EXPLORING FIRST YEAR MEDICAL STUDENT LEARNING EXPERIENCES IN AN INTERDISCIPLINARY THERAPEUTIC ENZYME DESIGN LAB INTEGRATING BASIC SCIENCES AND ENGINEERING

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Carle Illinois COLLEGE OF MEDICINE

INTRODUCTION

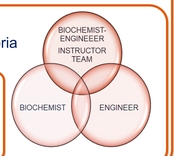
- Carle Illinois College of Medicine has developed engineering-infused curriculum aligned with its mission to train future physician-innovators to transform and democratize health care.
- Phase 1 curriculum is taught by Instructor teams of basic scientists, clinicians, and engineers.
- For the ***Foundations: Molecules to Populations*** **course,** an **engineer-biochemist instructor team** (Bhalerao-Yodh) developed a **therapeutic enzyme design lab**[1] for Carle Illinois inaugural student class as a way to implement its engineering-integrated curriculum at the basic science level.

PHASE 1 FOUNDATIONS: MOLECULES TO POPULATIONS COURSE

Week 2: Biochemical Basis of Disease
- Proteins, Enzymes, Static & Dynamic Equilibria in Biochemical Systems

Therapeutic Enzyme Engineering/Design Lab

A basic-science-engineering activity that integrates biochemistry, informatics, product design and marketing communication.



- For the 2nd run of this lab, the same instructor team **piloted a mixed-methods research study** to evaluate student learning experiences and outcomes from this integrative activity. This poster outlines the results of this study.

STUDY AIM

RESEARCH QUESTIONS TO STUDY EFFECTIVENESS OF ENZYME-ENGINEERING DESIGN LAB

Q1: To what extent do student artifacts reflect attainment of activity learning goals?

Q2: What are the student perceptions of this activity?

REFERENCES

1. Yodh, J. and Bhalerao, K. (2019, May) Poster Presentation at 7th *Internat. Conf. Assoc. Biochemistry Educators*, Tuscon, AZ.
2. Bhalerao, K. *ABE Principles: Biological (available upon request)*. 2017 ABE@ILLINOIS: http://abe-bhaleraolab.age.uiuc.edu.
3. *BRENDA, The Comprehensive Enzyme Information System.* http://brenda-enzymes.org.
4. *KEGG: Kyoto Encyclopedia of Genes and Genomes https://www.genome.jp/kegg/.*
5. *ACTIVASE/Alteplase https://www.activase.com/.*
6. Greene, J. C. (2007). *Mixed methods in social inquiry* (Vol. 9). John Wiley & Sons.

METHODS

ENZYME ENGINEERING LAB

PREPARATION
- Lecture: Enzyme Catalysis, Kinetics, Regulation
- Engineering Reading: Static and Dynamic Equilibria in Biochemical Systems[2]

LAB 1ST HOUR
- Create 5 teams of 6-8 students each
- Students use enzyme/genomic informatics databases BRENDA[3] and KEGG[4] to research genetics, physical properties, classification, kinetics, and structure-activity relationships for the commercial enzyme, **Alteplase**[5]

LAB 2ND HOUR

Teams present and submit a proposal for a re-engineered product design that includes a:

(i) new formulation of Alteplase including marketing name.

(ii) value proposition for the new product.

MIXED METHODS[6] STUDY

I. Learning Rubric

A rubric designed by the instructors was applied to each team's research summary and innovation proposal to assess attainment of the learning goals. Each assignment was rated by both instructors, and then individual ratings were discussed to reach a combined/resolved score.

MIXED METHODS RESEARCH STUDY QUESTION 1 *To what extent do student artifacts reflect attainment of activity learning goals?*	
LEARNING RUBRIC *Rating Scale: 1 – Inadequate, 2 – Adequate, 3 – Exceptional*	
RUBRIC QUESTION 1	1) How well did the students demonstrate knowledge of how to use KEGG and/or BRENDA informatics databases to obtain the enzyme class, sequence, organismal source, structure, kinetic parameters of the natural and synthetic variants of alteplase?
RUBRIC QUESTION 2	2) How well did the students demonstrate ability to propose a new formulation of alteplase based on knowledge obtained in #1?
RUBRIC QUESTION 3	3) How well did the students demonstrate an understanding of value propositions including Client and Customer Base?

II. Focus Group

A one-hour post-lab focus group with 5 student volunteers enabled exploration of student perceptions of the activity. Students were asked to discuss the following 7 questions during the session. Transcripts of audio-recorded session were used for inductive thematic analysis.

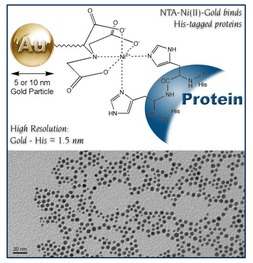
1. What were some aspects of this activity that you enjoyed?
2. What were some aspects of this activity you thought could be improved?
3. What aspects of this activity helped reinforce your learning of enzyme catalysis and kinetics?
4. Did this activity help you understand how to use KEGG and BRENDA database tools?
5. Did it help to work with the team on learning the informatics tools?
6. Did it help to work within a team on generating a value proposition?
7. Is there anything else you would like to say about this enzyme lab activity that we could apply for next year?

RESULTS

EXAMPLES OF NEW ALTEPLASE FORMULATIONS

Safeteplase™ - incorporate an allosteric inhibitor site to bind downstream inhibitors of enzyme to lower patient hemorrhage risk.

Clotbegone™ - incorporate a binding site for gold nanoparticles to increase efficiency of drug delivery and uptake and encapsulate within different size nanospheres to fine-tune effective dose and therapeutic time window.
(image right – from student team proposal)



DOCUMENT ANALYSIS USING THE LEARNING RUBRIC

1. Work produced by each student team was at an acceptable level with respect to all 3 learning rubric goals.

LEARNING RUBRIC - RESEARCH STUDY QUESTION 1: *To what extent do student artifacts reflect attainment of activity learning goals?*			
Rubric Questions - How well did students __?	Q1: Demonstrate knowledge of how to use KEGG and/or BRENDA informatics databases?	Q2: Demonstrate ability to propose a new formulation of alteplase based on informatics findings?	Q3: Demonstrate an understanding of value propositions?
Combined (Resolved) Rater Score	1 –Inadequate 2- Adequate 3- Exceptional		
AVERAGE (5 Student Teams)	2	2.2	2.2

2. Inter-rater differences may reflect raters' disciplinary backgrounds
(A low but consistent inter-rater reliability (53%) was observed.)

RATING DIFFERENCES DUE TO DISCPLINARY BACKGROUNDS (Example, Safeteplase) Learning Rubric Q2: Biochemist vs. engineering view of brainstorming		
Rater 1 (Engineer) Score 2 (adequate)	Rater 2 (Biochemist) Initial Score 1 (inadequate)	Resolution Combined/Resolved Score 2 (adequate)
"There is a kernel of an idea - the allosteric inhibition that could reduce or control its activity. How that affects the degradation is unclear."	*"More indepth research needed on downstream inibitor (PA1) mechanism of action and the proposed allosteric site features. Value proposition had incorrect information on impact of PA1 inhibition on activity."*	*Rater 2 (biochemist) increased score after discussing with Rater 1 (engineer) who clarified that engineering brainstorming sessions only require coming up with a generally plausible mechanim because there will be multiple iterations for the team to research further into molecular details and correct errors.*

INDUCTIVE THEMATIC ANALYSIS OF FOCUS GROUP: EXAMPLES

THEME 1: Incorporation of Informatics and visualization tools promoted creativity for applied learning.
"It made it more accessible because I don't have a strong protein engineering activity background compared to a lot of other people,"

"I thought the protein visualization tool was really cool. It's something I didn't know existed and it really made the creative process more tangible."

THEME 2: Adding a therapeutic application motivated learning.
"I think the value proposition was important because when I did basic research before, I never really looked into who would actually want this technology."

"Having a purpose made me want to engage with all the tools and having an overarching goal for why we are doing these things helps drive my learning."

THEME 3: Working in teams with students with different training backgrounds enabled greater understanding.
"I think having some people with more lower level (basic science) knowledge and other people with more industry or public health higher level experience really helped our group to see how the value proposition and innovation works"

THEME 4: Adding a competition element motivated team innovation.
"The competition gave me a lot of motivation to be better than other groups and come up with a different modification to make a better product."

CONCLUSIONS

1. **A mixed-method evaluation** demonstrated this lab exercise successfully engaged students in integrating basic and clinical sciences with engineering innovation.
2. **Learning activity structure** promoted creativity and teamwork between students with different training backgrounds that positively impacted students' motivation and their ability to apply foundational concepts to medical innovation.
3. **Significance:** Incorporation of an application-driven, team-based task which links basic science knowledge to product design and marketing provided the drive for learning and ideation.

FUTURE IMPROVEMENTS

RUBRIC

1. Provide students the rubric in advance to motivate better translation of group discussion into tangible outcomes on submitted summary.
2. Convert the rubric rating scale from a 3- to 5-point scale to further differentiate outcomes and address the impact of differences in rater's disciplinary background on inter-rater reliability.
3. Fine-tune rubric questions to better focus on how students apply foundational knowledge towards innovation.

LEARNING ACTIVITY

1. Work in smaller teams of 3-4 students so everyone stays engaged.
2. Provide more initial exercises on how to use information garnered from these databases to bring everyone to the same level prior to the innovation activity.
3. Provide follow-up opportunities for teams to take a deeper dive into their innovation proposals.

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