Pacific Northwest
NATIONAL LABORATORY

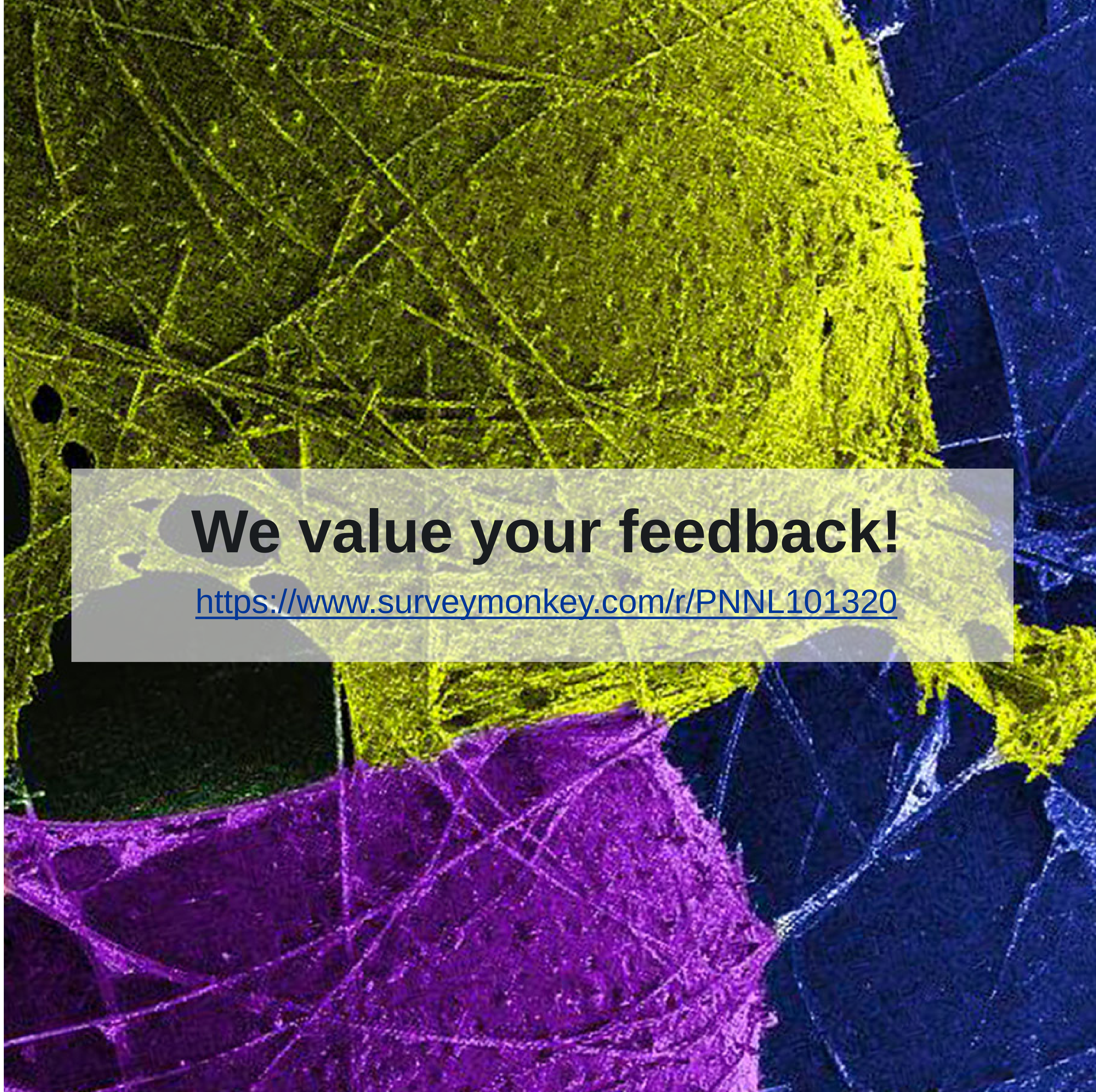
Solving the World's Biggest Problems on the Smallest Scale

Heather Olson, Chemist

Pacific Northwest National Laboratory

U.S. DEPARTMENT OF ENERGY BATTELLE

PNNL is operated by Battelle for the U.S. Department of Energy



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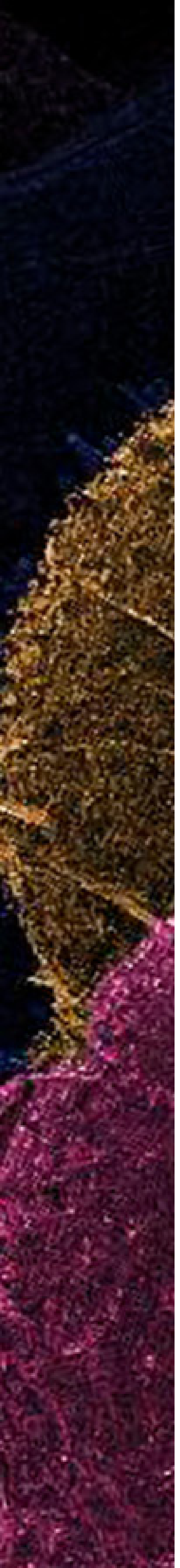
https://www.surveymonkey.com/r/PNNL101320



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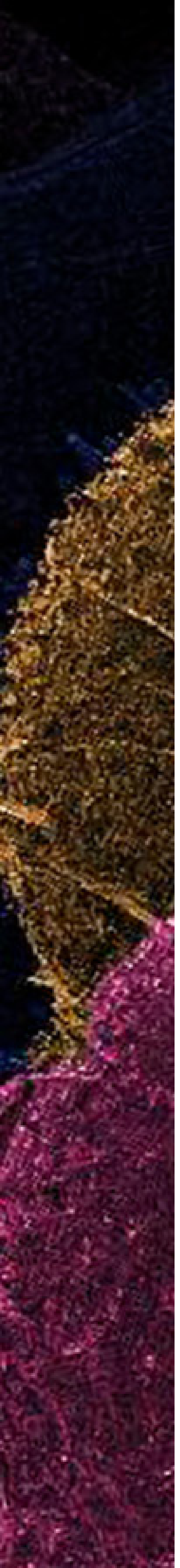
1 of 17
U.S. DOE Labs



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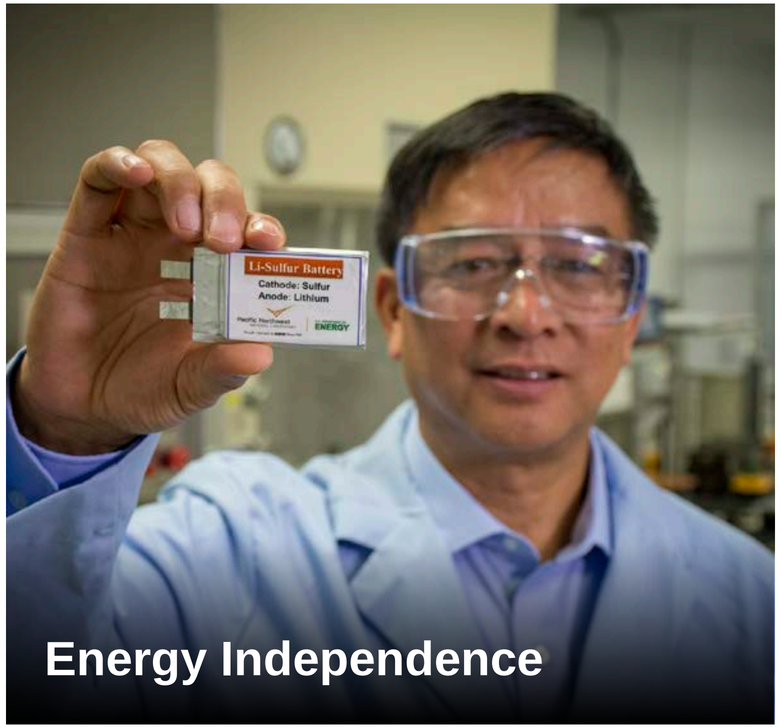
PNNL is Focused on **DOE’s MISSIONS** and Addressing Critical **NATIONAL NEEDS**

Scientific Discovery



Energy Independence

National Security

Environmental Management

PNNL is an ECONOMIC ENGINE

4,722
Employees

265
Inventions

$1.46B
Total Economic Output

$1.01B
Annual Spending

88
Patents

7,180
Jobs Generated
in Washington

$465M
Total Payroll

34
Licenses

193
Companies
with PNNL Roots

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50+ Years

Developing Goodwill

	Philanthropic Investments	Team Battelle Volunteer Hours	Community Organizations
Decades	$28.5M	347,000	>120
FY19	$0.52M	30,000	56

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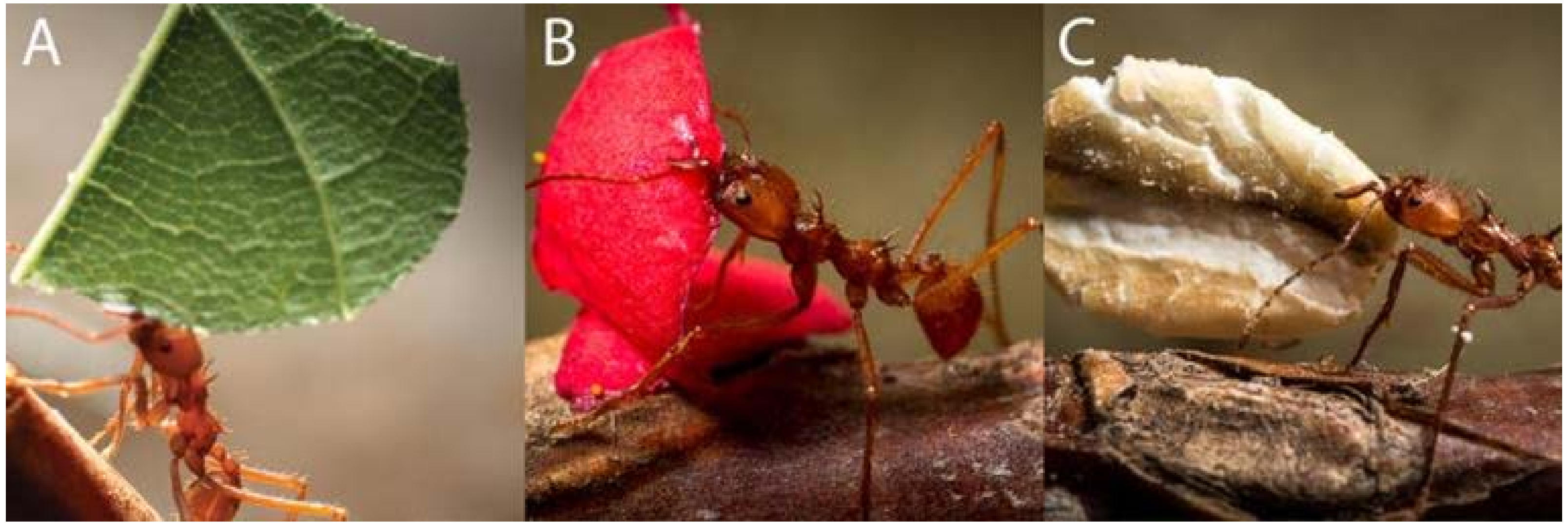
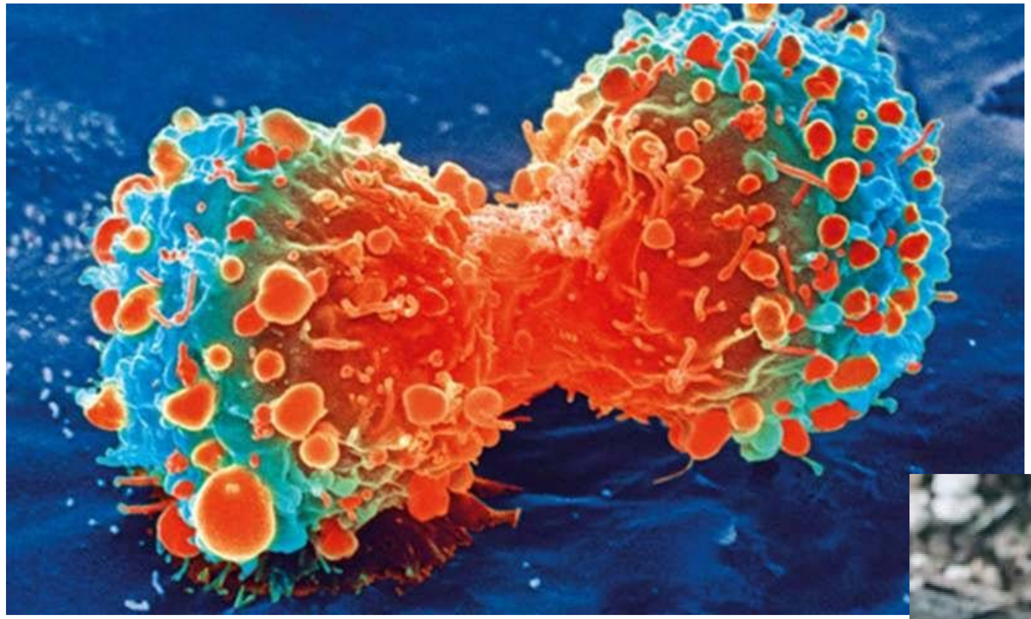
Have you ever wondered…

- How ants became farmers?
- How diabetes happens?
- What makes a cancer cell different from a normal cell?
- How certain plants can still grow with little rain?





Analysis On All Scales

Researchers at PNNL work to understand big-picture problems by looking at the small-scale details. For example, looking at bacteria that exist in the rhizosphere of a tree can tell us something about the forest that tree resides in, just like a small detail in a room can say something about the city that room exists in.

To accomplish this, we use chromatography, a laboratory technique for separating a mixture. We then use mass spectrometry, a tool that measures how much mass a molecule contains, to identify the compounds in our complex samples

What's an OMIC?

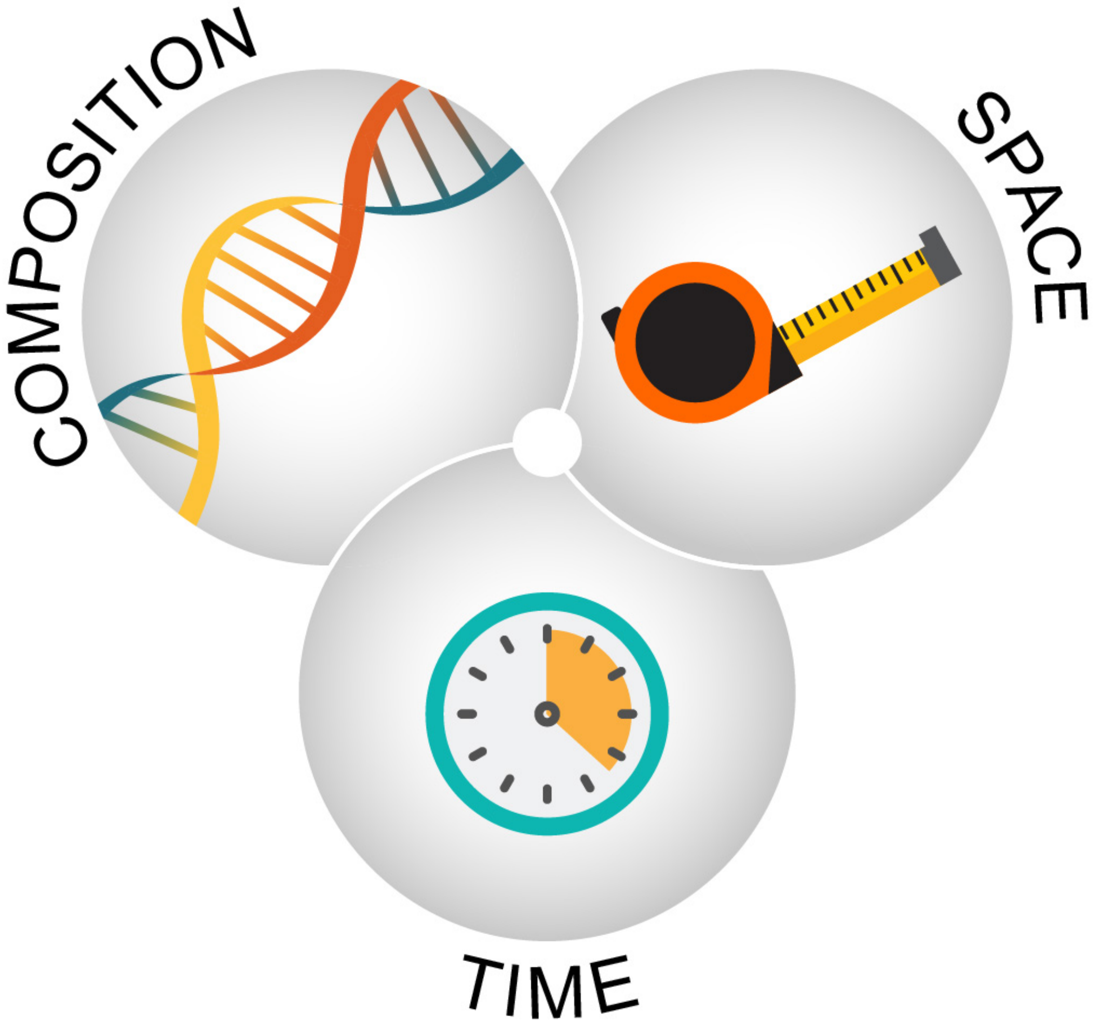
Related measurements or data from such interrelated disciplines as genomics, proteomics. transcriptomics or other fields. Many of these fields have a name that ends with the suffix -omics.

Omics aims to characterize and quantify groups of biological molecules that help scientists understand the structure, function, and dynamics of an organism.

-omic	What it studies	Information it provides
Genomics Transcriptomics	DNA RNA	Identity Translation to Structure
Proteomics	Proteins	Function/Structure
Metabolomics Lipidomics	Metabolism	Function

How we use the -OMICS toolkit

Composition: Lipidomics, Metabolomics, Proteomics



Space: Molecular level interactions between systems

Time:
Obtain “snapshot” pictures of multi-omic levels during several occurrences and piece together a systems biology picture

Ant Farmers

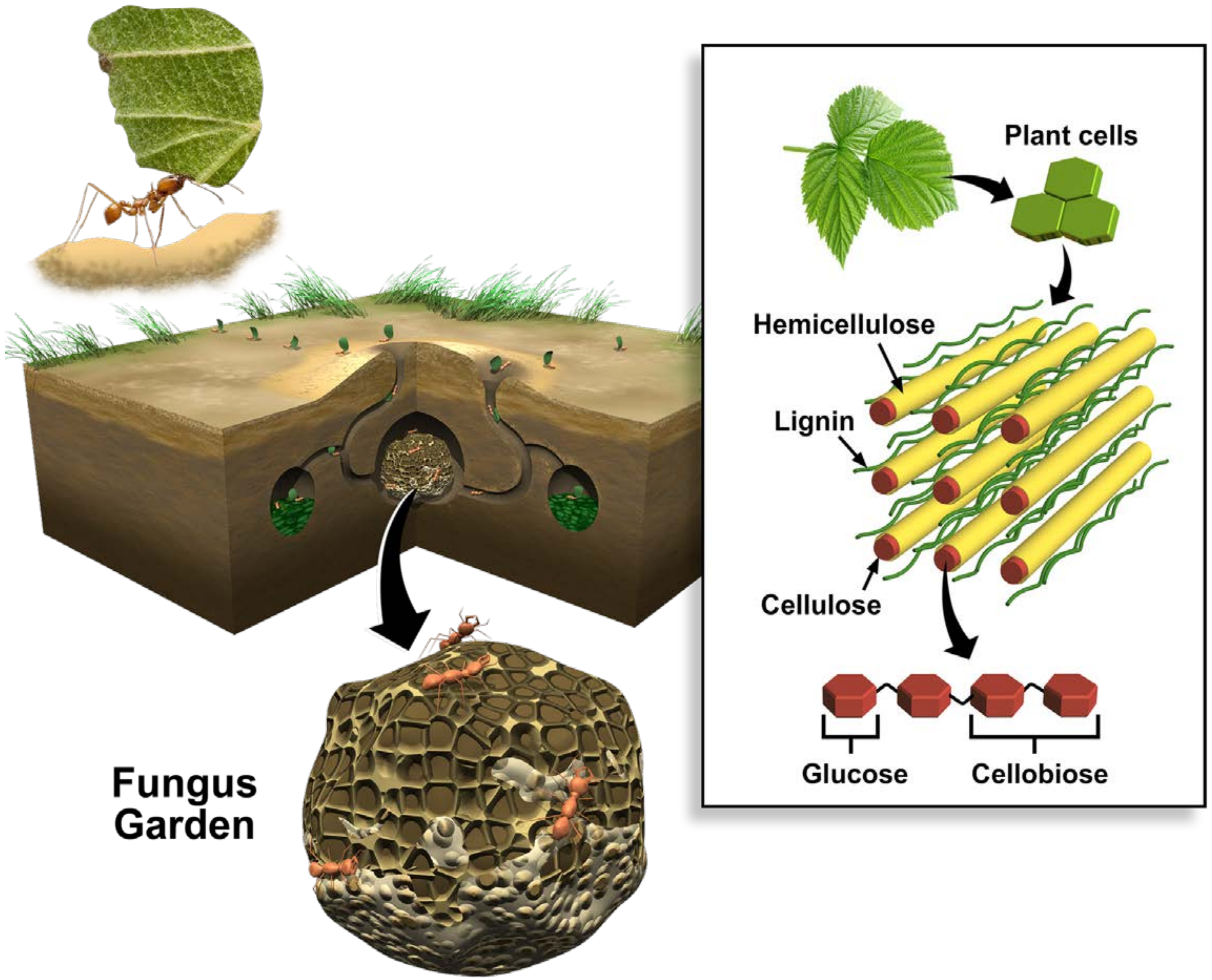
Researchers at PNNL study a fascinating symbiotic system between ants, fungi, and bacteria where ants actively cultivate fungus much like humans farm crops as a food source.

The Fungal Garden:

Leaf-cutter ants cut leaves from nearby trees and carry leaf fragments to the fungus garden

The fungus grows on the plant matter and breaks it down into simple sugars

Bacteria further transform the simple sugars derived from plant matter into amino acids, vitamins and additional nutrients useful for the ant and the fungus



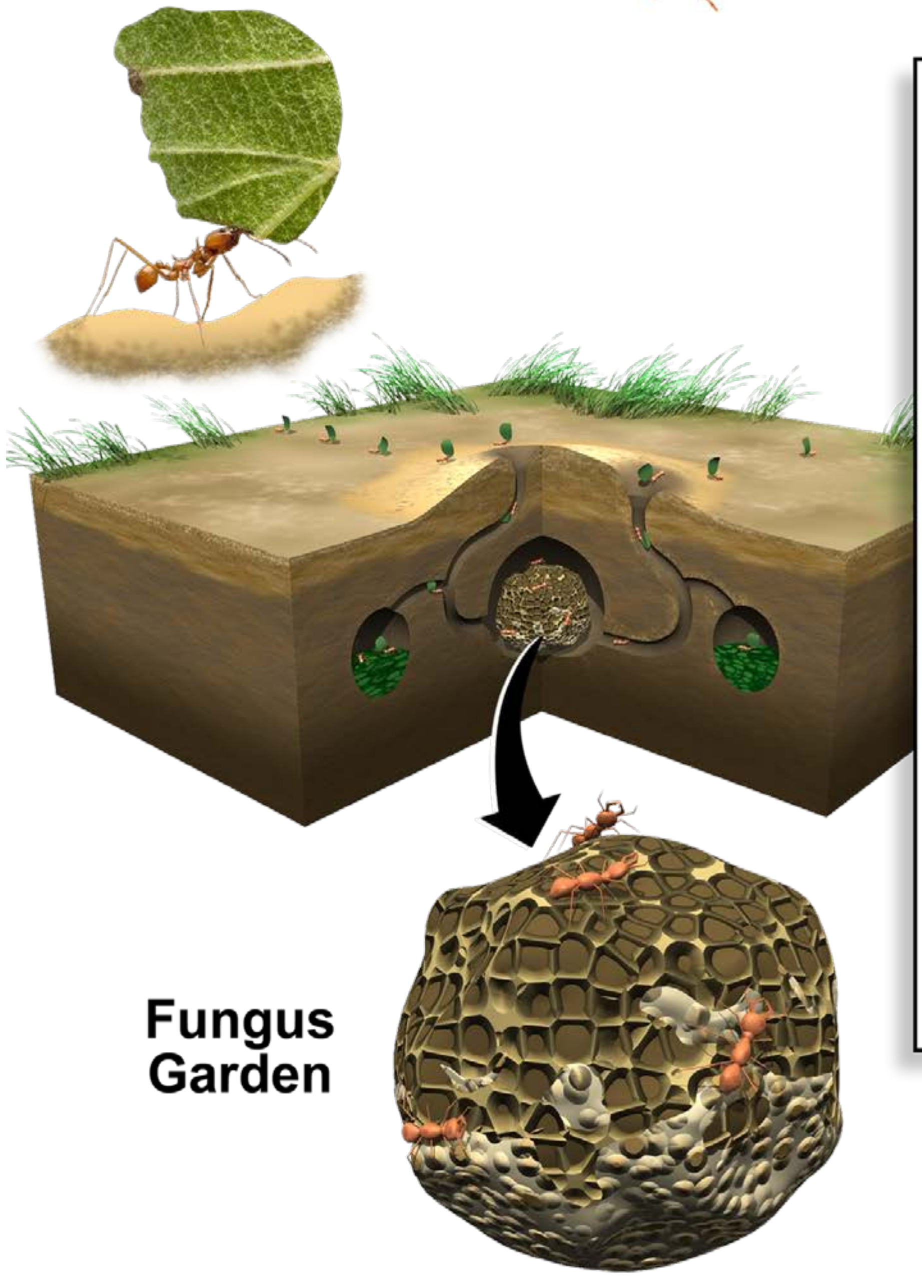
Ant Farmers

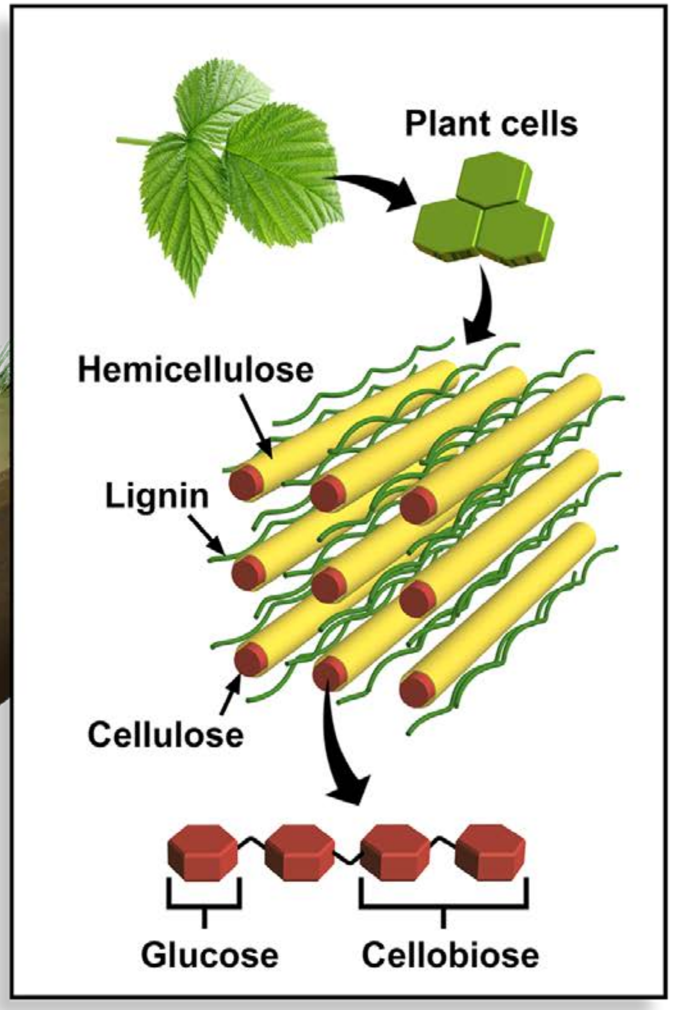
The Fungal Garden:

Antibiotic-producing bacteria protect the garden from bacterial and fungal parasites and pathogens

The fungus produces gongylidia, or specialized hyphal swellings, that ants consume and feed to larvae in the colony

Scientists then take samples from the garden and run analyses to better understand how it all works





Why Ants?

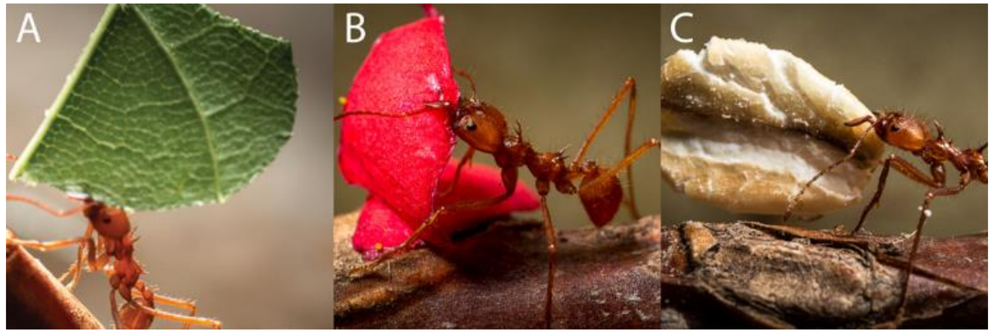
Studying the Garden

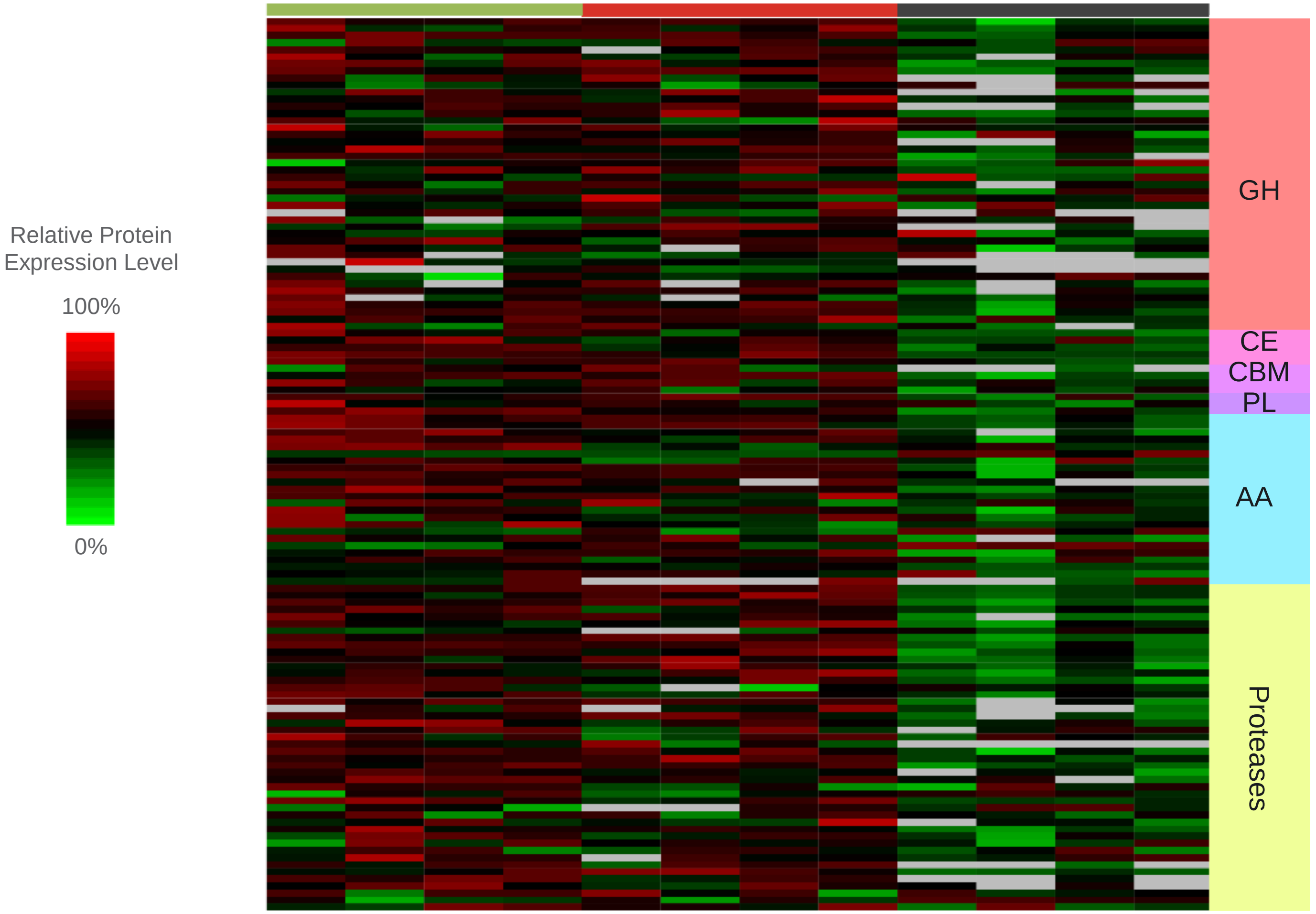
Scientists study this ant farming process in order to learn from efficient processes in nature and apply them to human challenges. For example, by understanding how leaf matter is broken down to valuable molecules in fungus gardens, scientists can discover more efficient ways to create biofuels from plant biomass.

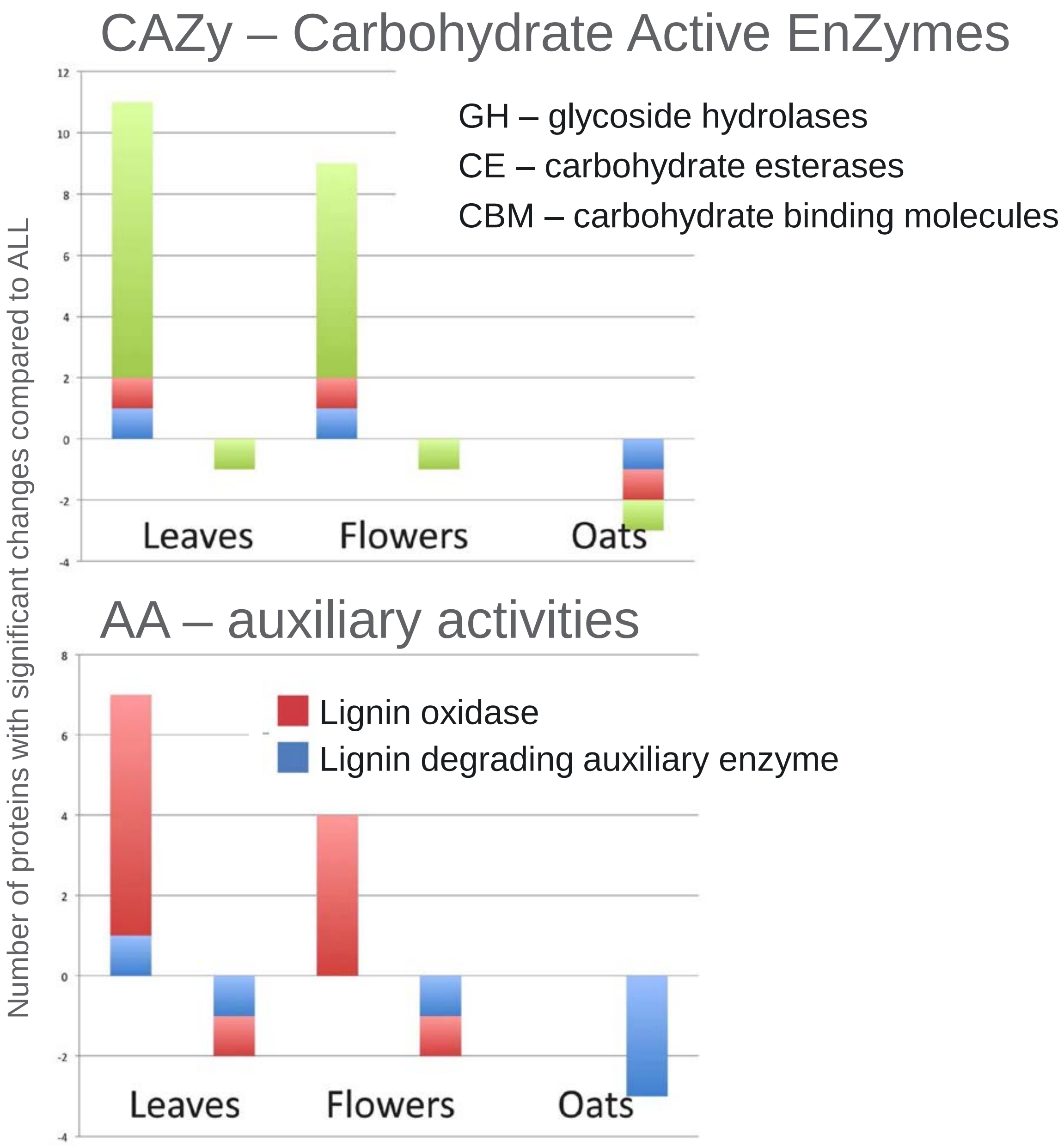
Using Omics

By looking at proteomics, lipidomics, and metabolomics, scientists are able to figure out what role the ant, fungus, and bacteria play in this symbiotic process.

The fungal garden ecosystem of leaf-cutter ants produces specific enzymes in response to different plant substrates



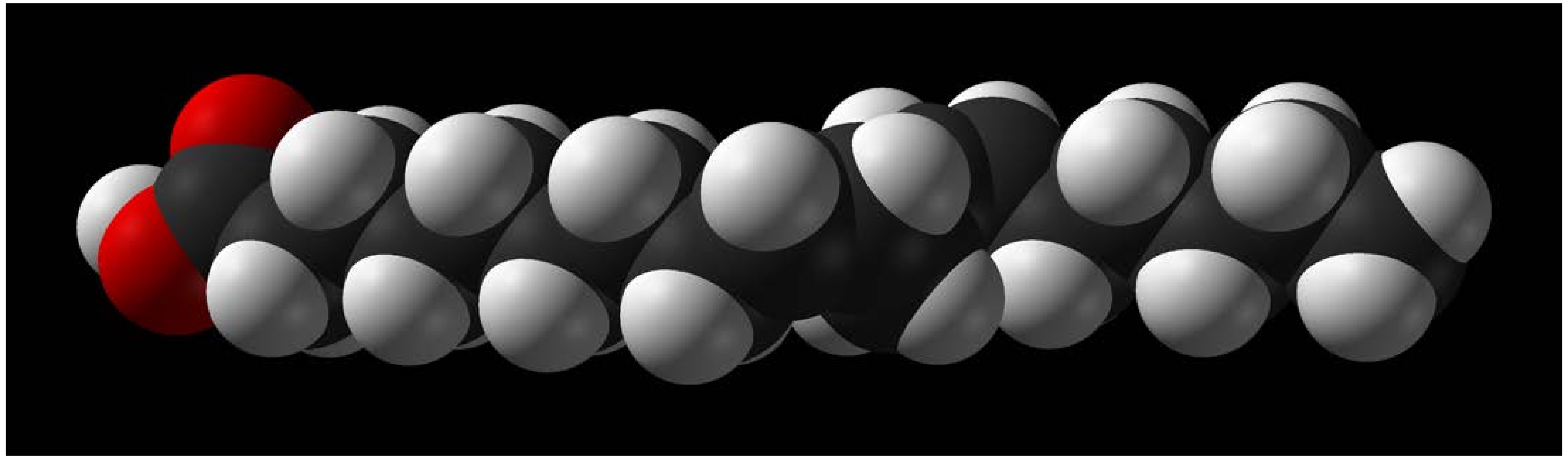




Molecular Ecology (2016), 25: 5795–5805

A Tale of Two Lipids: Chemical Attraction or Repulsion?

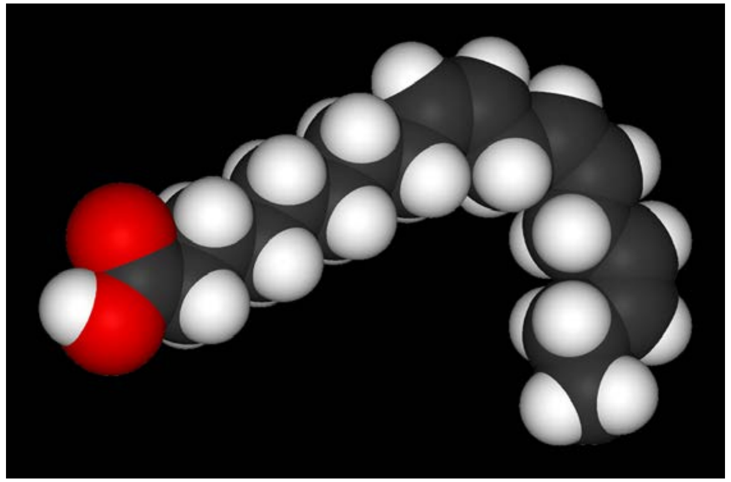
Linoleic Acid



18 Carbons, 2 double bonds

Linoleic Acid attracts ants

Linolenic Acid



18 Carbons, 3 double bonds

Linolenic Acid makes ants aggressive

Linolenic acid is found in leaves and in the tops of the ant gardens, but linoleic acid is found in the bottom of the garden after the bacteria and fungi have broken down the lignins and cellulose

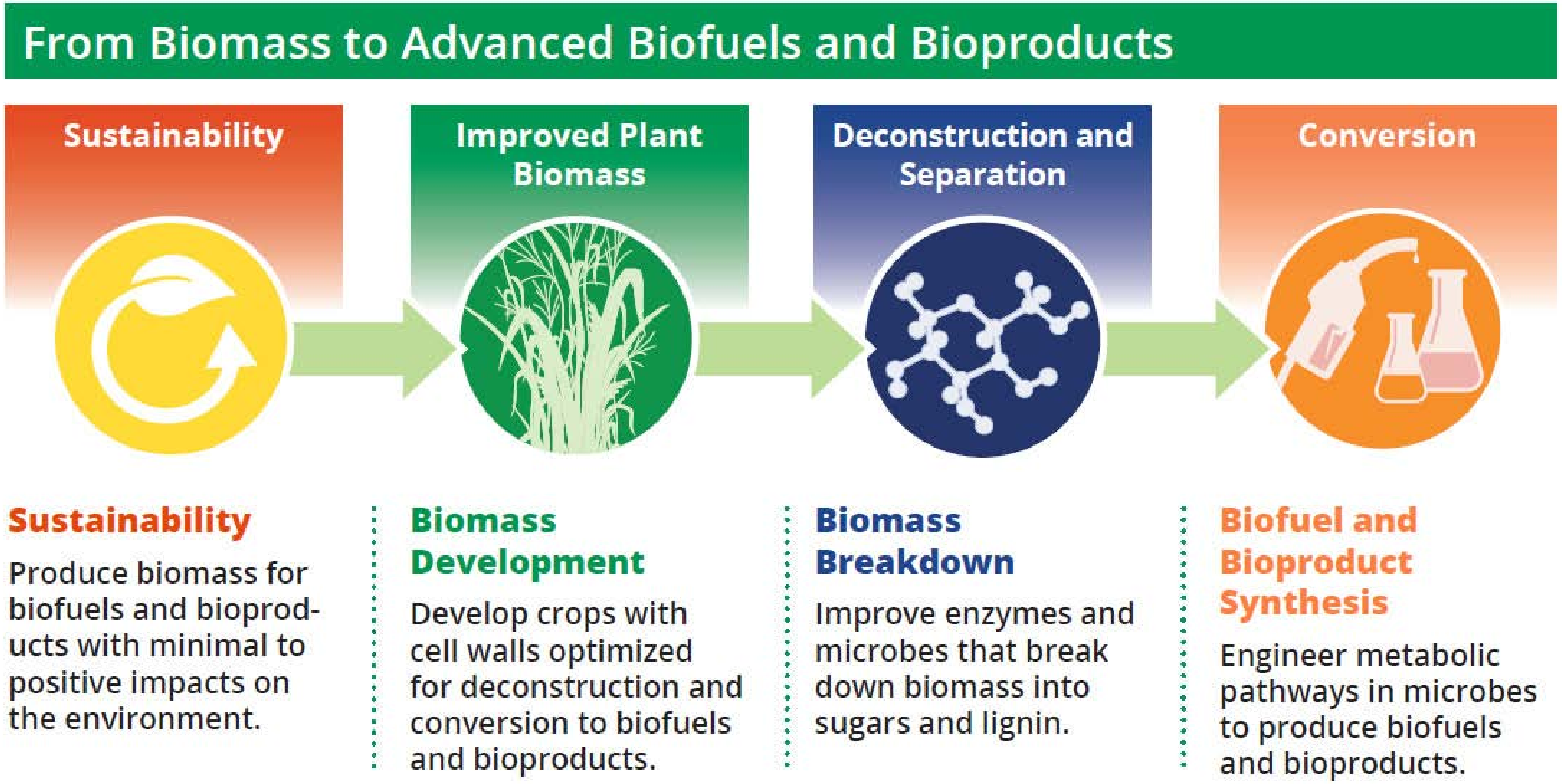
D paper disks contain solvent only control

B paper disks contain Linoleic acid (18:2)

L. Khadempour, et al., **C. Currie**, **E. Baker**, **K. Burnum-Johnson**. From plants to ants: Fungal modification of leaf lipids for nutrition and communication in the leaf-cutter ant fungal garden ecosystem bioRxiv, (2020) A paper disks contain **Alpha-linolenic acid (18:3)**

D paper disks contain solvent only control

What Does This Have to do With Humans?



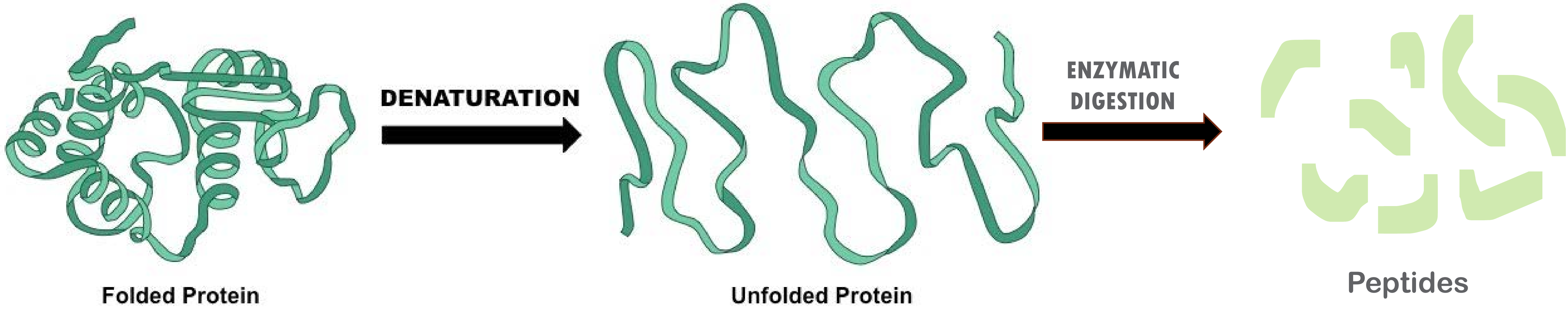
Just like cooking spinach makes it easier to digest, some fungi can break down plant cell walls, including lignin. That makes it easier for other organisms to use the carbon that is in those cell walls.

The bioenergy industry can't yet efficiently and affordably break down lignin, which is needed to transform non-food plants such as poplar trees into biofuels. Learning how fungi break down lignin and cellulose could make these processes more affordable and sustainable.

Magnitude of the Puzzle

The human body with all its various organs contains nearly 100 trillion cells. There are about 10,000 proteins per human cell, not all of them having the same structure or function. Understanding how the human body works (or doesn't in the case of some diseases) is one of the main goals in systems biology. We use proteomics, lipidomics and metabolomics to try to fit the puzzle pieces together.

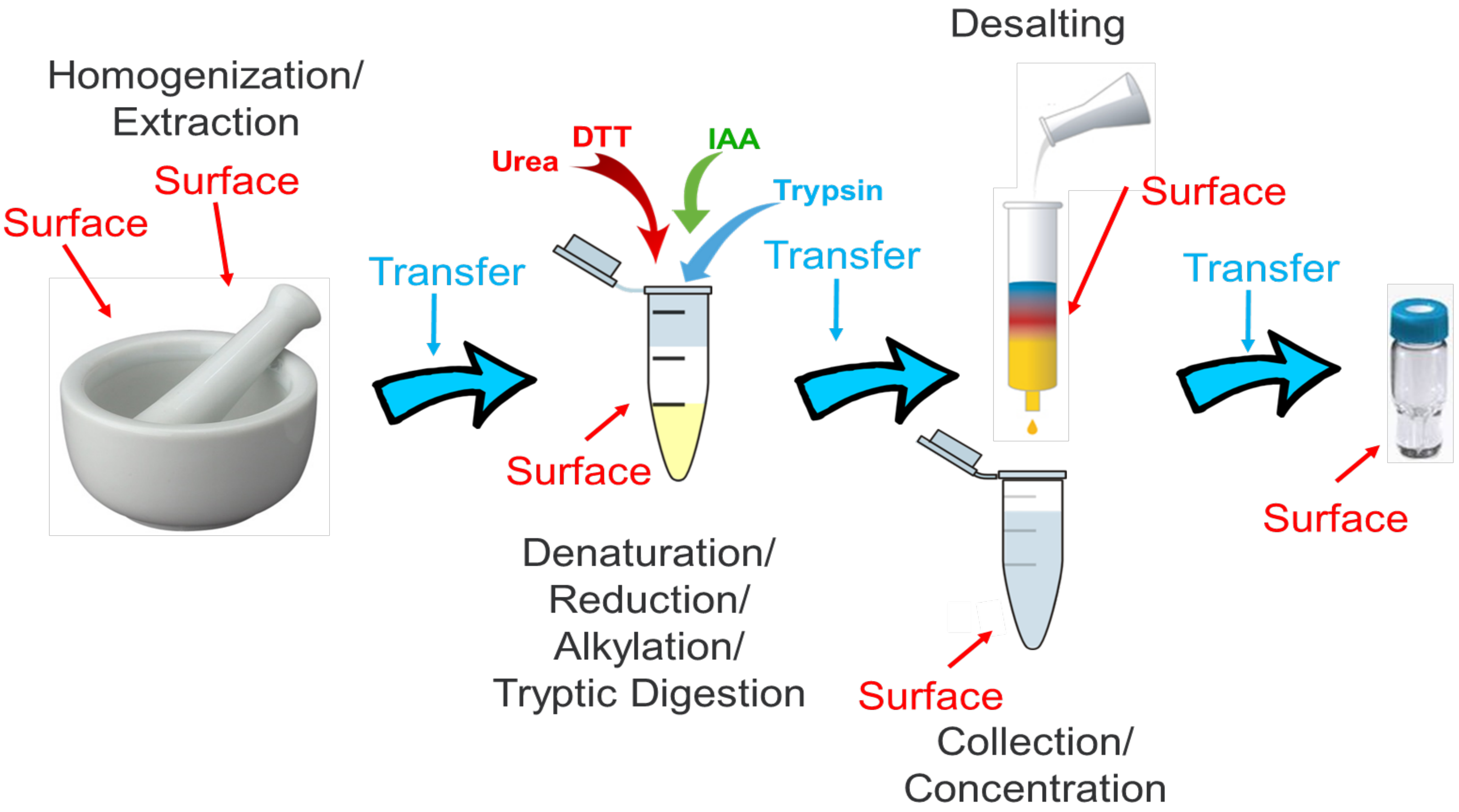
Digesting Proteins - it's not like how your stomach does it (or is it?)



Folded proteins give structure and function, but are very difficult to study, so we need to unfold them using chemicals and/or heat.

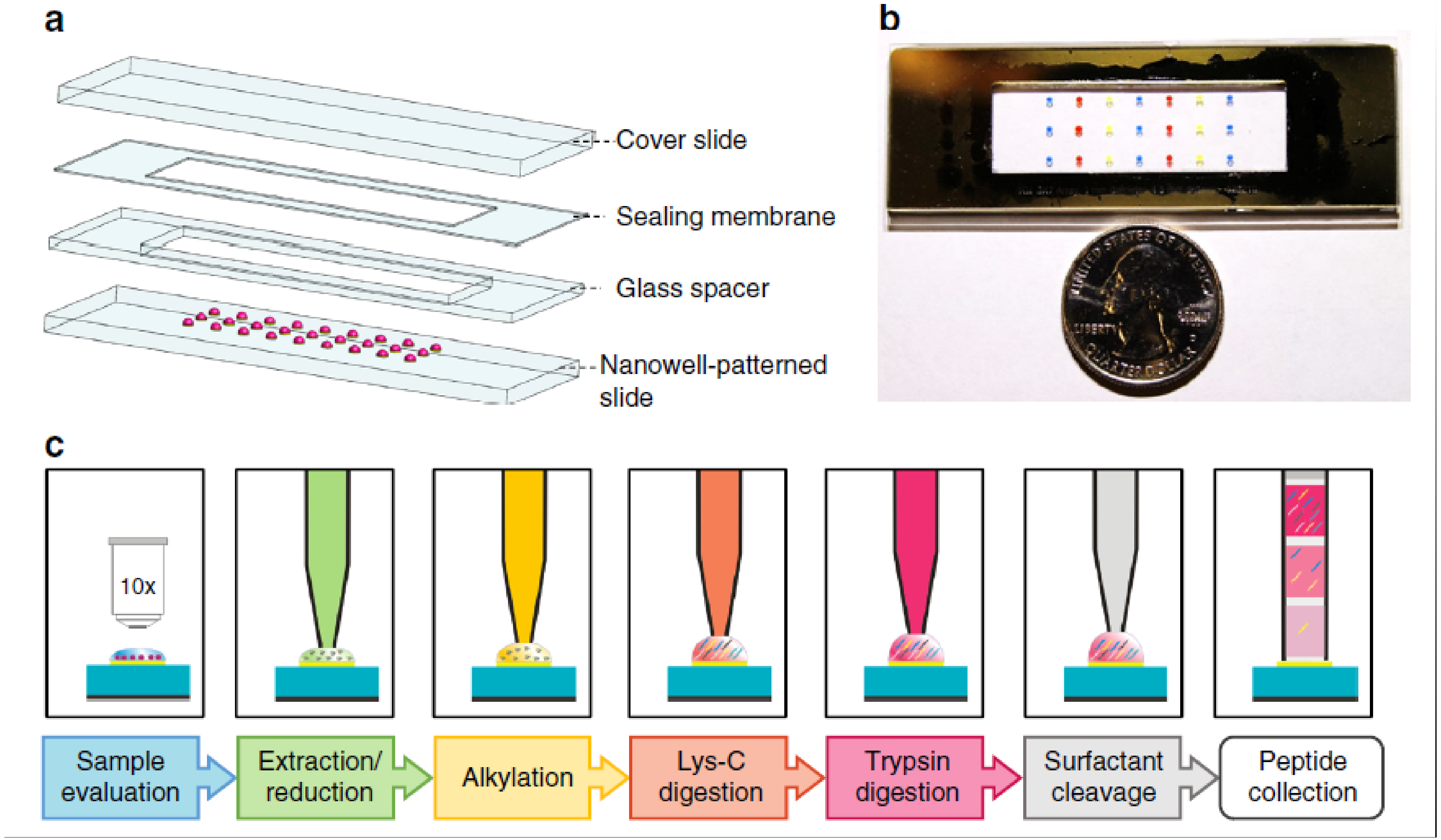
Once unfolded, we use enzymes such as trypsin (like what is found in your stomach) to digest the proteins into smaller amino acid chains called peptides.

Standard Proteomic Digestion Procedure



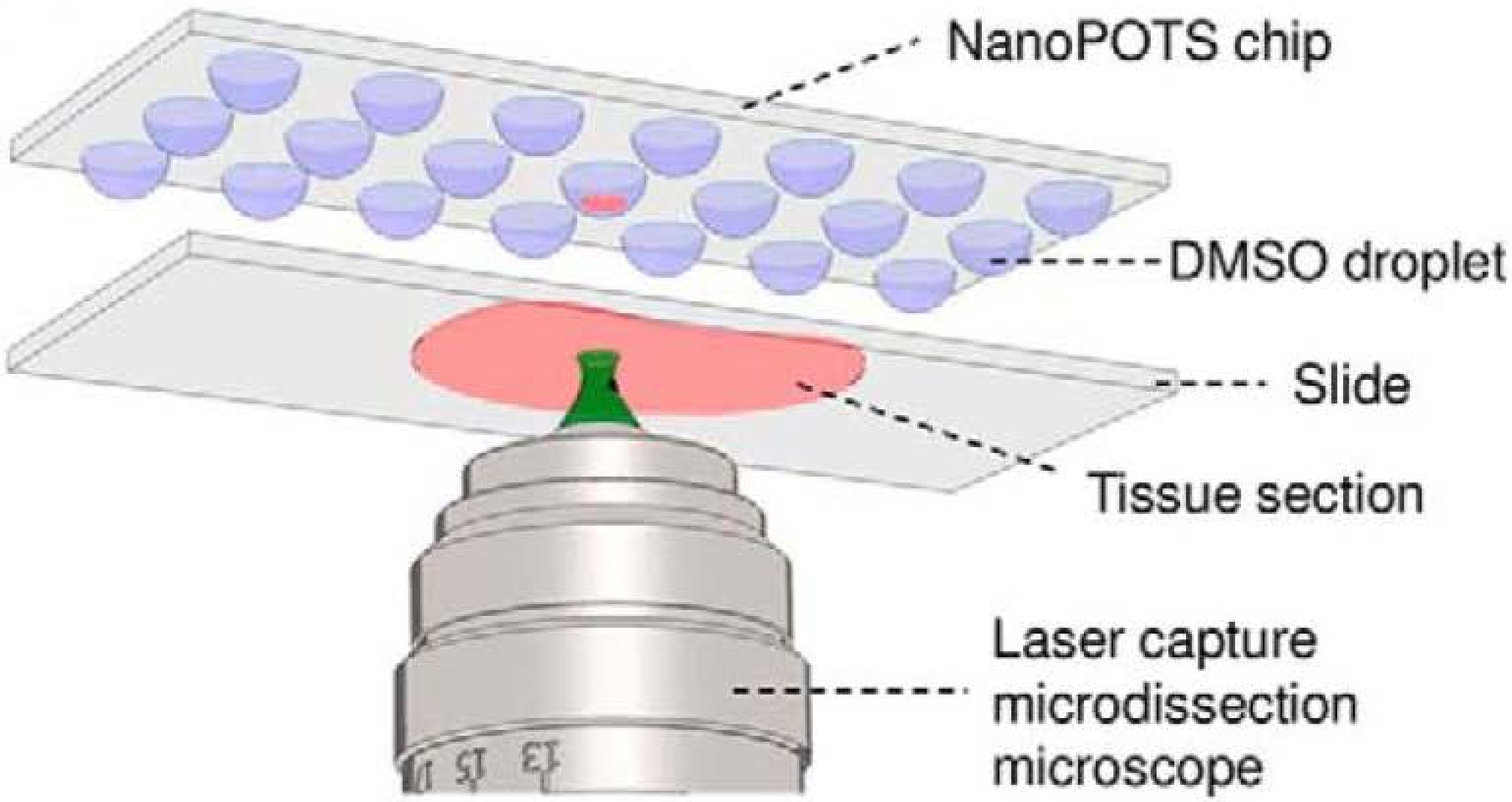
Each time a new surface is encountered, proteins/peptides are lost

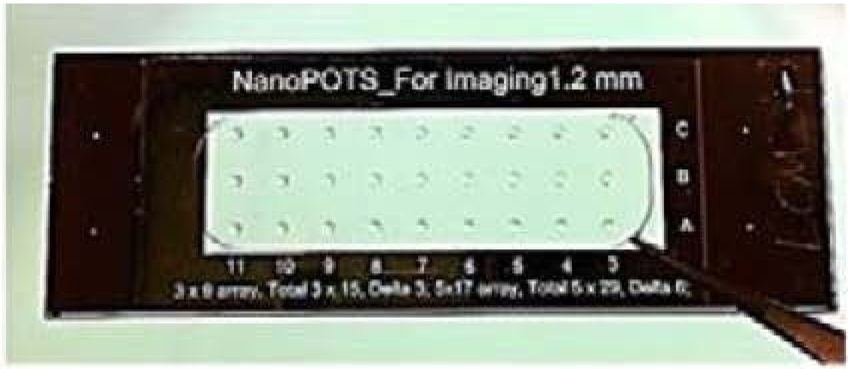
Going Nano: Reducing Surface Area Issues



Working in nanodroplet sample sizes reduces the surface area to the extreme

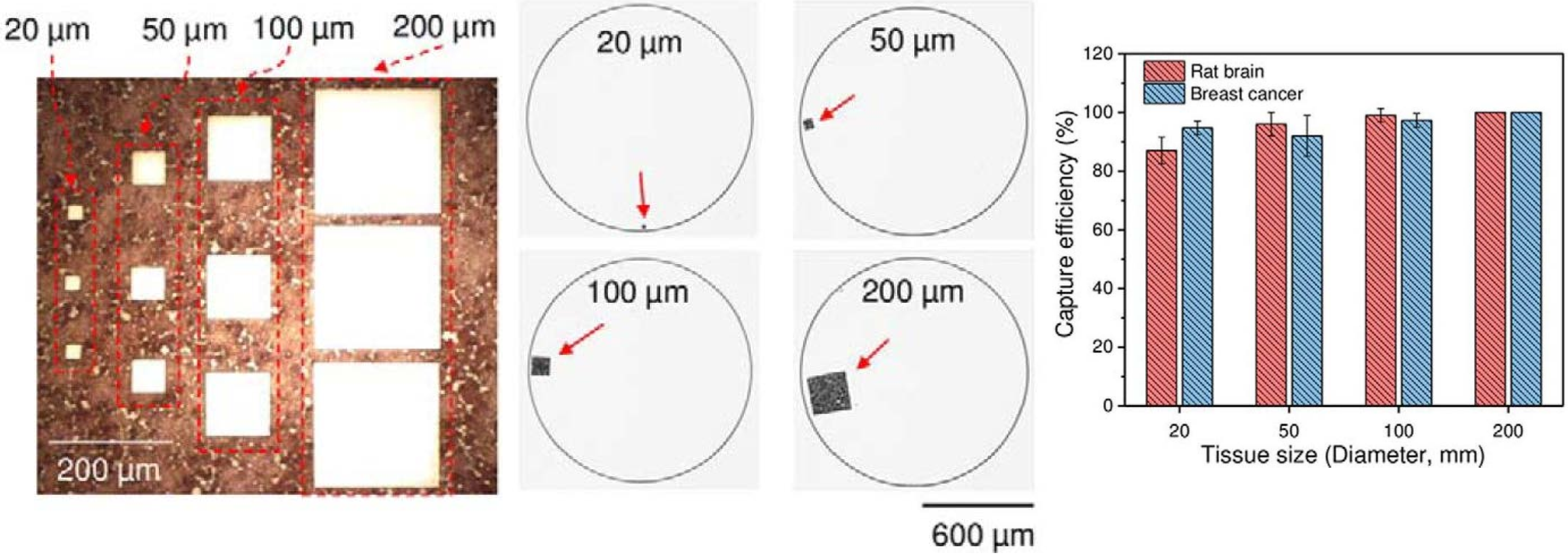
Working Upside Down





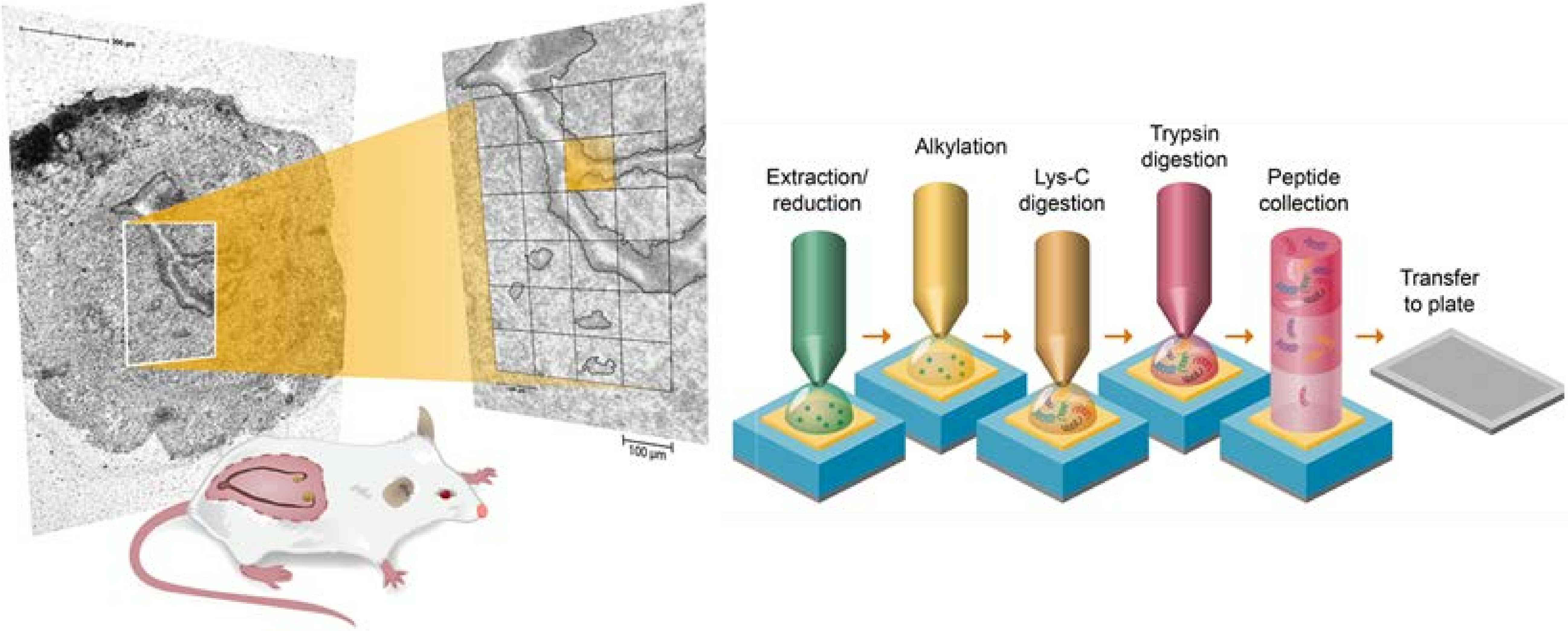
Samples are collected onto the chips (slides) using a special microscope that performs dissection at the same time as the researcher is viewing the cells

Tissue Limbo – How Low Can You Go?



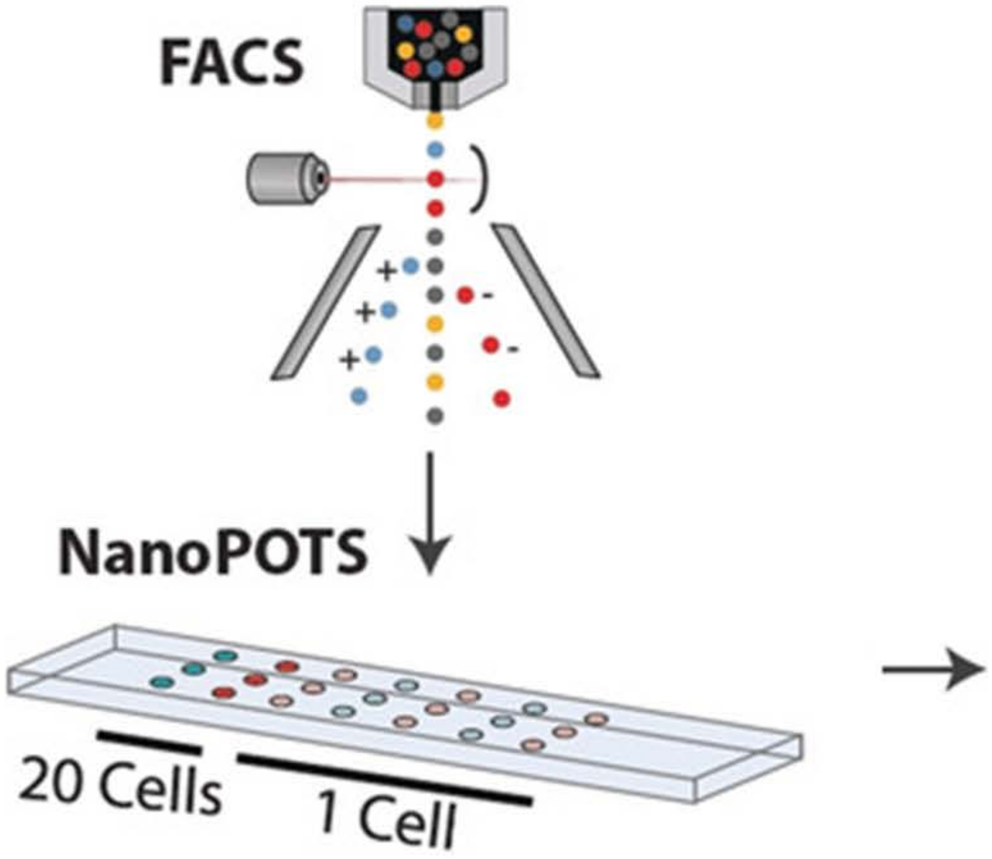
Efficiency of tissue collection is maintained fairly well, even on an order of magnitude

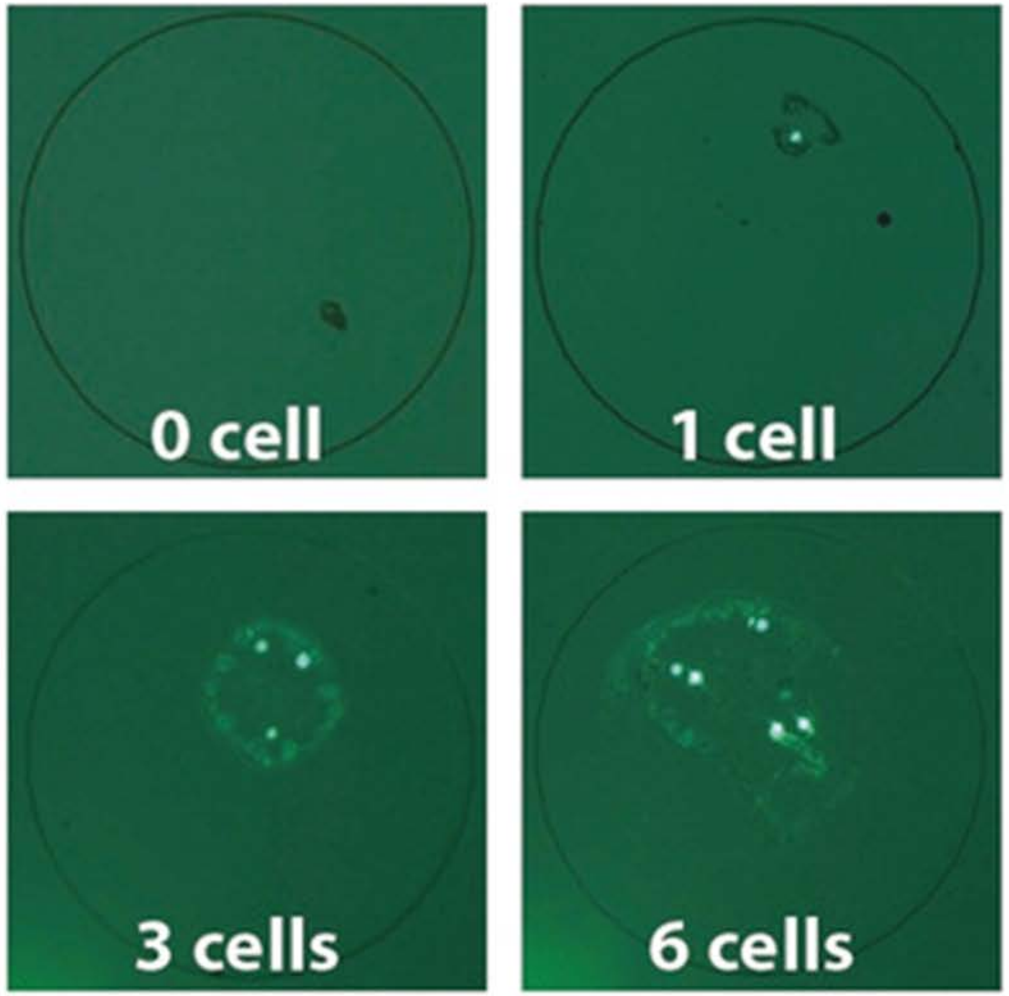
Zooming In On The Problem



Having a higher level of resolution enables researchers to gather a much larger amount of data, thus a greater understanding of the questions being asked about a disease.

Tackling the Tiny: Looking at Single Cell -Omics





Using fluorescence-activated cell sorting (FACS), we can find the cells of interest (e.g. cancer) and collect individual cells to perform –omics analyses.

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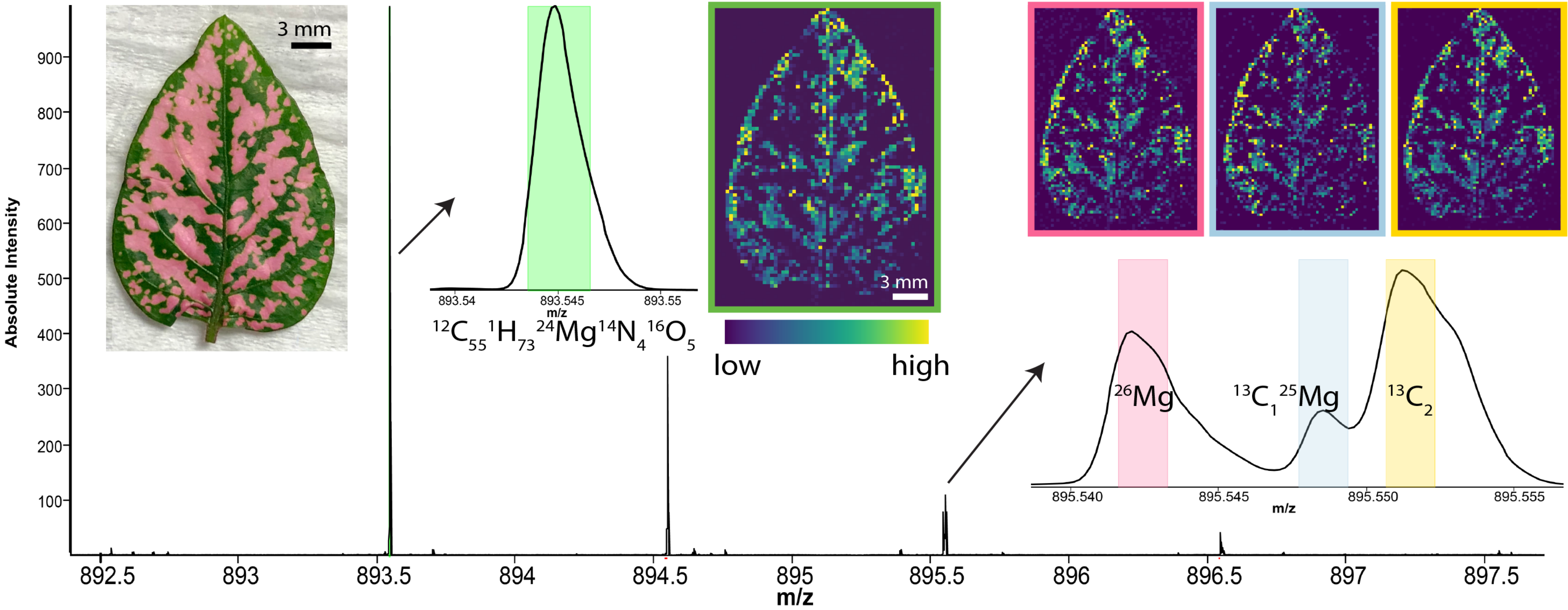
What does a Mass Spectrometer Look Like?

Pictured here is a Fourier Transform Ion Cyclotron Resonance (FT-ICR) instrument. It is similar to an MRI, but much more powerful.

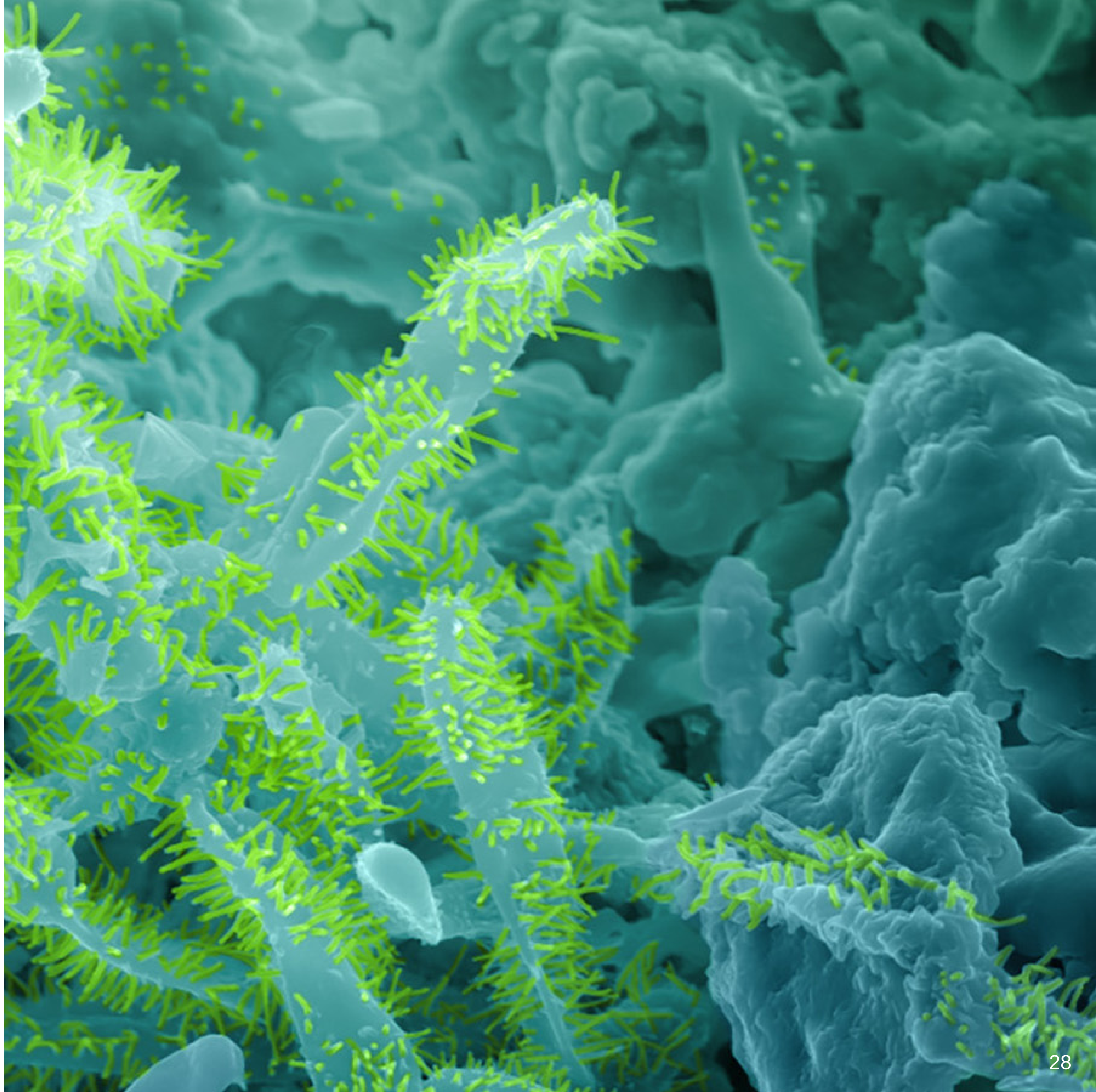
Putting it all together



Using the lasers we discussed previously, we can turn the MS instrument into a type of microscope to observe the chemical changes across an entire leaf.

Thank you

Dr. Kristin Burnum-Johnson
Dr. Paul Piehowski



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Join us for our next webinar

Implementing a Vision to Create and Deploy the Airport Risk Assessment Model (ARAM)

Tuesday, November 10, 2020 | 7:00 pm

Zoom

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THANK YOU!

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