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Escape Genetics: An Interactive Classroom Review Session

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The activity described here provides the time and space for college-level students to complete a series of genetics-based problems as a fun, interactive, and fast-paced way to review course content near the end of a semester. Using the template of an escape room not only offers additional exposure to course material, but also simulates some of the time-induced stress experienced by students during a final exam. Having students work together in teams further allows individuals to reflect on their own personal strengths and weaknesses for specific topics covered in the provided clues, while facilitating peer-modeling of successful problem-solving by their teammates.

Keywords: genetics, review, game, problem-solving, escape room

Introduction

Allotting time at the end of a semester to review an entire course-worth of material can be daunting for both the instructor and the students. The objective of this activity is to provide an enjoyable and active environment where students can self-assess their understanding of a variety of topics (especially those involving problem-solving). Described here is an example used in an upper-level genetics course one or two weeks prior to the final exam.

Over the past decade, recreational escape rooms have been popping up all over the world, sending paying participants on quests that involve solving a series of riddles and games to "escape" a room within the allotted hour. These adventure games are not only enjoyable, but also encourage problem solving and collaboration among the participants. While a number of programs with this framework have been designed for primary and secondary classroom settings and are available online, this set-up, including a collection of problems, is designed to challenge 3000-level college genetics students. Although this activity easily lends itself to modifications, the problems highlighted here will come from the following topics within the field of genetics: Punnett squares with Mendelian patterns of inheritance and other extensions, mitosis/meiosis, transcription/translation, chromosome mapping, BLAST searches, epistasis, and population genetics. Additional topics could also be incorporated into this activity, including reading pedigrees and understanding cloning techniques.

While ideally set up during a laboratory meeting, this activity could alternatively be used in a classroom setting, depending on individual time and enrollment constraints. In its original design, this activity limited participation to approximately eight students per one-hour session, having two different groups of students attending the first- or second-half of a 3-hour laboratory meeting and allowing the instructor 30 minutes to re-set the room in between. The initial set up for a room should take no more than an hour, and likely much less, according to its complexity.

Student Outline

Objective

- Review material from lectures to be better prepared for the final exam, specifically in a 3000-level Genetics course with the materials presented here.

Introduction

Due to the nature of this activity, students are provided limited, if any, information or materials prior to their entrance into the laboratory. They may be informed as to the nature of the activity for that day (i.e., it will involve a review) and be given instructions about any elected restrictions. (It may be desired to limit or encourage cell phone usage or web access, depending on the specific problems selected or designed. As written, this activity utilizes a number of scientific websites and benefits from the availability to use internet search engines.)

Materials

A moderate initial financial investment is required for this lab (about $100-150) to purchase a variety of keyed or combination locks and small safes. A total of about 10-15 programmable, lockable items would be ideal, as well as a few supplemental materials, described later. These items can be purchased online or at any number of hardware, specialty, or department stores. After initial purchases are made, no additional costs should be necessary for future iterations of this activity. (Costs can also be curbed if loans or donations are available.) Specific items that can be used include: traditional combination locks, bicycle locks, programmable combination padlocks, alpha-numerical padlocks, keyed padlocks, directional padlocks, bags or boxes that can be closed with the locks you have available, money boxes, lockable suitcase straps, travel-sized mini-safes, "invisible" pens with low-powered UV light source, digital LED message fans, remote-controlled key fobs, USB flash drives, timers, and calculators. Providing an assortment of writing utensils and highlighter is also necessary, as is having a computer available in the classroom to access scientific websites (e.g., NCBI's BLAST database). Examples of problems and clues are included as appendices, along with their answers.

Figure 1. Example of labeled microcentrifuge tubes used in clue that requires students to put samples in the correct order, according to the sequential labs completed during the semester.

Figure 2. Clue provided on the back of a 24-piece puzzle. As Dolly the sheep was cloned in 1996, the correct answer to this clue would be 9-9-6.

Figure 3. Examples of padlocks and luggage straps used in this activity.

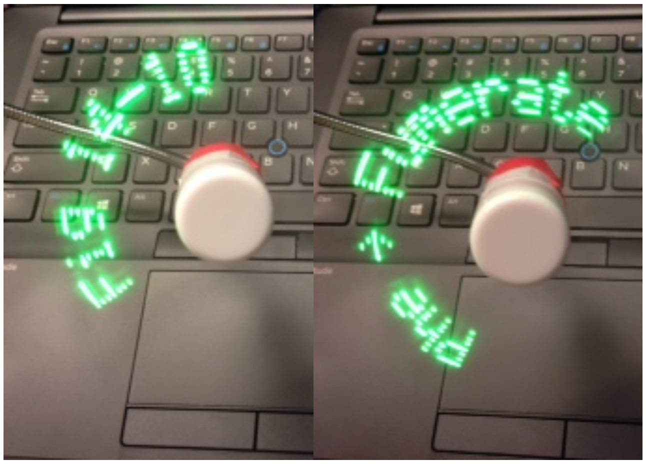

Figure 4. Clue provided on a digital LED message fan that plugs into a USB port. Used with biochemical pathway provided in Appendix L.

Figure 5. Padlocks used with the clue provided in Appendix H.

Notes for the Instructor

This activity will require multiple clues to be scattered throughout a room, many of which need to be hidden or locked until a previous clue is solved; however, it is important to have multiple clues (ideally, half as many clues as participants) available at the onset of the activity to insure that all of the students are actively engaged in finding a solution to one of the problems presented initially. Table 1 lists the design of one game set-up option. The individual problems/clues used may require significant personalization/modification, depending on what topics are covered in a specific course and what room facilities are available to house this activity. Marking certain locks with stickers or other tags to coordinate them with their specific clue for opening them can increase the speed of the activity. Incorporating an overarching theme can also add another layer of enjoyment to the activity. For the problems included in this description, characters and concepts from the BBC sci-fi show, Doctor Who, were utilized; but other TV shows, movies, books, campus traditions, historical figures, etc., could alternatively provide inspiration.

When setting up the room, it may be possible to incorporate some hiding places within your space for the clues (with or without using locks), but you may also find it helpful to incorporate stand-alone items that can be locked (such as latched boxes or zippered bags, assuming a lock fits in the latch or zipper eyes). If you are short on lockable areas, it is also possible to use more than one lock to secure a single hiding location.

In addition to initial planning and adjustments to match clues with specific topics covered in your course, there will be about 30 minutes required each time to set/reset the pieces before the students arrive. After that, the role of the instructor is limited to giving modest hints, policing for any cheating, reminding about the time limit, and keeping students away from restricted areas of the room in use. It will probably be helpful, if not necessary, to restrict access to specific regions of a room/lab that are not to be included in the escape activity, as there will likely be some classroom/lab storage areas or pieces of equipment that cannot be locked-up or moved. This can be accomplished by stringing up "do not cross" tape around the off-limits areas. The addition of a course textbook somewhere in the room can be helpful for students to use, but you may also choose to allow them online access to class notes, etc.

This lab activity works best with a group of about 6-8 students, so it may be helpful to split larger classes into multiple groups that participate at different times or on different days. It is reasonable to have two groups meet during a 3-hour lab period, with a 30-minute reset time between groups. Incentivizing students with a small amount of extra-credit for a successful escape and/or the best time can further ensure participation within a group and minimize information breaches to later groups.

Acknowledgments

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About the Author

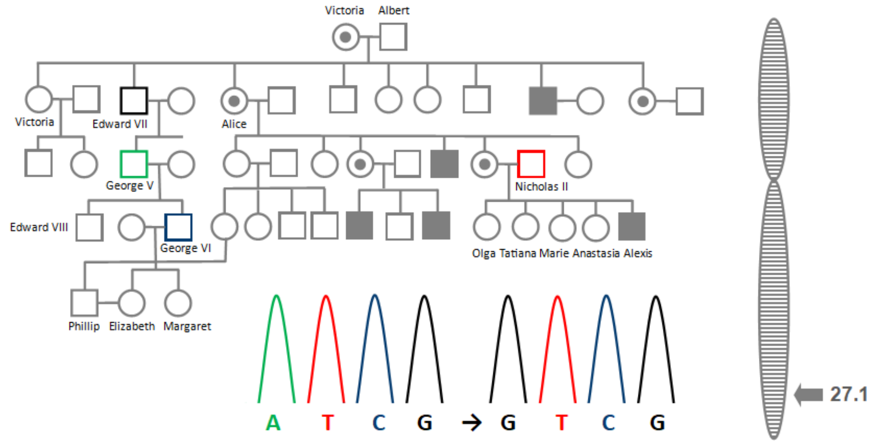
Jennifer Schroeder earned her Bachelor's degree in Chemistry from Rose-Hulman Institute of Technology and her Ph.D. in Biomedical Sciences with a concentration in Molecular Pharmacology and Experimental Therapeutics from the Mayo Clinic College of Medicine. She is currently an associate professor of Biology at Young Harris College, where she began teaching in 2010. She primarily teaches courses in cell biology and genetics. Her other teaching interests include pharmacology, cancer biology, and epigenetics.

Table 1
Example of a game set-up matrix

The problem titles listed in the top row should all be available to the students without the need to unlock anything, although some may be hidden within the playing space. Subsequent rows in each column indicate the problems that are only available after the preceding problems were correctly solved, which allowed students to open locks and/or gain access to keys. Of note, three different locks were used here to gain access to the safe and two locks each were used to gain access to the TARDIS from the cabinet or to open the locked diary. The end goal (finding the sonic screwdriver in the safe, in this case) would occur only by solving the last puzzle (i.e., the chocolate hint that will help open the safe), which should require that all other problems be solved first.

Jig-saw puzzle (Figure 2, provides clue to open lock below)	**Snails (Appendix M, clue opens lock on item below)**	**Agouti (Appendix G, clue opens lock on item below)**	**Squash (Appendix B, clue opens lock on item below)**	**Hemoglobin gene loci (Appendix A and padlock in Figure 3A, releases next item)**	**Plasmid RE digest map (Appendix J, clue helps open locked cabinet that holds item below)**	**Banana genome (Appendix K, clue opens padlock that releases item below)**
Dolly bag (contains item below and one contig piece)	**Large compartment of book bag (items below found within)**	**Small compartment of book bag (items below found within)**	**Blue lock box (items below found within)**	**Bad Wolf thumb drive (Appendix F)**	**TARDIS from cabinet**	**TARDIS key**
LED fan (Figure 4, directs to a figure in the provided textbook with the following)	**Textbook (containing one contig piece), Lab notebook, Recombination problem (Appendix C, opens lock to help gain access to safe)**	**Watch and psychic paper (Appendix H); Zipper pouch (containing contig piece and ABO problem, Appendix D)**	**Labeled tubes (corresponding to entries in lab notebook, Figure 1)**	**BLAST (correct answer, as seen in Figure 3B, helps open locked cabinet that holds item below)**		
Biochemical pathway (Appendix L, directional padlock provides access to the next item)	*****Safe (Appendix I; opened using Hershey-Chase clue and/or contig)**	**2 Hearts (Figure 5, releases key for next item)**	**Bowtie lock containing Ood problem (Appendix E, opens lock that would help gain access to safe)**	**TARDIS from cabinet (contains quiz questions from Appendix A and a contig piece)**		
Diary		**Diary (containing contig pieces and Hershey-Chase clue)**	*****Safe (CONTAINS END GOAL, in this case a sonic screwdriver to open the door)**	**British flag (see lock in Figure 3C-D, helps provide access to the ***safe)**		

Appendix A: Multiple Choice Questions on Class Content, Using A Pedigree, and Loci Identification



The picture of the X chromosome above is used with a combination lock (see Figure 3A) that includes letters and numbers to identify the correct location of the gene associated with hemophilia in the royal family. ANSWER: Xq27.1

The correct answers to the questions below can be combined with the color letters from a Sanger sequencing chromatogram and a pedigree of hemophilia in the Victorian royal families with specific “numbered” royals similarly color-coded (provided above). Corresponding three-number lock could have some reference (e.g., sticker, ribbons) to Britain or royalty (Fig. 3D).

ANSWER: **1)** C = blue = King George VI = 6, **2)** T = red = Nicolas II = 2, **3)** G = black = Edward VII = 7 (i.e., 6 2 7)
(unused option: A = green = George V = 5)

Questions that are bigger on the inside

1. The first time you see tetrads in meiosis is in
   - A. Anaphase I.
   - T. Metaphase II.
   - C. Pachynema.
   - G. Diplonema.

2. Wrinkled peas are due to a mutation in which gene?
   - A. HexA
   - T. SBEI
   - C. SRY
   - G. GAPDH

3. Which of the following plasmids is/are transferred via horizontal gene transfer?
   - A. F factor only
   - T. R plasmid only
   - C. Col plasmid
   - G. Both F factor and R plasmid

Appendix B: Squash Epistasis Dihybrid Cross

Corresponding three-number lock could have some reference (e.g., sticker) to squash or the colors mentioned below. This problem asks students to determine the phenotypic ratio of white, yellow, and green squash following a dihybrid cross with yellow and white squash, which follow an epistatic pattern of inheritance. As white squash have the *A*--- genotype, yellow are *aaB*-, and green are *aabb*; the cross would include *aaBb* (yellow) and *AaBb* (white) from the option list.

ANSWER: Performing a dihybrid cross of these would result in a 4:3:1 phenotype ratio (alternatively, one could use the non-simplified 8:6:2 ratio).

Options:

aaBb

AaBb

aabb

Color Genotypes:

Yellow squash________________

x

White squash________________

Phenotype ratio (white : yellow : green):

Appendix C: Chromosome Mapping (Recombination) Data Set

To be used with a combination lock. As these locks are rarely programmable, the numbers below would likely need to be changed to result in distances between genes that match the available combination lock. Of note, the combination lock must include three numbers (i.e., no zeros) to be used here. One could have students calculate the distances between 4 genes, but for this problem the chromosome number (5) was used as the first number of the combination.

ANSWER: 5-21-5 (chromosome 5 and then 21mu between AB and 5 mu between BC)

Determine the distance between genes A, B, and C on chromosome **5** using the following reCOMBINATION data:

Phenotype	Number
ABC	378
abc	372
Abc	102
aBC	98
ABc	17
abC	23
AbC	6
aBc	4

Appendix D: Blood-Typing For Mastery of Dihybrid Crosses and Bombay Phenotype

Corresponding four-number lock could have some reference (e.g., sticker) to parents or blood. Note that *fut1*-/- genotypes will result in O-type blood, regardless of the presence of any I^A or I^B genes.

ANSWER: 4 0 4 8

Determine the chance (i.e., the number out of 16) that Melody will have **A, B, AB, or O** blood type, given her parents' genotypes below:

Amy (I^A I^B, fut1-/-)

Rory (I^A I^A, fut1+/-)

Appendix E: Hardy-Weinberg Equilibrium Problem

Corresponding four-number lock could have some reference (e.g., sticker, label) to aliens, HW, or an equal sign.

ANSWER: 0 6 0 4

After genotyping 25 Oods (a futuristic alien species), it was discovered that 9 of them were homozygous dominant for red eyes, which is controlled by a single autosomal gene, *hvmd*. What are the expected frequencies for the dominant and recessive alleles of *hvmd* in this population?

p = ___ . ___   q = ___ . ___

Appendix F: DNA Sequence for a BLAST Database Search

Corresponding four-letter lock could have some reference (e.g., sticker, collar) to a dog/wolf. The text below is to be saved as a file on a flash drive under the name "blaidd ddrwg" (Welsh for "bad wolf"). Students would need access to a computer with a USB port and the internet to be able to copy-paste this sequence in the nucleotide BLAST search engine maintained by NCBI (**https://blast.ncbi.nlm.nih.gov/Blast.cgi**).

ANSWER: Either PIDD or LRDD, depending on how the top hits for this sequence are listed on the day of the search.

gcagctgctgccgcaggagatgcttcagaggattcggacgcagggtccagggcgctgcctttcctgggcggcaaccggctgagcttggacctgtaccccgggg gctgccagcagctgctgcacctgtgtgtccagcagcctctgcagctgctgcaggtggaattcttgcgtctgagcactcacgaggaccctcagctgctggaggcc accctggcccagctgcctcagagcctgtcctgc

***Discover my real name before I BLAST off!**

Appendix G: Punnett Square for Agouti Mouse Genotype-Phenotype Relationship

Corresponding three-number lock could have some reference (e.g., sticker) to a mouse or the color yellow, or a yellow mouse. Students should be provided with yellow highlighter in order to color in all the yellow mouse genotypes (i.e., *Gg*), noting that *gg* genotypes would be embryonic lethal and should NOT be colored yellow.

ANSWER: 3 ("three"), 1, 3

Yellow mice (due to agouti gene)

Gg	GG	GG	Gg	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG
Gg	GG	GG	Gg	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG
Gg	Gg	GG	Gg	Gg	Gg	GG	Gg	Gg	Gg	GG	Gg	Gg	Gg	GG	Gg	Gg	Gg
Gg	GG	GG	Gg	GG	Gg	GG	Gg	GG	GG	GG	Gg	GG	Gg	GG	Gg	GG	Gg
Gg	GG	GG	Gg	GG	Gg	GG	Gg	GG	GG	GG	Gg	Gg	GG	GG	Gg	Gg	GG
Gg	Gg	GG	Gg	GG	Gg	GG	Gg	GG	GG	GG	Gg	Gg	Gg	GG	Gg	Gg	Gg
GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	Gg	GG	GG	Gg	Gg	Gg	Gg	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	Gg	GG	GG	gg	GG	GG	Gg	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	Gg	GG	GG	gg	GG	GG	Gg	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	Gg	GG	GG	gg	Gg	Gg	Gg	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	Gg	GG	GG	gg	GG	GG	Gg	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	Gg	GG	GG	gg	GG	GG	Gg	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	Gg	GG	GG	Gg	Gg	Gg	Gg	GG	GG	GG	GG	GG
GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG

Appendix H: Sequence of mRNA for Translation Clue

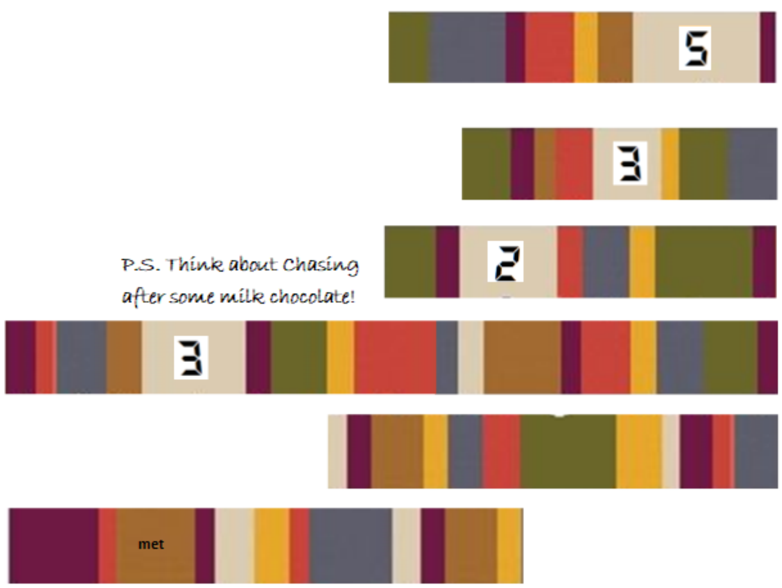
Sequence listed below is to be written with "invisible" UV pen on a piece of paper or tape, Students should also have access to a low-power UV light source and a codon table. Translation of this sequence into one-letter amino acid codes spells out "TIMEY WIMEY," which could correspond to the time on a STOPPED watch or clock found somewhere in the room, perhaps hidden. Corresponding three- or four-number lock could have some reference (e.g., sticker) to where the "invisible" code was written or UV (best NOT to use time or a clock for the reference, as that would negate the need to actually translate the sequence).

ANSWER: Your choice, within the limits of time (i.e., 4:01, 12:35, 23:59). For this set-up, these were used with two heart-shaped combination locks (see Fig. 5) set to open according to a clock stopped at 3:21 and 15 seconds (i.e., 3-2-1 and 0-1-5). To make it a little clearer for the students, one of the locks was literally labeled "second."

ACG AUC AUG GAA UAU UGG AUA AUG GAG UAC

Appendix I: Contig and the Final Clue

The fragments below would need to be divided up and hidden in various boxes throughout the game to tests students' ability to reconstruct a chromosome map from "shotgun sequence" (i.e., contig) fragments. It would also be helpful to provide a clue as to what the four numbers are supposed to represent. In this case, the clue ("P.S. Think about Chasing after some milk chocolate!") was supposed to direct the students to thinking about the Hershey-Chase experiments that used P-32 and S-35 radiolabels. Using an actual candy bar, just the wrapper, or even a picture of a chocolate bar could be also a helpful. Again, access to the clue plus all of the numbered fragments should require that the students complete all the activities/problems; one or more of these should probably be hidden until the second-to-last problem is solved.



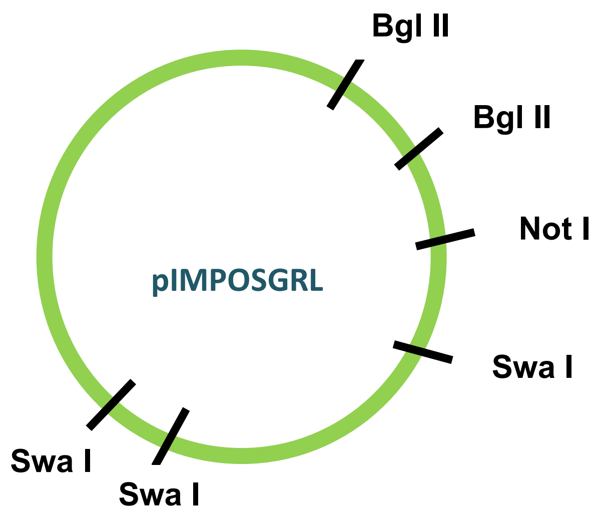
ANSWER: 3 2 3 5 (These pieces align left to right, starting with the bottom fragment and working up.)

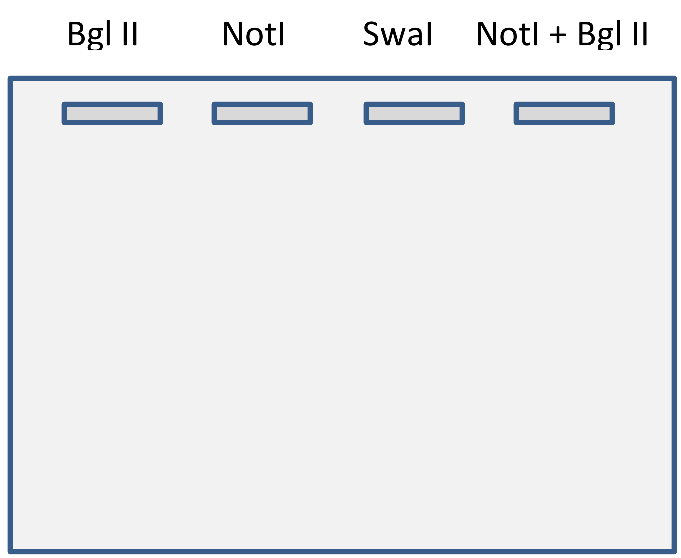
Appendix J: Understanding Restriction Digests

Plasmid map shown below can be used to determine the number of RE digest fragments that would be created using the enzyme (combinations) listed on the picture of the agarose gel.

ANSWER: 2 1 3 3 (representing the number of fragments in the four lanes of the gel

"Run (a gel) you clever boy and remember!"





Appendix K: Understanding Haploid and Diploid Numbers

The description and image of banana chromosomes below (which I usually cut up and have them arrange to produce the clue using the letters written above each chromosome) are used to have students show that they know that diploid numbers are twice that of the total number of different chromosomes, which is the N value used to determine 3N for triploidy, too.

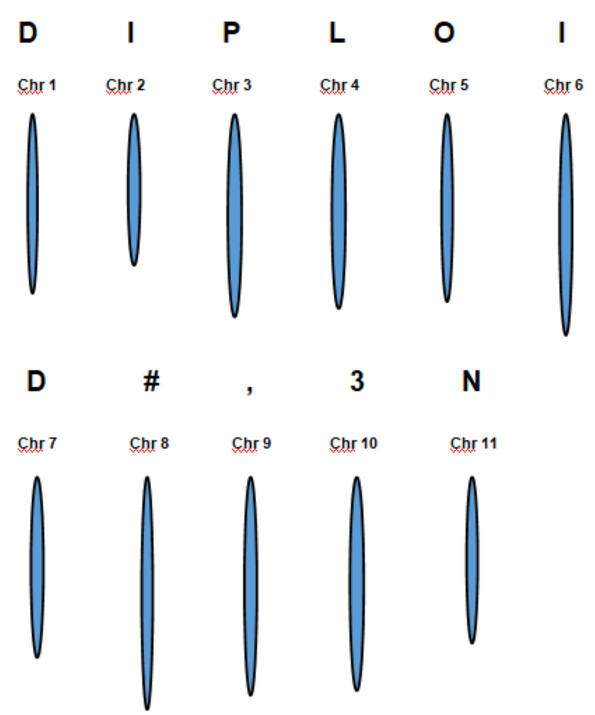
ANSWER: 2 2 3 3 (i.e. 2 x 11 = 22 and 3 x 11 = 33)

Monkey sez: **"Always take a banana to a party, Rose; bananas are good!"**

While wild bananas contain seeds, the cultivated Cavendish variety is seedless (i.e., sterile because they have an odd number of chromosome sets).

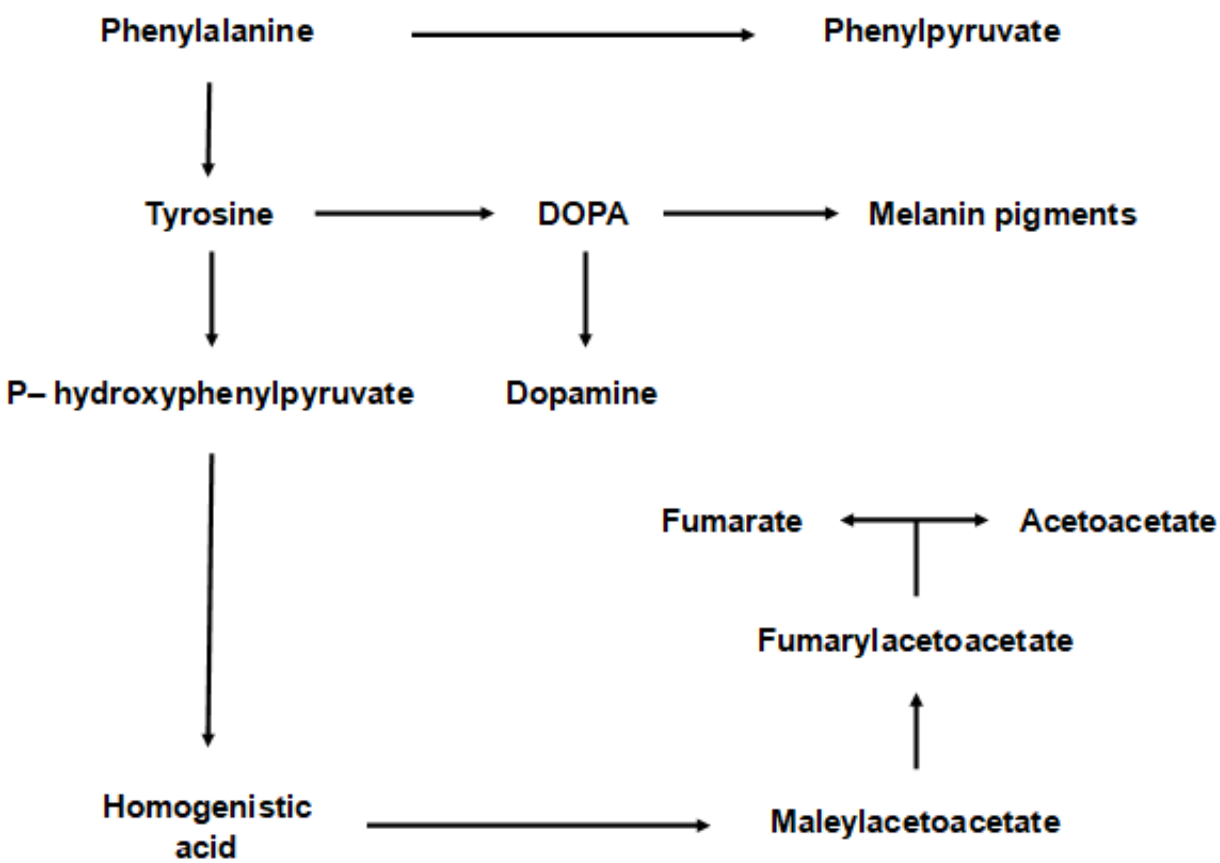
Thankfully, the cultivated bananas are parthenocarpic and do not require fertilization to produce fruits. However, since they don't undergo sexual reproduction, there is a legitimate concern that this monoculture will be wiped out by a virus in the near future.

Banana (*Musa acuminate)* genome:

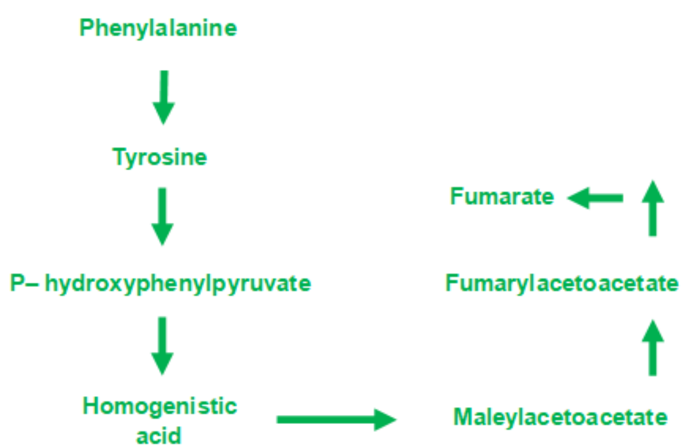


Appendix L: Biochemical Pathway from Phenylalanine to Fumarate

Using the arrow directions on the following image that would be required to move from phenylalanine to fumarate. This could correspond to the directions that are used on a directional padlock.



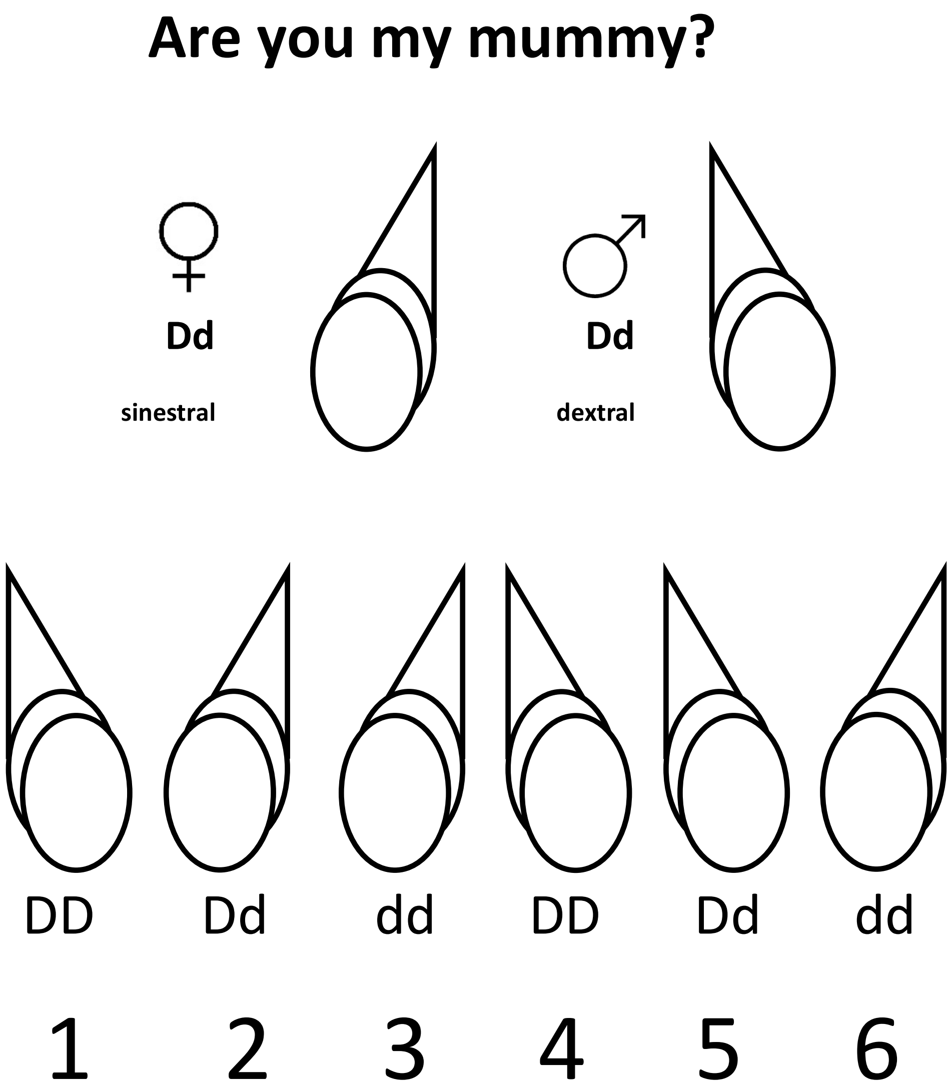
ANSWER: down, down, down, right, up, up, left



Appendix M: Maternal Effect

Using an example based on the maternal effects observed in *Lymnaea peregra* snails, students are asked to use the provided phenotype and genotype data to determine which of the offspring could possibly be from the provided female. In this species, the genotype of the mother determines the phenotype of the offspring, with the dominant genotype being associated with dextral coiling.

ANSWER: 1-4-5 (because a mother with a DD or Dd genotype would only create offspring with dextral coiling)



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