Undergraduate Students' (Mis)understandings of Mutation

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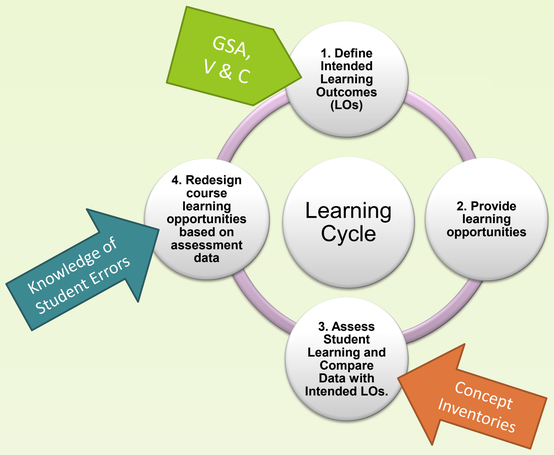
Background

Evidence is Crucial to the Continuous Improvement of Courses and Programs



Learning about Genetics is Important, but Challenging

- Nearly 60% of entering STEM students do not graduate
- 80% for under-represented students (Maltese and Tai, 2011)
- Genetics is a well-known point of difficulty (Cimer, 2012; Doughtery, 2009)
- Integration of genetic knowledge and technology into modern life is high
- Citizens will need to make decisions regarding ethical uses of genetic technology

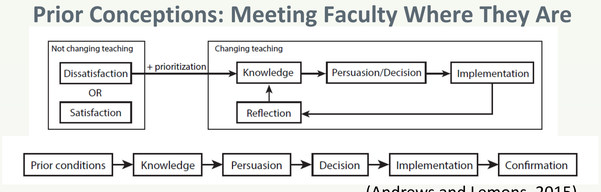
Known Difficulties

- Complex terminology and concepts (Bahar 1999, Raia 2005)
- Critical reasoning and problem-solving (Facione 2015, Karagoz and Cakir 2011)
- Pace of change/ambiguity/lack on consistency (Gericke and Hagberg 2007)
- Multiple scales and relationships among scales
  - Micro-meso-macrocosm (Niebert and Gropengiesser 2015)
  - Symbolic and mathematical (Sutton, 1996)

Prior Conceptions: Meeting Students Where They Are

- What is a mutant?
- What is a mutation?
- How do you know that?
- Where did you learn it?

Prior Conceptions: Meeting Faculty Where They Are



(Andrews and Lemons, 2015)

- Faculty persist in the "way they were taught"
  - Personal evidence over data (Andrews and Lemons, 2015)
- Habit change
  - Make it personal, make it visible, make it easy

Objectives

- To design an easy-to-use, short assessment tool for mutation concepts than can provide instructors with valid and reliable data as well as be used to measure learning gains related to an instructional intervention
- To identify common student errors that may include true misconceptions, as well as factual errors and terminology misuse that can be targeted for instructional intervention

Methods

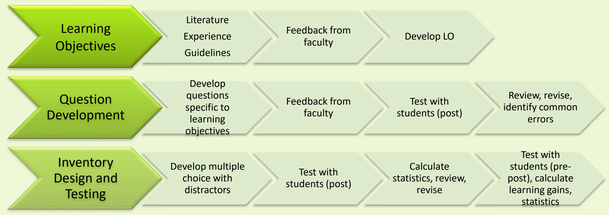


Figure 1. Inventory Development, Design, and Testing Workflow

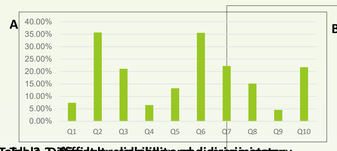
Table 1. Mutation Concepts and Learning Objectives

Concept	Learning objective Students should be able to:	GSA Genetics Learning Framework example Learning Objectives
Mutations are changes to DNA.	Define mutation.	
Mutations can be point mutations or involve larger segments of DNA. These may or may not have different outcomes at the protein level.	Categorize changes to DNA and predict the outcome of these changes on a protein produced from the altered DNA using the genetic code.	"Explain how the genetic code relates transcription to translation"
In multicellular sexually reproducing organisms, mutations may occur in somatic cells or in germ-line cells.	Differentiate between somatic and germline mutations and predict the inheritance patterns of each type of mutation	"Compare and explain the inheritance of germline and somatic mutations." "Distinguish between loss of function and gain of function mutations and their potential phenotypic consequences."
Mutations may be induced by physical, chemical or biological processes.	Predict the nature of changes to DNA exposed to intercalating agents, base analogs, and radiation.	"Describe how mutations arise and how environmental factors can increase mutation rate. "

Results

Table 2. Difficulty, reliability, and discriminatory power of items in Pedigree Concept Inventory

Learning objective Students should be able to:	Item	Sample Size (n)	Index of Difficulty	Discrimination Index	Point-biserial Correlation
Define mutation.	1	121	0.31	0.52	0.31
	2	121	0.51	0.63	0.65
	3	121	0.37	0.60	0.38
Categorize changes to DNA and predict the outcome of these changes on a protein produced from the altered DNA using the genetic code.	4	121	0.34	0.30	0.13
	5	121	0.43	0.55	0.34
	6	121	0.68	0.65	0.48
	7	121	0.54	0.73	0.46
Differentiate between somatic and germline mutations and predict the inheritance patterns of each type of mutation	8	121	0.49	0.70	0.44
	9	121	0.65	0.65	0.40
	10	121	0.56	0.66	0.39
Mean			0.49	0.60	0.40



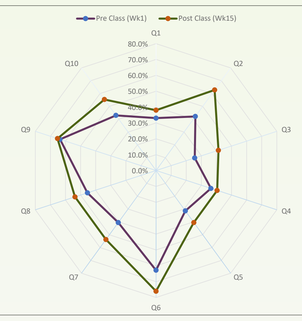


Table 3. Difficulty, reliability, and discriminatory power of items in Pedigree Concept Inventory

	PRE (WK1)	POST (WK 15)	SIG DIF?
Q1	33.1%	38.0%	no
Q2	42.1%	62.8%	** 0.0002
Q3	25.6%	41.3%	** 0.0021
Q4	36.4%	40.5%	no
Q5	31.4%	40.5%	no
Q6	62.8%	76.0%	** 0.0088
Q7	40.5%	53.7%	**0.0160
Q8	45.5%	53.7%	no
Q9	63.6%	65.3%	no
Q10	43.0%	55.4%	** 0.0158

Figure 2. Learning Gains (A) and Comparison of Pre-test and Post-Test Percent Correct (B). n =121

Table 5. Representative Changes in Student Errors

Define Mutation	Correct	Referencing Functioning as main Criterion	Mutations are only in coding region	Error in cause-effect reasoning	A Mutation is Any Change
Q2 A change in the DNA sequence of a promoter region leads to the overexpression of gene XYZ. (Yes, Change in DNA)	20.66%	-11.57%	1.65%	-10.74%	
Q3 The DNA corresponding to an intron splice site is changed, resulting in inclusion of an intron in the mature mRNA. (Yes - Change in DNA)	15.70%	-2.47%	-4.1%		-4.1%
Categorize changes to DNA	**Correct**	**Trouble with Central Dogma**	**Trouble Reading Univeral Code Table**	**Errors with Fine Detail of Central Dogma**	**Making Assumptions/ Magical Thinking**
Q6. If codon 6 is changed from UCU to CCU, what would be the effect on the protein sequence? (Mis-sense)	7.8%	-8.0%	0.0%	-0.8%	-7.4%
Q7. If the wild-type DNA from question 2 had been TAC TTG ATG CTT CGA GAT instead of TAC TTG ATG CTA TCG AGA, what would be the effect on the encoded protein? (Frameshift)	13.22%	-7.44%		4.13%	-9.92%
Differentiate between loss of function and gain of function mutations	**Correct**	**Mistakenly Referencing Dominance**	**Gene Presence = Gene Expression (not all genes are in all cells)**	**Mistakes in Defining Cancer Suppressor**	**Relating Loss and Gain of Function to Cell, not Protein Function**
Q10. A tumor suppressor gene encodes a protein that normally functions to stop the cell cycle. If this translocation affected that tumor suppressor gene, would you expect this mutation to be considered a loss of function mutation or gain of function mutation? (loss of function because tumor suppressor proteins normally act to stop the cell cycle, but the mutant cannot.)	12.85%	-4.05%	-1.55%	-5.70%	-1.57%

Table 4. Student Errors Regarding Learning Objective 1 with Student Examples

Learning Objective 1: Define mutation.		
Theme	Student Error	Student Example(s)
Definition	Mutation is any change in RNA or protein in the absence of DNA change	Yes, appears to be an insertion mutation because a new amino acid was added to the sequence
	Mutations can only be in the coding regions.	No, Just gene expression is being changed--expressitivity doesn't equal a mutation.
	Mutation requires a functional or phenotypic change	No because there is no change in the function of the rna or proteins
	Assuming the event is a normal process	This is not a mutation, but rather a result of alternative splicing.
	Arguments related to necessity for recurrence	no. more than likely happen once
Central Dogma	Failure to understand the central dogma	yes It is cutting the actual length of it's DNA
	Error in cause-effect reasoning	Yes, An over expression of a gene can lead to a mutation.
Over-reaching	Unsupported assumptions and conjecture	This could be a mutation. A mutation that codes for the protein is not working correctly then this could cause failure, this would lead to a different protein then what you would have. This is a mutation that could be harmful to the organism.
Anthropomorphic	Cellular components have human characteristics	Yes, because if it is not suppoesed to be there then it a mutation. The ribosome did not intend for it to appear thus it is a mutation.

Table 5. Student Errors Regarding Learning Objective 2 with Student Examples

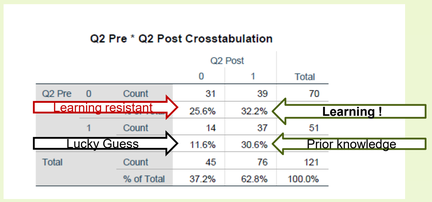
Learning Objective 2: Categorize changes to DNA and predict the outcome of these changes on a protein produced from the altered DNA using the genetic code.		
Theme	Misconception	Student Example
Central Dogma	Basic issues with understanding central dogma including terminology and inability to read a codon table	UAA would signal a stop codon so the transcription would halt
	More nuanced mechanistic problems with central dogma	It would give the protein a second start codon that goes with TAC.
Over-reaching	Unsupported assumptions and conjecture	A stop codon will render the protein non-functional.
Anthropomorphic	Cellular components have human characteristics	DNA needs GAA.

Table 6. Student Errors Regarding Learning Objective 3 with Student Examples

Learning Objective 3: Differentiate between somatic and germline mutations and predict the inheritance patterns of each type of mutation.		
Theme	Misconception	Student Example(s)
Somatic/germline	Misunderstanding relationship of meiosis and mitosis to development, somatic tissue, and/or germline tissue	yes, since the error happened in meiosis, there would be a risk for the kids to have the translocated and develop cancer since it is a germline mutation. Meiosis affects reproduction so that is how it used affect the kids.; Yes because it would transfer to gametes
	Misunderstanding meiosis and mitosis	No because the the error was in meiosis, and meiosis leaves room for genetic diversity and crossing over. Therefore there is a very low chance her kids would have kidney cancer too because meiosis would produce gametes different than the orginal; because half on the genes go to one side and the other half goes to the other.
Over-reaching to other genetic aspects than somatic/germline	Mendelian inheritance patterns or ideas determine outcome	No the kids could get that half from their father; they may receive the mutation, but they may receive the normal gene from the mother; Cross breeding of the two trees.
	Gene expression rather than genetic differences explains mosaicism	Different genes acting in different spots
	Probability of recurrence, not inheritance, determines outcome	Yes because it happened during meiosis and it could happen when her body creates gametes; If he had kids after cancer yes the probability is there because that is now in the gene pool to happen. no. more than likely happen once
Nature of genes, alleles, and mutations	Conflating gene and allele	Because yellow and red are on the same allele, this is possible. Mutation in one of the two sets of genese that created a new allele encoding for yellow.
	All genes are not present in all cells	possibly, if his kids inherited his kidney genes that would; No, the cancer chromosome isn't connected to the reproductive organs
	Misunderstanding mutation	No, hers is a mutation not inherited gene defect.; no. translocations are not hereditary

Table 7. Student Errors Regarding Learning Objective 4 with Student Examples

Learning Objective 4: Predict the nature of changes to DNA exposed to intercalating agents, base analogs, and radiation (ionizing and non-ionizing).		
Theme	Misconception	Student Example(s)
Mutagen mechanism	Misunderstanding mutagen mechanism	It may be that ethidium bromide interacts with the DNA molecule in a why in which it sticks or binds to it. When the mutated DNA is exposed to more ethidium bromide again, a reaction occurs, breaking the chemical off of the DNA.; no, it binds with dividing cells.
	Bromouracil is equivalent to uracil	Uracil could be paired with Guanin and adenine which would result in mutated mRNA and mutated proteins as a result.
	DNA replication occurs in non-dividing cells	No, because the replication of this sequence would change it back to a normal sequence once replicated.
Mutation definition	Any DNA change is a missense mutation	Missense mutation, which means only one base pair is changed.transversion
Over-reaching	Overstating evidence far beyond data given	It has built up an immunity so when re added it is able to resist it affecting it.; Change the process of replication of the dna
	Magical thinking to explain the data	Because the bacterial cell will recognize that there are too many mutations occurring it will reverse back to wildtype to attempt to stop further mutations and start from a baseline. Unfortunately for the bacterial cell this allows us to treat with an antibiotic and without any prominent mutations leading to an antibiotic resistance, the cell will be wiped out.



Q2 Pre * Q2 Post Crosstabulation

			Q2 Post 0	Q2 Post 1	Total
Q2 Pre	0	Count	31	39	70
		%	25.6%	32.2%	
	1	Count	14	37	51
		%	11.6%	30.6%	
Total		Count	45	76	121
		% of Total	37.2%	62.8%	100.0%

Figure 3. Representative Crosstabulation Analysis Showing Learning and Learning Resistance in Pre-test/Post-test Data

Conclusions

- A short, easy-to-use assessment tools was iteratively designed and tested.
- Data from the assessment were shown to be valid and reliable.
- Normalized learning gains were observed following instruction.
- Student written responses showed student errors in many concepts, particularly with respect to:
  - defining mutation as any change,
  - understanding hereditary consequences of mutation for somatic and germline tissues,
  - different terminology and processes related to central dogma
- Analysis of student understanding pre-instruction and post-instruction showed student learning as well as resistance to learning.

Informing Instruction

- Somatic and germline inheritance is a real struggle for students ~ 53% correct in the post (with a great deal of variability)
- Mutation is ANY change
  - Closely related to Cause/Effect reasoning
  - Emphasize Heritability
- Defining a stop codon
  - Transcription vs Translation (~50% of responses pre indicated a nonsense mutation stopped transcription, not translation)
  - Closely related to Central Dogma issues (don't assume students know the basics)
- Magical Thinking
  - Push students to provide a mechanism for their explanations

Future Directions

- The "Tools for Assessment in Genetics (TAG) grant includes 5 short Concept Inventories
  - Mutations & Pedigrees (Validation done Fall 2018, writing papers)
  - Epistasis & Epigenetics (Open ended Questions done Fall 2018, starting theme coding)
  - Polygenic Inheritance, Hardy-Weinberg Calculations & Microevolution (LOs scheduled for Summer 19)
- Ho: Misconceptions Differ in their Persistence
  - What are the misconceptions surrounding these concepts?
  - Which misconceptions stick and which resolve in freshmen vs seniors/grads?
- Ho: With data, we can make more effective, targeted interventions
  - Learning activities designed to specifically address known and common misconceptions

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