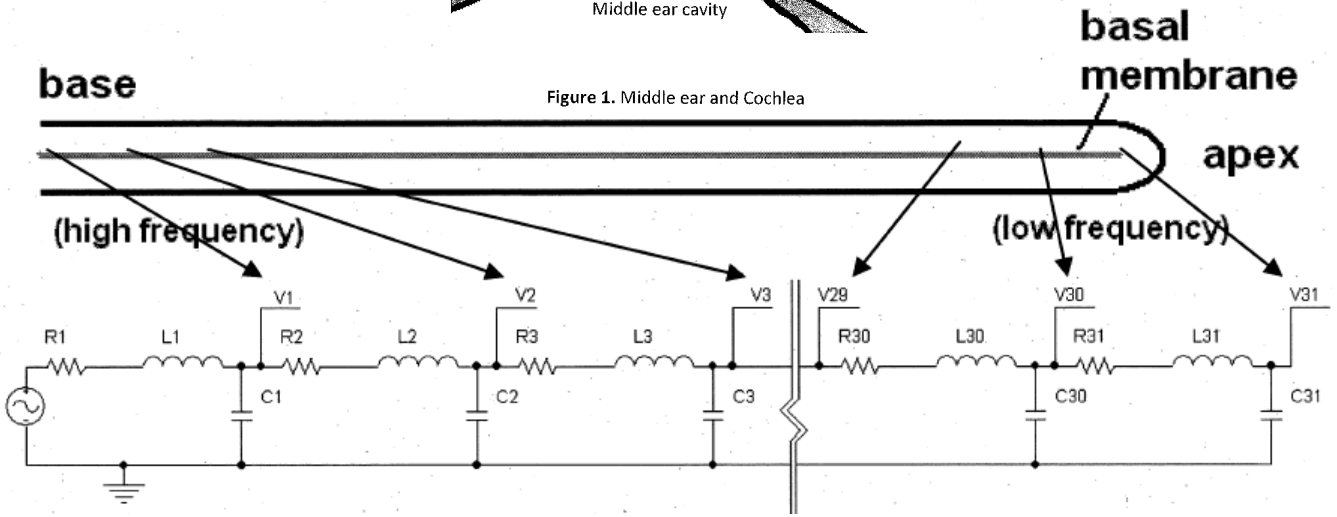


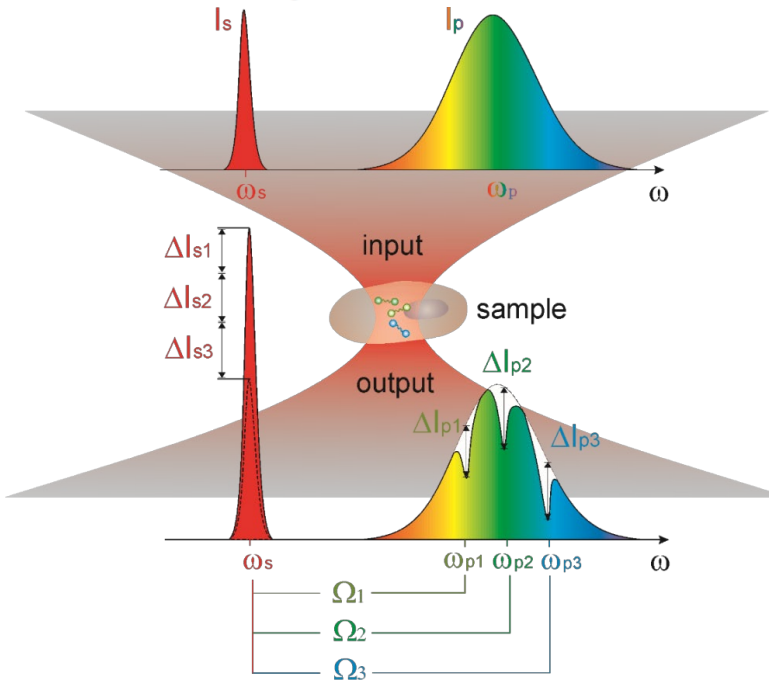
Figure 1. Middle ear and Cochlea

Light: Science & Applications (2015) 4, e265; doi:10.1038/lsa.2015.38

www.nature.com/lsa

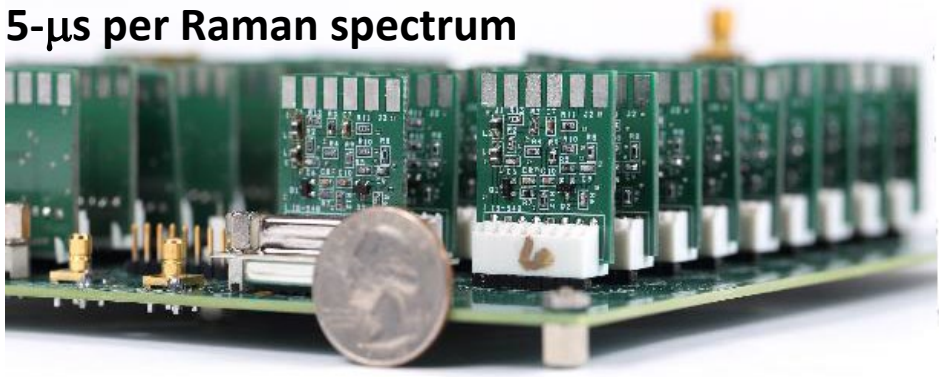
Microsecond scale vibrational spectroscopic imaging by multiplex stimulated Raman scattering microscopy

Chien-Sheng Liao[1,*], Mikhail N Slipchenko[1,*], Ping Wang[1,*], Junjie Li[2], Seung-Young Lee[1], Robert A Oglesbee[3] and Ji-Xin Cheng[1,3]



32-channel tuned amplifier

5-μs per Raman spectrum

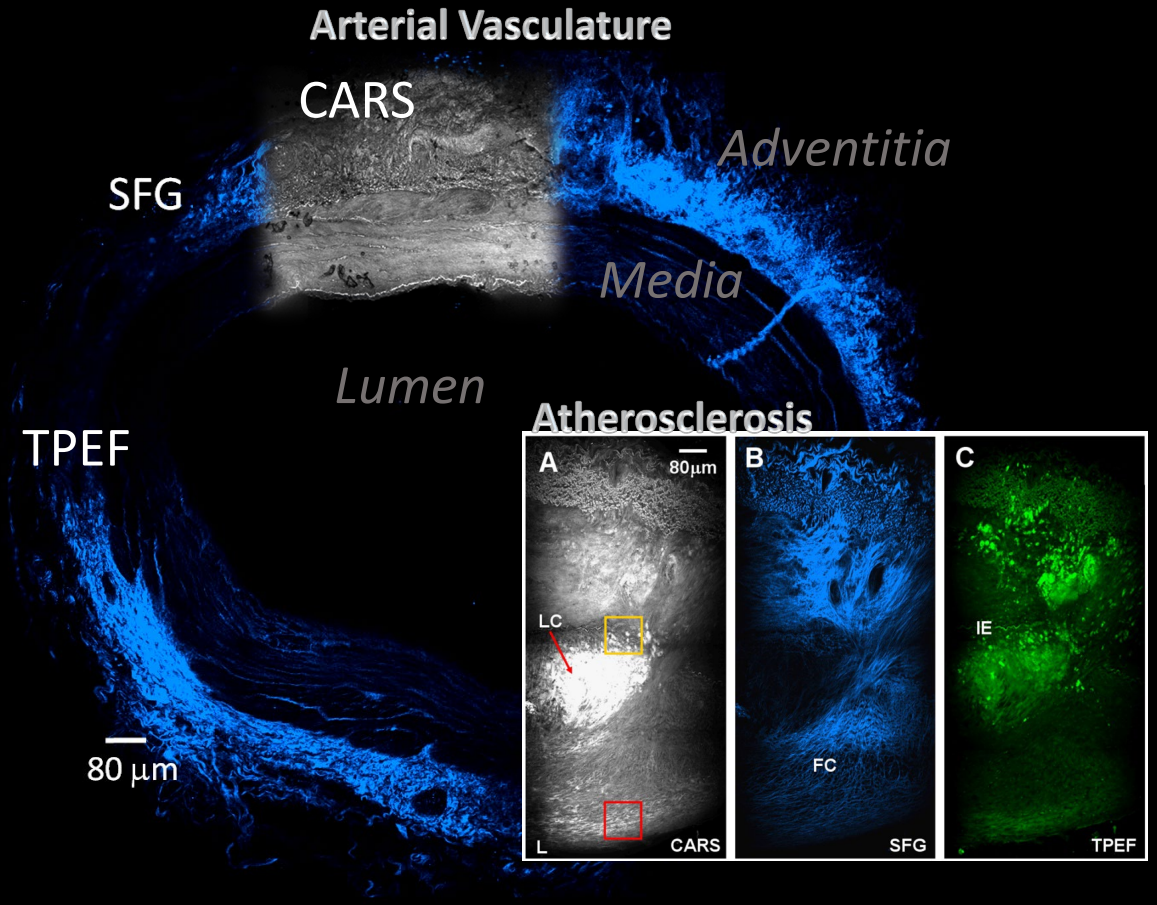


Top Story in 2015, Biophotonics Magazine

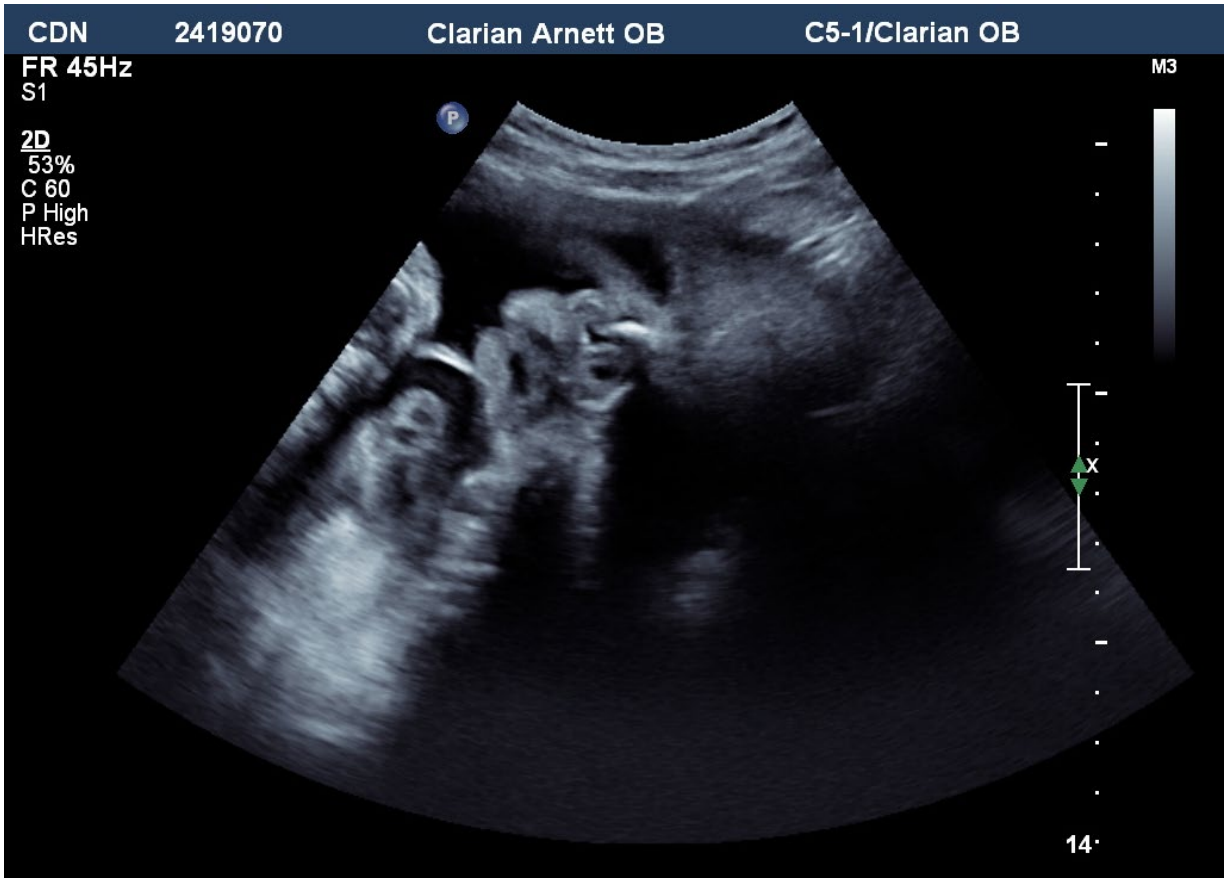
US 9,222,878 B2; US 9,068,949 B2

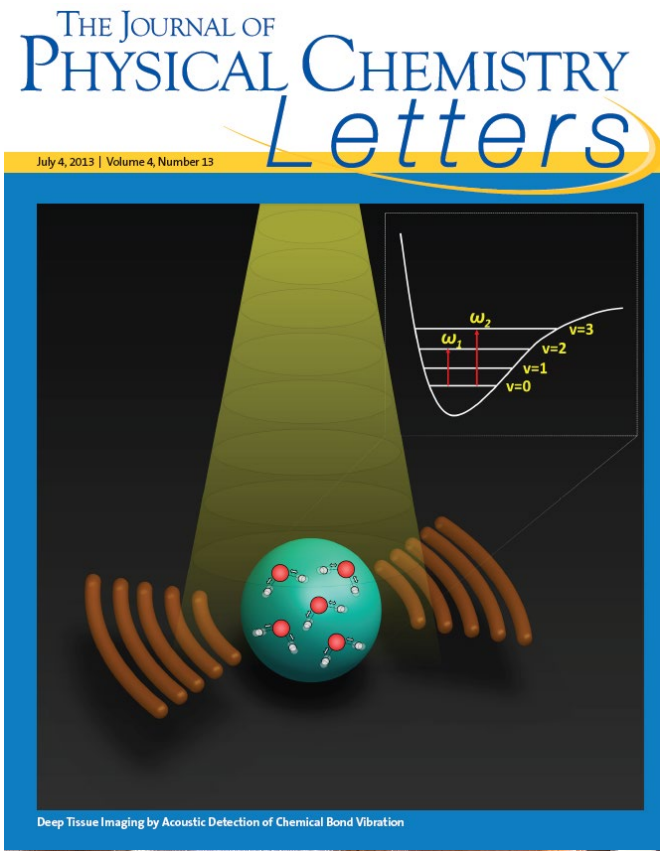
Sci & Eng Grant from Keck Foundation 2015

Barrier to Patient: Limited Imaging Depth



Story 3: new idea from hospital visits in 2009

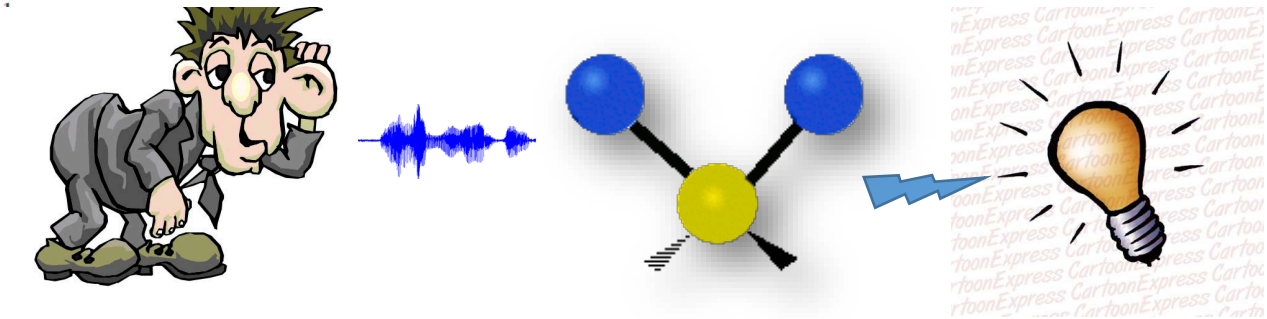


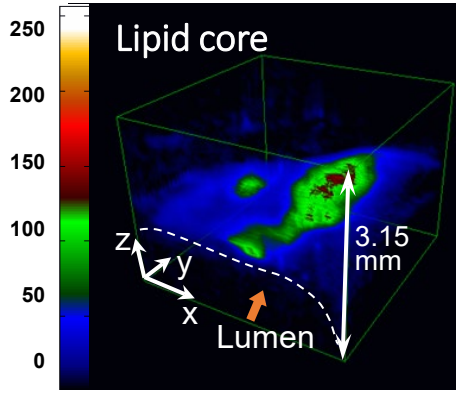


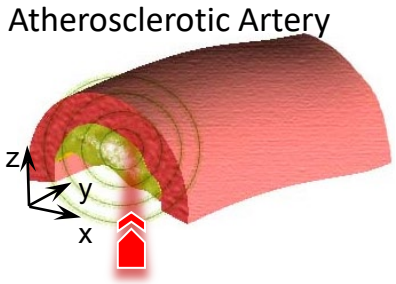
PHYSICAL REVIEW LETTERS PRL 106, 238106 (2011)

Label-Free Bond-Selective Imaging by Listening to Vibrationally Excited Molecules

Han-Wei Wang,[1] Ning Chai,[2] Pu Wang,[1] Song Hu,[3] Wei Dou,[4] David Umulis,[1,4] Lihong V. Wang,[3] Michael Sturek,[1,5] Robert Lucht,[2] and Ji-Xin Cheng[1,6,*]







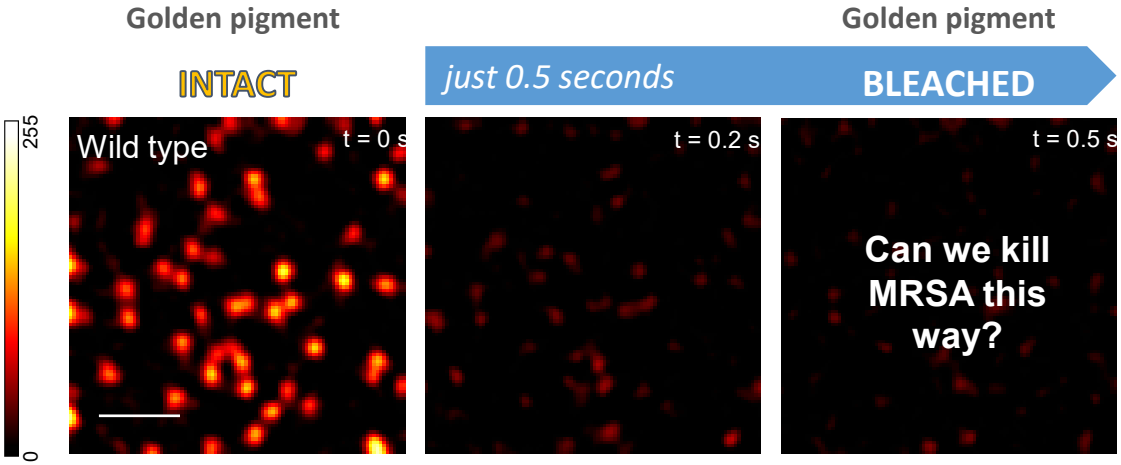
- R21 GM015901
- R01 HL125385
- AHA National Innovation Award
- R01 HL125385-05A1

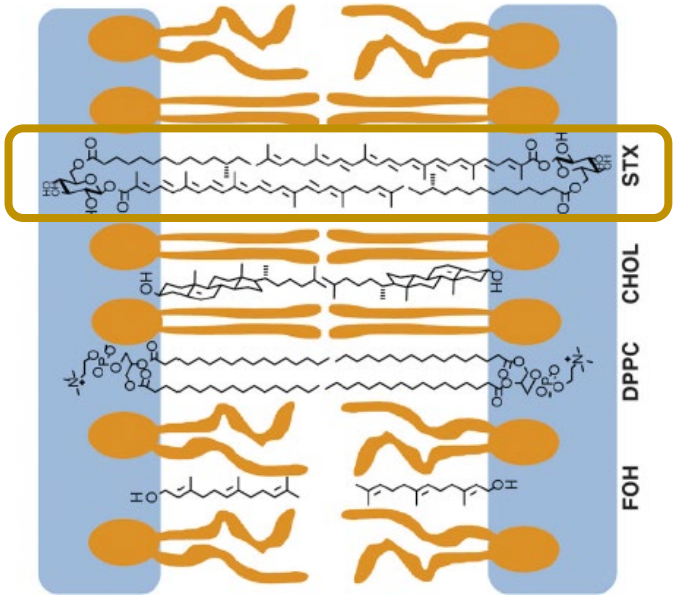
VibroniX Inc

Cofounders: Ji-Xin Cheng, Pu Wang, 2014

Story 4: Innovation is driven by the opposite

Transient absorption imaging of Methicillin-resistant S. Aureus (MRSA), 2017





Advanced Science 2019; US 11,013,933 B2, issued 5/25/2021

Photobleaching the golden pigment Revives H_2O_2

How Light Turns Ordinary Hydrogen Peroxide into a MRSA Treatment

BU engineers have invented a new blue light therapy that can kill MRSA without antibiotics

By Kat J. McAlpine. Photos by Jackie Ricciardi.

As a kid, I skinned my knees on a range of surfaces, from our asphalt driveway, to wood chips on the playground, to the concrete deck of our town pool. I usually cried, not because of the fall itself, but because I knew any scrape deep enough to bleed would attract the attention of my parents and cause them to reach into the medicine cabinet for that dreaded bottle of hydrogen peroxide. Oh, the stinging!

But now, a few decades later, I've finally found a reason to appreciate hydrogen peroxide. It turns out that it's powerful enough to kill a particularly lethal kind of antibiotic-resistant bacteria—as long as it's combined with a blue LED light or laser.

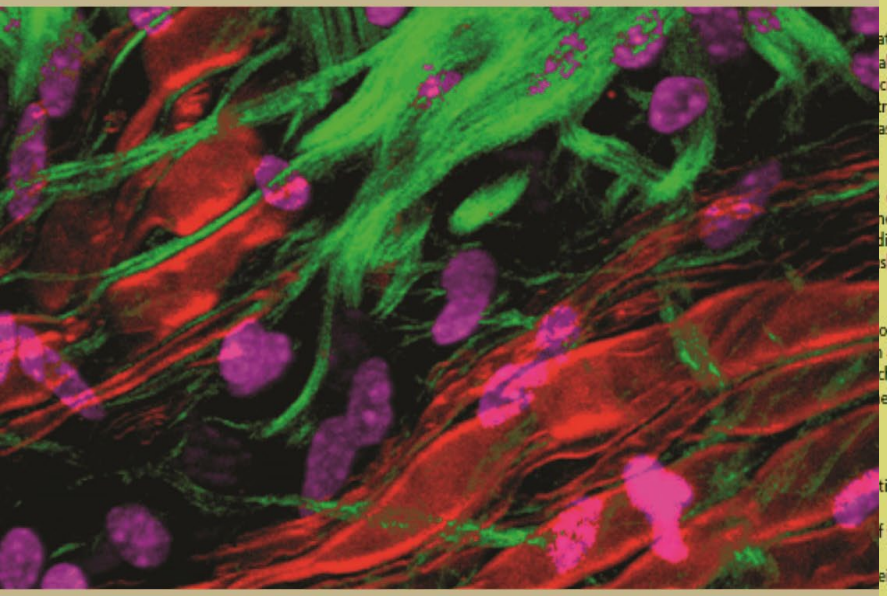
Photonics researchers at Boston University have developed a drug-free treatment for tough-to-treat

Year 2019 **Pulsethera Inc, co-founded by Cheng, Qian and Mansour**

SERIES IN CELLULAR AND CLINICAL IMAGING

AMMASI PERIASAMY, SERIES EDITOR

Coherent Raman Scattering Microscopy



Edited by

Ji-Xin Cheng

X. Sunney Xie

CRC Press
Taylor & Francis Group

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Stimulated Raman Scattering Microscopy

Cheng
Min
Ozeki
Polli

ELSEVIER

Stimulated Raman Scattering Microscopy

Techniques and Applications

Edited by

Ji-Xin Cheng

Wei Min

Yasuyuki Ozeki

Dario Polli

ELSEVIER

Story 5: Thinking out of the Raman Box

Cheng & Xie, *Science*, 350, 1054 (2015)

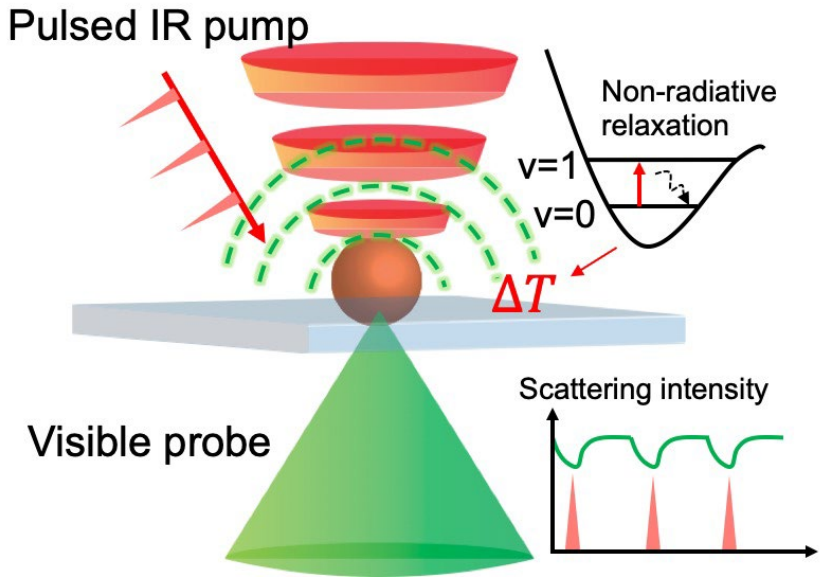
Raman scattering
~ 10^{-30} cm^2/sr/molecule

Mid-infrared absorption
~ 10^{-22} cm^2/molecule

Groups	Frequency [cm^-1]	IR Absorbance [10^3 M^-1 cm^-1]	IR X-Section [10^-16 cm^2/molecule]	Raman Scattering Activity [A^4/amu]	Raman X-Section [10^-30 cm^2/sr/molec]
6-Trehalose-Azide	2127.17006	1691.24080	1.01852	43.85929	0.42108
4-C≡C	2198.17733	50.42692	0.03037	546.33668	4.97113
4-C≡N	2323.74137	100.87151	0.06075	227.73876	1.88884

Calculation: Dr. Zeke Piskulich in QC group

Mid-infrared photothermal (MIP) imaging



- **A pulsed mid-IR laser (red) induces a temperature rise, changing the local refractive index;**
- **A probe beam (green) is used to detect the photothermal effect.**

Zhang D, Cheng JX. Sci. Adv. 2016 2(9):e1600521, confocal MIP
Sci Adv 2019 5(7), eaav7127 wide-field MIP
Light S&A 2019, phase-MIP; Nat Comm 2021 lock-in free MIP
JACS, 2021; Nat Comm 2022; Sci Adv 2023
For a Review, Bai, Cheng, Sci. Adv. 2021 7:eabg1559

US 11,280,727 B2, Mar 22, 2022
Licensed to photothermal Spec Corp

From Paper to Product

RESEARCH ARTICLE

IMAGING

Depth-resolved mid-infrared photothermal imaging of living cells and organisms with submicrometer spatial resolution

10.1126/sciadv.1600521

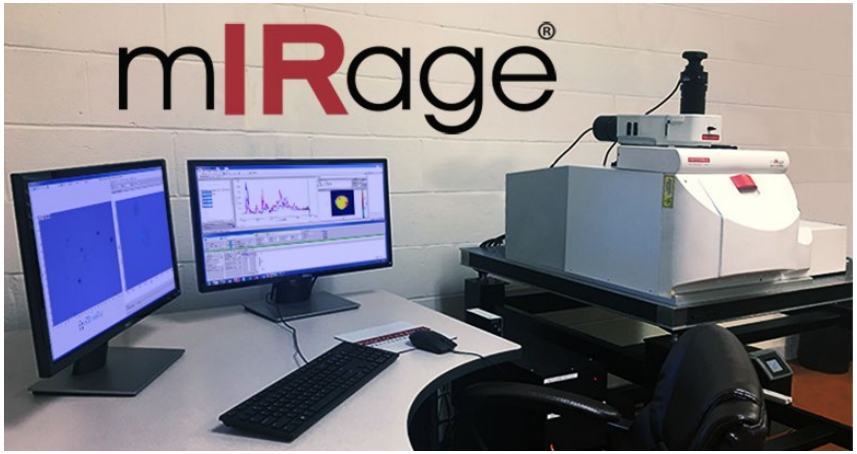
Delong Zhang,[1] Chen Li,[2] Chi Zhang,[1] Mikhail N. Slipchenko,[1,3] Gregory Eakins,[4] Ji-Xin Cheng[1,2,5]*

Chemical contrast has long been sought for label-free visualization of biomolecules and materials in complex living systems. Although infrared spectroscopic imaging has come a long way in this direction, it is thus far only applicable to dried tissues because of the strong infrared absorption by water. It also suffers from low spatial resolution due to long wavelengths and lacks optical sectioning capabilities. We overcome these limitations through sensing vibrational absorption–induced photothermal effect by a visible laser beam. Our mid-infrared photothermal (MIP) approach reached 10 μM detection sensitivity and submicrometer lateral spatial resolution. This performance has exceeded the diffraction limit of infrared microscopy and allowed label-free three-dimensional chemical imaging of live cells and organisms. Distributions of endogenous lipid and exogenous drug inside single cells were visualized. We further demonstrated in vivo MIP imaging of lipids and proteins in *Caenorhabditis elegans*. The reported MIP imaging technology promises broad applications from monitoring metabolic activities to high-resolution mapping of drug molecules in living systems, which are beyond the reach of current infrared microscopy.

INTRODUCTION

Today, infrared spectroscopic imaging has broad applications, ranging from heritage material characterization to cancer grading (*1*–*4*). Since the publication of Coblentz's high-quality spectral database in 1905 (*5*), technological advances, including the development of Fourier transform infrared (FTIR) spectroscopy (*6*), FTIR imaging (*7*), a focal plane array detector (*8*), and new light sources such as synchrotron (*9*, *10*) and quantum cascade laser (QCL) (*11*, *12*), have improved the measurement of infrared absorption for each spatially resolved pixel. In particular, modern QCL has enabled discrete frequency infrared imaging, where specific vibrational bands are pinpointed to accelerate the imaging speed while offering sufficient chemical information (*12*). Despite these advances, a few fundamental limitations of infrared microspectroscopy have prevented its application in in vivo imaging and diagnosis. First, accurate measurement of absorption in biological harnessing the thermal lensing effect. In this mid-infrared photothermal (MIP) scheme, infrared absorption at the focus causes a temperature increase that locally changes the refractive index, which consequently affects the propagation of the probe beam. This perturbation to the probe beam is effectively detected via a dark-field geometry. Our MIP scheme avoids the abovementioned problems encountered in infrared imaging. First, because we probe a visible beam at a fixed wavelength, the artifact due to wavelength-dependent scattering of the infrared beam is eliminated. Second, the spatial resolution in MIP microscopy is determined by the wavelength of the probe beam, which is much shorter than that of the mid-infrared beam. Third, MIP provides three-dimensional (3D) sectioning capabilities through nonlinear signal generation via a pump-probe mechanism, which is out of reach by linear absorption–based infrared imaging. Finally, water absorption of the visible probe

Craver Award Speech, SciX Meeting, Oct 2016
Meet Dean Dawson & Roshan Shetty (CEO of Anasys)



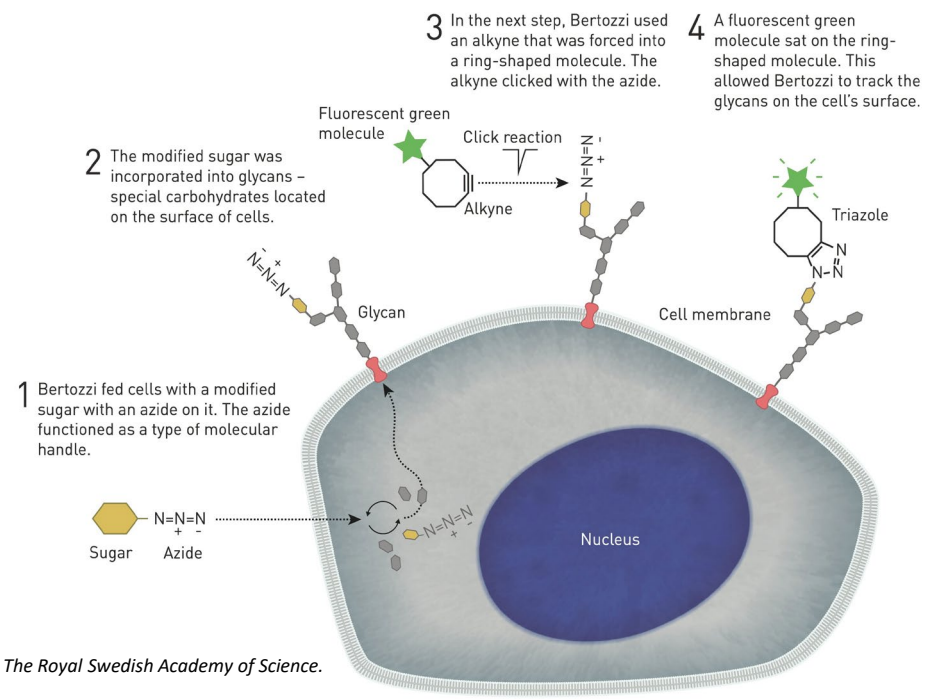
mIRage™
Anasys Instrument Inc, April 2018
now
Photothermal Spectroscopy Corp

mIRage™ has been delivered to ~70 labs in 8 countries

Click-free MIP Imaging in the Silent Window

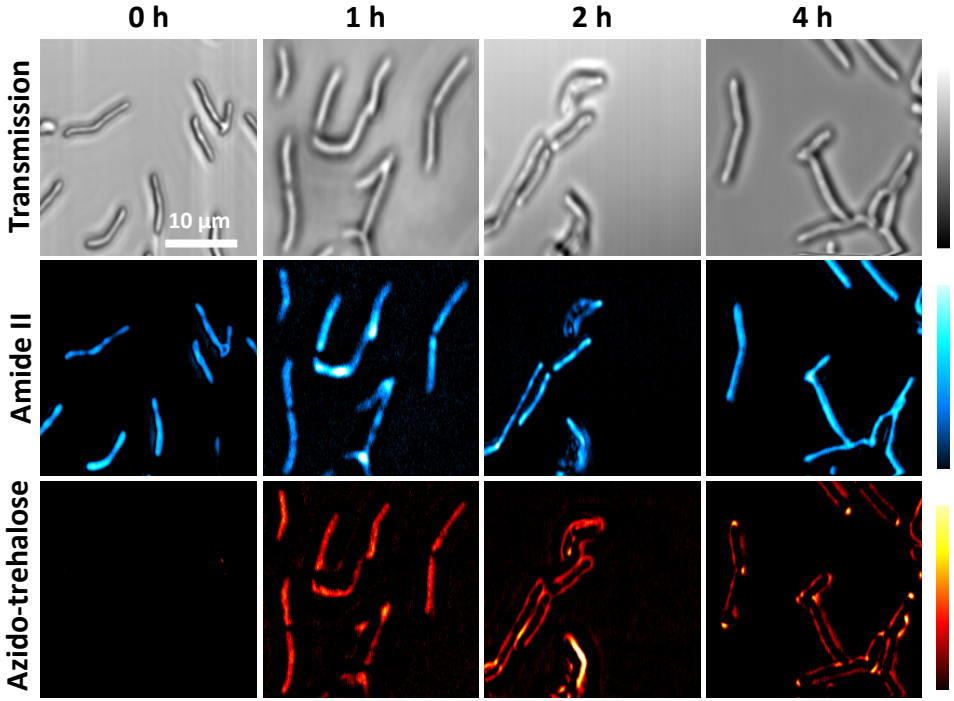
chemical bond as GPS of molecules

Click Chemistry: Azido-sugar for glycan tracking



The Royal Swedish Academy of Science.

MIP: Direct imaging of azide in mycobacteria



Thank you!