Tiny Earth:

crowdsourcing antibiotic discovery

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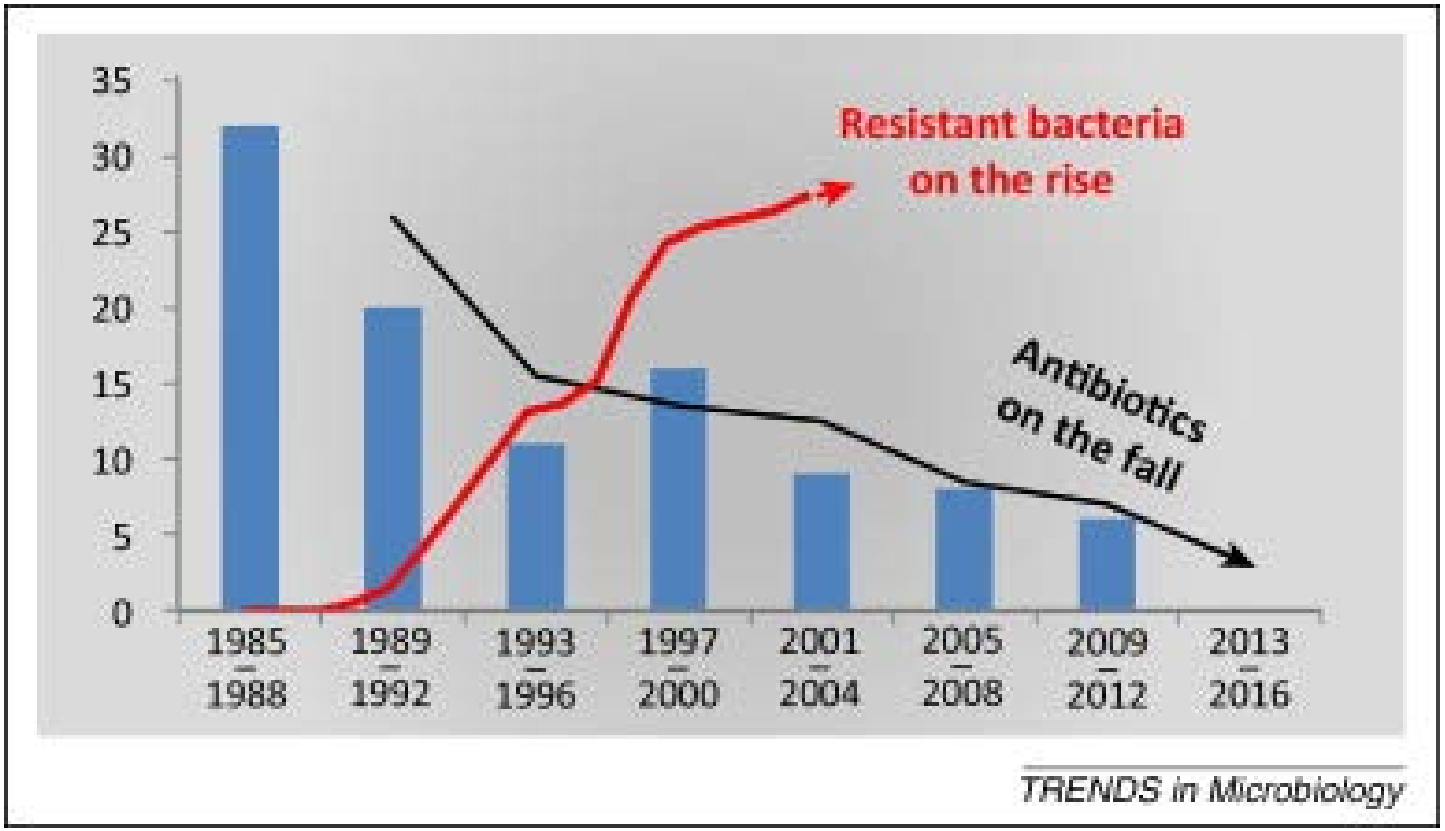
Forces Driving Tiny Earth

- Need for more STEM and STEM-literate college graduates
- Soil crisis
- **Antibiotic crisis**

A Growing Crisis

Increasing Resistance Among Pathogens

Shrinking Pipeline of New Antibiotics



Report Led by Lord Jim O'Neill

Health

Take over pharma to create new medicines, says top adviser

By James Gallagher
Health and science correspondent, BBC News
Send email to with subject "Shared from BBC News"

https://www.bbc.com/news/health-47719269

Review on Antimicrobial Resistance
Tackling drug-resistant infections globally

TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY:
FINAL REPORT AND RECOMMENDATIONS

THE REVIEW ON ANTIMICROBIAL RESISTANCE
CHAIRED BY JIM O'NEILL

MAY 2016

https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf

What is Tiny Earth?

- Introductory undergraduate course in which students discover antibiotic-producing bacteria from soil
- Started in 2012 at Yale with 6 students; now ~10,000 students/year
- Instructors are trained to maintain course fidelity
- At end of course, send bacteria to Chemistry Hub

According to the US Department of Commerce, women have seen no employment growth in STEM jobs since 2000.

Women = 24% of STEM workforce

Women & Minorities =

- 70% of College Students
- 45% of STEM Degree Holders

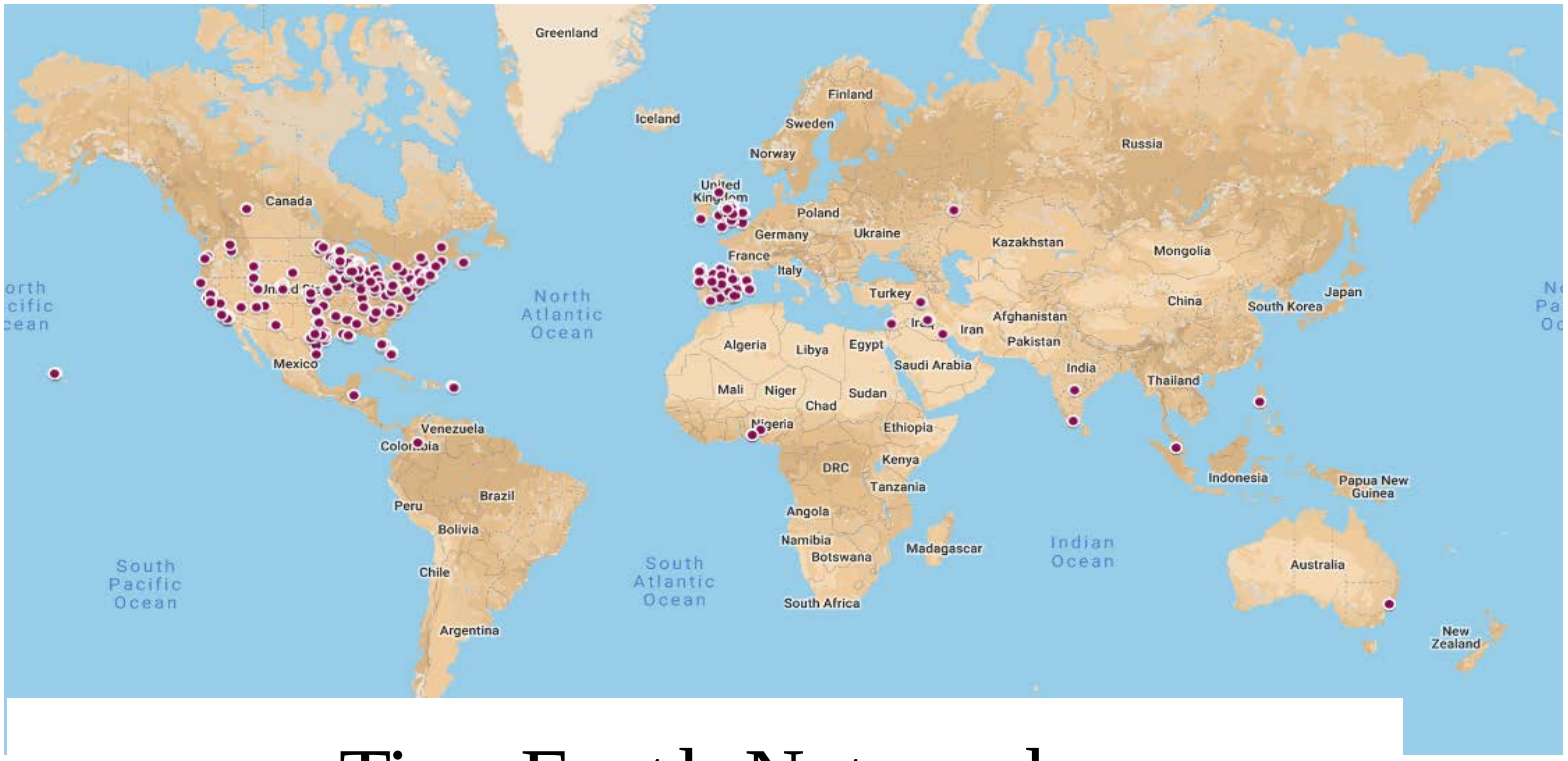
The Department of Commerce's Women in STEM: A Gender Gap to Innovation (August 2011) revealed that, although they represent a mere 24% of the STEM workforce, women earn on average 33% more when they work in these high-growth fields.

In K-12 education, girls and boys don't significantly differ in their abilities in math and science, but do differ in their interest and confidence in STEM subjects

In higher education, the rates of science and engineering coursetaking for women shift at the undergraduate level and gender disparities begin to emerge

In the STEM workforce, women remain underrepresented in the science and engineering workforce, with the greatest disparities occurring in engineering, computer sciences, and physical sciences

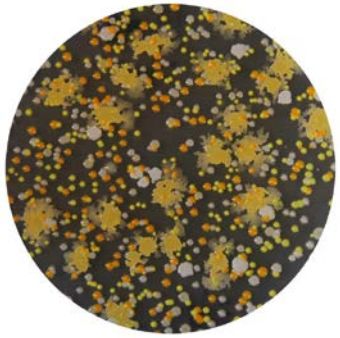
Growth of Tiny Earth Network



Tiny Earth Network
10,000 students per year

Identify antibiotic-producing soil bacteria

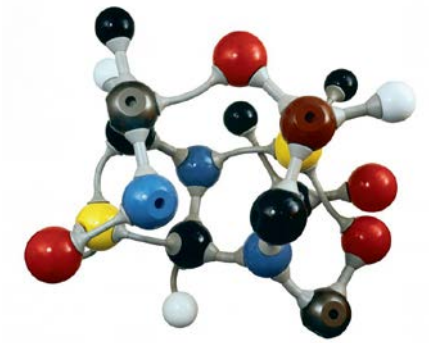
Collect soil sample



Grow bacterial colonies

Isolate bacteria

Test for antibiotic activity against six ESKAPE relatives + yeast and protist



?

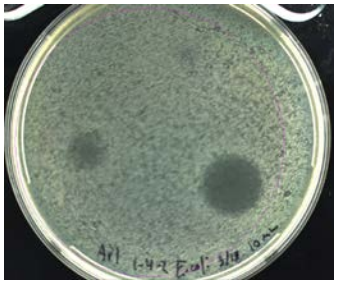
- This course focuses on examining soil. (nature's natural pharmacy)
- This is particularly relevant since more than 2 out of every 3 antibiotics in use are derived from soil bacteria and fungi.
- Through a series of student-driven experiments, students collect soil samples, grow bacterial colonies, isolate bacteria, test for antibiotic activity (against clinically-relevant microorganisms), and characterize those showing inhibitory activity.
- Students input information on each sample into our database throughout the course.
- (We are currently fundraising to establish a chemical hub to provide the missing link with the pharmaceutical industry.)
- Tiny Earth's approach provides a platform to crowdsource antibiotic discovery by tapping into the intellectual power of many student researchers concurrently addressing a global challenge and advances promising candidates into the drug development pipeline.

Tiny Earth Chemistry Hub

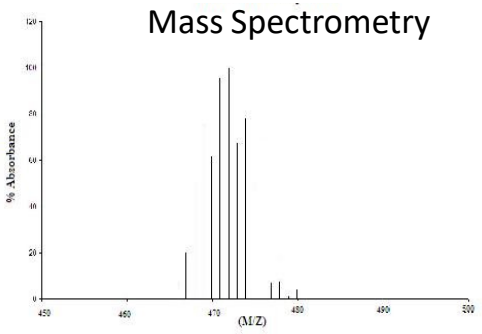
Tiny Earthlings
sign MTA
send strains to Wisconsin

Methanol
Culture
extract

2-Butanol
culture extract



Ethyl Acetate
Culture extract



PacBio genome sequencing

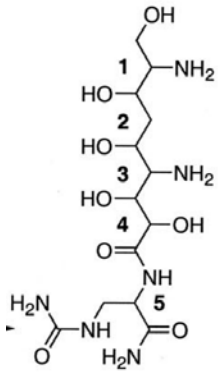
JGI
JOINT GENOME INSTITUTE
DEPARTMENT OF ENERGY

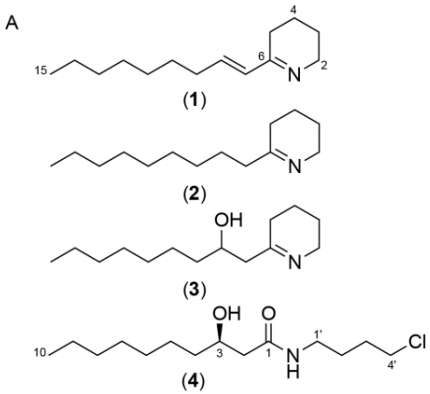
The Tiny Earth Chemistry Hub

- Distributed network headquartered at the Wisconsin Institute for Discovery
- Partner Chemists —
  - Jason Crawford (Yale)
  - Marcy Balunas (U Conn)
  - Pieter Dorrestein (UCSD)
  - Frank Schroeder (Cornell)

Why We Still Discover New Antibiotics in the Soil Microbiome (that Big Pharma Missed)

- New screening methods
  - Plant disease assay
  - Bacterial mixtures
  - Bacterial stress





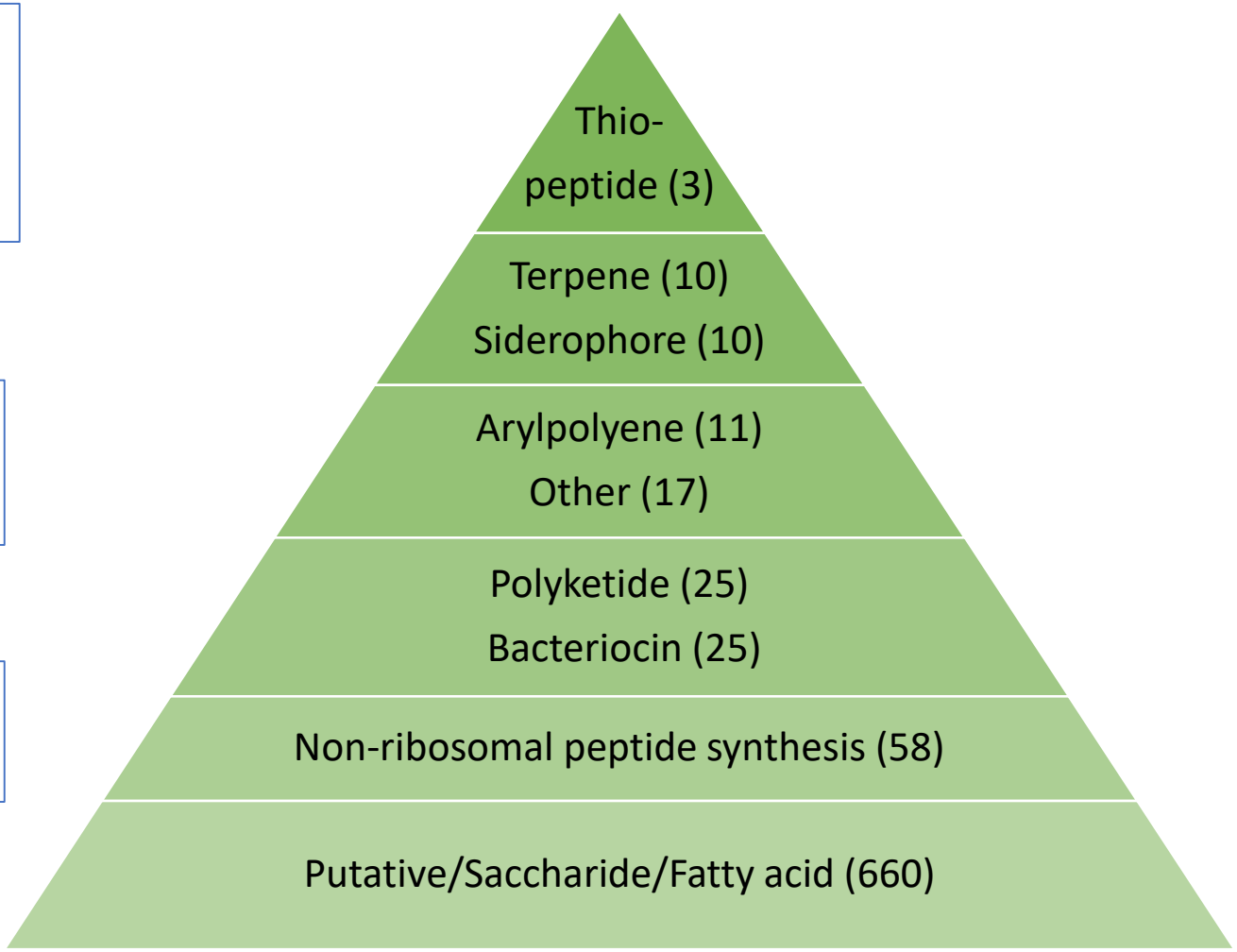
- New targets
  - *Acinetobacter*
  - Gram-negative bacteria
  - Oomycetes
  - Narrow spectrum of target species
- Soil diversity coupled with prioritization
  - Volume of screening—99% rediscovery ok
- Methods innovation
  - Students not bound by dogma—PDA

Novel biosynthetic gene clusters

Tiny Earth antimicrobial-producing isolates

22 sequenced genomes

824 BGCs



APE = aryl polyene, usually a pigment

Tiny Earth Future

- Expand network worldwide
- Continue to build strain collection
- Expand structural chemistry effort
- Expand efforts to educate the public about antibiotics and soil
- Funding

Tiny Earth Leadership

Nichole Broderick (U Conn)
Amanda Hurley
Jen Heinritz
Mara Beebe
Marc Chevrette
Deepa Acharya

Controlled Sm tx had no stable long-term effect on the prevalence of Sm and Tet ARG in flowers, leaves, and soil samples of orchards, nor did it significantly alter the bacterial populations of the soil