HHMI
HOWARD HUGHES
MEDICAL INSTITUTE

Hands-on Learning and Diversifying Science

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SOME BIOLOGICAL PROPERTIES OF α ACETYL TRILYSINE:

Effect on growth of *E. coli.* lysine auxotroph and use in derepression of lysine pathway

Richard Losick

A Senior Thesis

Submitted to the Chemistry Department of Princeton University

in Partial Fulfillment of the Requirements for the Degree of

Bachelor of Arts

May 1, 1965

spun down during linear growth. Crude extracts were assayed for the specific activities of aldolase, dihydrodipicolinic acid reductase, and racemase (VII). For aldolase and racemase growth on α acetyl trilysine caused about a two-fold increase in specific activity over the control. For dihydrodipicolinic acid reductase, however, specific activity increased fifteen-fold.

TABLE VII

Specific Activity of the Enzymes

Peptide	aldolase	dihydrodipicolinic acid reductase	racemase
α acetyl trilysine	7.7	0.153	0.0106
lysine	2.8	0.010	0.0063

page — 1 the cut off at n = 4 is also appropriate as a model system

fig 19 — between cu2 1 & 2 ?

page 7 — .96 ml 1M KHCO3 to what? its really .096

page 16 — pyridoxal P

page 16 table III — units of decarboxylase more appropriate than conc.

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page 24 — should have pointed out initial rate of growth on peptide same as lysine

page 39 bottom argument n.g.

Fig 7 misnomed — Growth not rate of growth
growth on α-acetyl Tetra should be explained
does impurity of ε acetyl tetra explain this

Fig 8

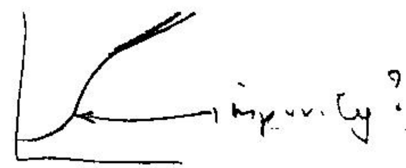


Fig. 9 - average growth rate includes
speed up due to ε acetylated impurity

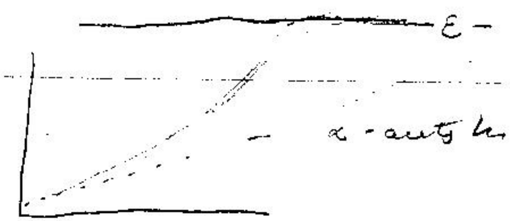


Table VII units?

Page 39 — bad K_m for enzyme.

Fig 11 DAP = really lysine?

THE JOURNAL OF BIOLOGICAL CHEMISTRY

Author(s):

Richard Losick and Charles Gilvarg

Title:

Effect of α-acetylation on Utilization of Lysine Oligopeptides in <u>Escherichia Coli</u>

Comments:

This paper contains a clear and concise presentation of new material and I recommend acceptance for publication in the J. Biol. Chem. The following comments are intended to help improve the paper if the authors so desire.

Fig. 5, 6 and Discussion, p. 16 - It is not indicated whether the size of inoculum affects the subsequent Klett unit/hour linear growth rate achieved on a given concentration of α-acetyltrilysine. This question becomes especially important in view of the extended discussion on p. 16 of the postulate that the linear growth rate reflects dilution of a constituent, such as a transport system, essential for growth on α-acetyltrilysine. Such a theory predicts that the absolute linear growth rate established for any given α-acetyltrilysine concentration will be proportional to the inoculum size. If this is not so, the theory may need to be modified or discarded.

this shows the referee really read, understood and appreciated the paper

Table 2 - The enzymes assayed are assigned different trivial names in the legend and in the table proper (e.g. aldolose <u>vs</u> condensing enzyme) which is quite confusing.

Figure 2 - The legend might more clearly indicate that (b) represents a reconstructed mixture while (c) is chromatography of the actual mix obtained after acetylation. This is very clear in the text but less clear in the figure.

Reasons for Joining a Lab

Learning something, however tiny, that no one ever knew before!

Having a mentor

“Mentor, a trusted counselor or teacher.”

My Princeton mentor sent me to MIT!

What I do at Harvard

The Problem

Many students who enter college indicating a intention to major in science fail to do so.

Students from disadvantaged backgrounds are at highest risk for dropping out of science.

Why

Large and impersonal entry level science courses.

Disconnect between learning science and doing science.

1. Increasing Diversity in Science

2. Creating cross-disciplinary project laboratories

3. Activity- based learning in large courses

IDEAS

Increasing Diversity and Educational Access to Science

Aimed at entering students with a strong interest in science who come from disadvantaged backgrounds.

I scour the freshman class to find such students!

Principal features

The key feature is to engage students beginning in their *first* year in a long-term, inquiry-based project with a Professor.

Students are paid for doing research during the term and full time over the summer in lieu of conventional jobs.

A community is created in which upper classmen help mentor entering students.

•58 current and past students: 22 are African American, 11 are Hispanic, 2 are from rural school systems, 13 are from economically disadvantaged backgrounds, and 9 are from developing countries.

•Among the 30 alumni, 29 remained science majors and all remained in research.

• Among alumni, 2 are in MD/PhD programs, 16 in or are applying to MD or DMD programs, 10 are either in graduate school in a STEM field or applying.

Endicott House

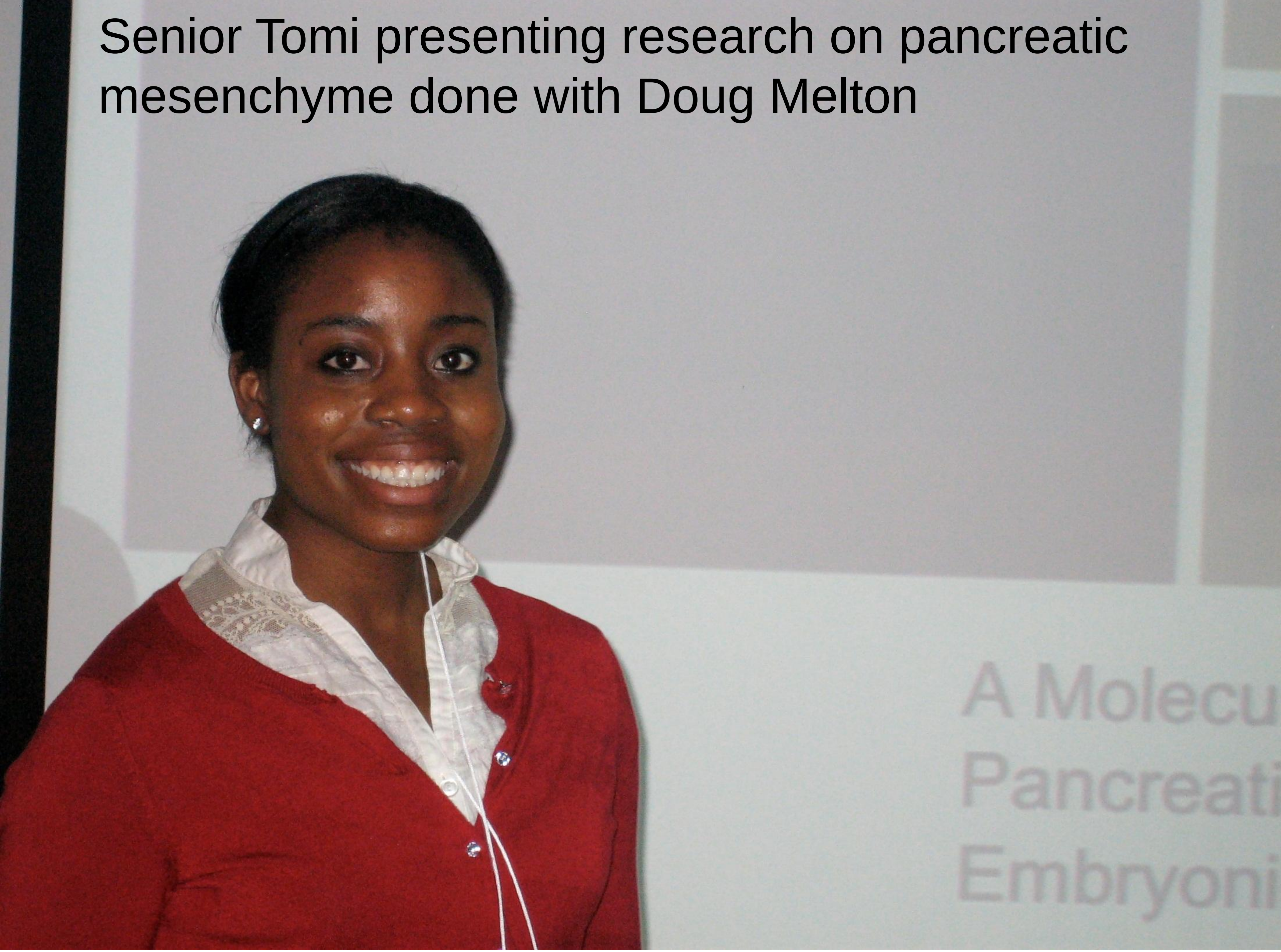

Shola in residency at Columbia
Sawalla at Harvard Med
Tobi Harvard Med
Diana Stanford Med
David in Media Lab at MIT
Egle doing PhD at Stanford
Vera doing PhD at Penn

Ying Qi “Shirleen” Soh
David Page’s Group

David Sengeh
Biomechatronics Group
Media Lab

http://globalchallenge.mit.edu/teams/view/192

Senior Tomi presenting research on pancreatic mesenchyme done with Doug Melton



Sam presenting on fungal diversity research with Anne Pringle

Sam will be going to graduate school at Michigan State in Plant Biology!

Michael: “I want to prove theorems. I want to discover something new and make a contribution to mathematics….”

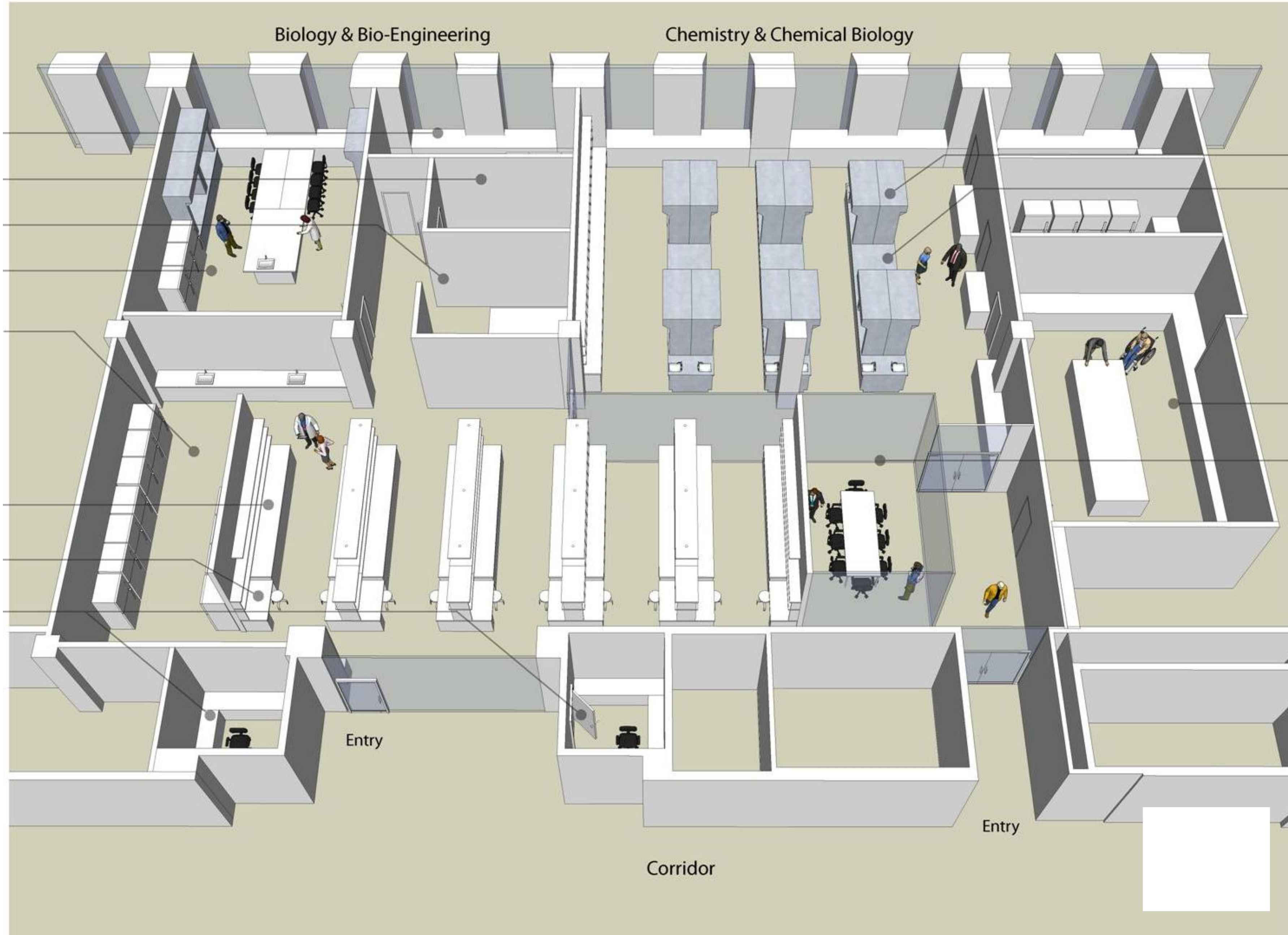
Rediet came to Harvard from Ethiopia with a love for mathematics. She will study “algebraic combinatorics” with Richard Stanley of MIT.

Seeding IDEAS!

HOFSTRA UNIVERSITY

OHIO STATE

MICHIGAN STATE


Biology & Bio-Engineering
Chemistry & Chemical Biology
Entry
Entry
Corridor

Undergraduate Research Laboratories in Science & Engineering

Multiple disciplines in the same facility

organic chemistry, bioengineering, stem cells, molecular biology , neurobiology

The cheese project, Spring 2010

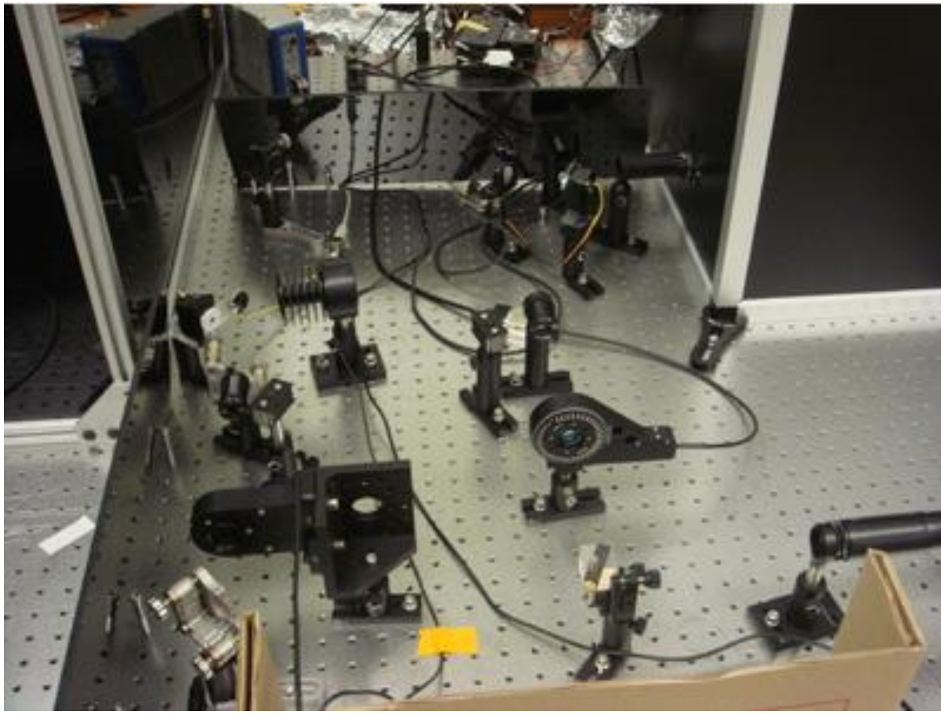
Exploring the microbial diversity in cheese

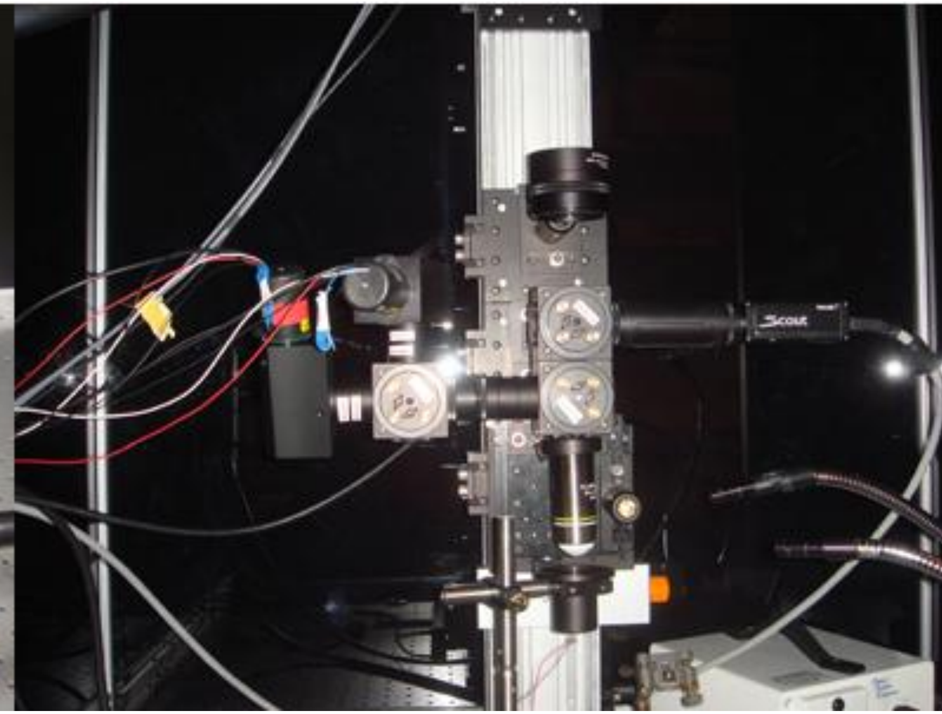
Sample collection (and tasting) at Formaggio Kitchen

→ Culturing microbes in the lab → Extraction of DNA from isolates →

→ Extraction of community DNA → PCR and clone library construction →

Sequence-based identification of microbial species





Z-stack from bottom to top of zebra fish brain after laser activation of a neuron

Two other projects!

Life before proteins: copying genetic information without enzymes

Students determined reaction rates for non-enzymatic polymerization of RNA.

Identification of the DNA target sequence recognized by the neuronal protein, THAP5

Students used SELEX to determine the DNA-binding site for a regulatory protein implicated in neurological movement disorder (dystonia).

Teaching Molecular Biology (MCB52)

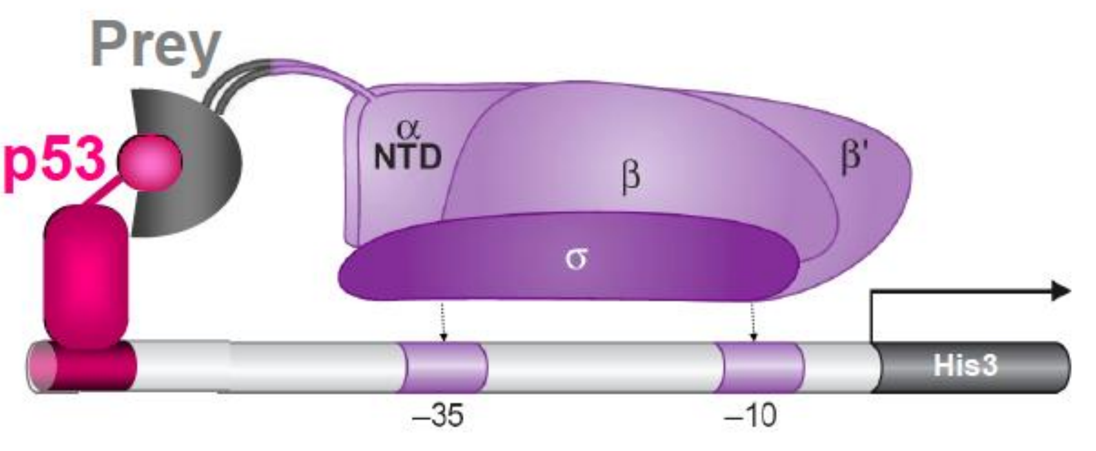
How do we introduce “ownership” and “discovery” into large laboratory courses?

How do we actively engage students in large lectures?

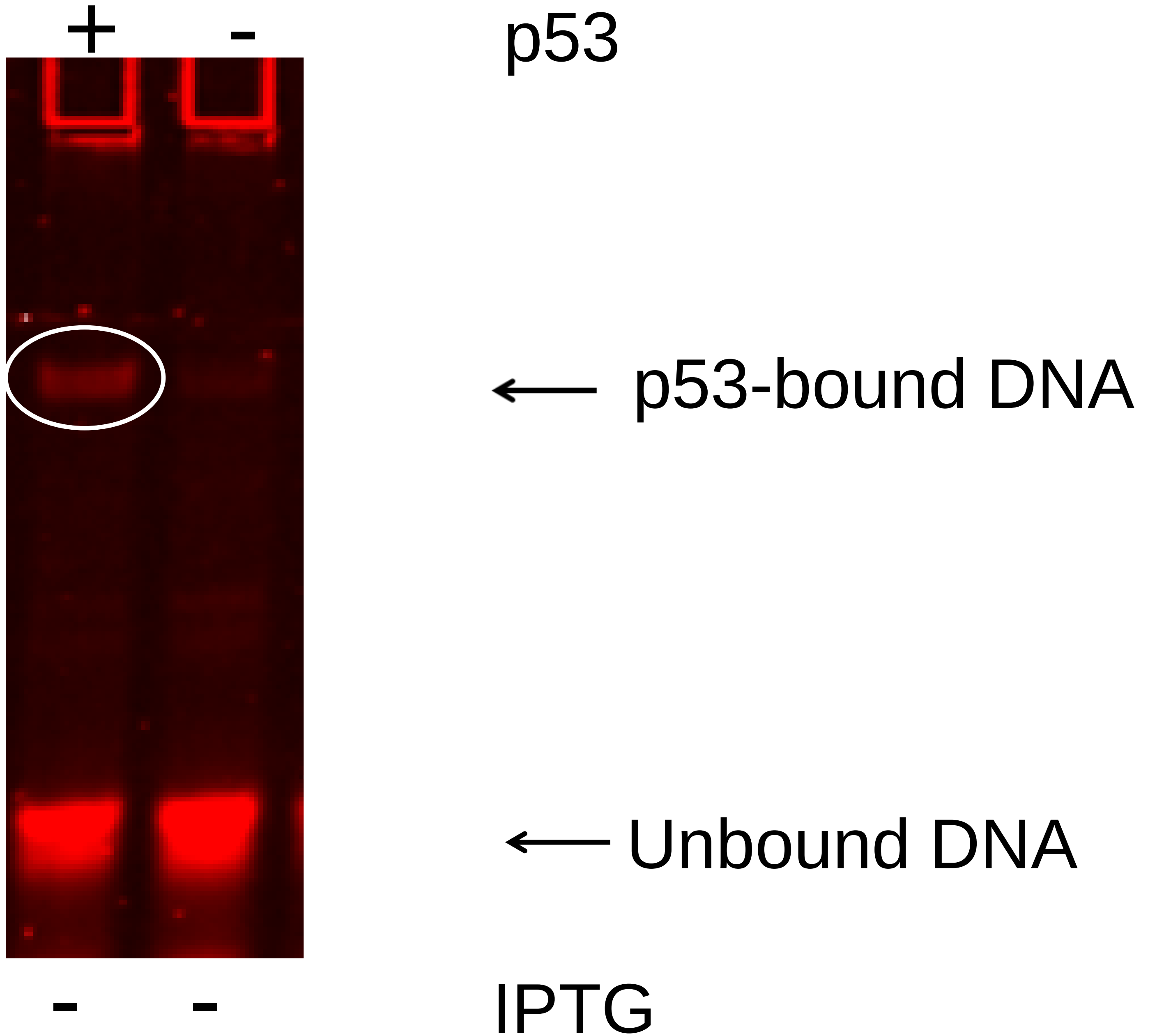
Bacterial Two-Hybrid with p53

- Students get their own hits, send samples for sequencing, and BLAST the results to identify their hits.

- Teams of students pick the best hits, clone genes into a vector for IPTG-induced expression, check for expression by western blot, and then perform EMSAs.



Students' Electrophoretic Mobility Shift Assays



A Sampling of the Exciting Results!

- 108 unique hits
- 9 hits appeared two or more times
- 2 known interactors
- Several hits with similarity to known interactors
- Many with connections to cancer
- Multiple hits with little known information

MCB52 students in action

Discussing two-hybrid on the white board

Stunts!

Crab claw model for RNA polymerase

A, P and E sites on the ribosome

SCIENCE EDUCATION

Changing the Culture of Science Education at Research Universities

W. A. Anderson,[1] U. Banerjee,[2] C. L. Drennan,[3] S. C. R. Elgin,[4] I. R. Epstein[5], J. Handelsman,[6] G. F. Hatfull,[7] R. Losick,[8*] D. K. O'Dowd,[9*] B. M. Olivera,[10] S. A. Strobel,[6] G. C. Walker,[3] I. M. Warner[11]

Professors have two primary charges: generate new knowledge and educate students. The reward systems at research universities heavily weight efforts of many professors toward research at the expense of teaching, particularly in disciplines supported extensively by extramural funding (*1*). Although education and lifelong learning skills are of utmost importance in our rapidly changing, technologically dependent world (*2*), teaching responsibilities in many STEM (science, technology, engineering, and math) disciplines have long had the derogatory label "teaching load" (*3*, *4*). Some institutions even award professors "teach-

Science and teaching go hand-in-hand

I am a better teacher for being a scientist.

But I am also a better scientist for being a teacher.