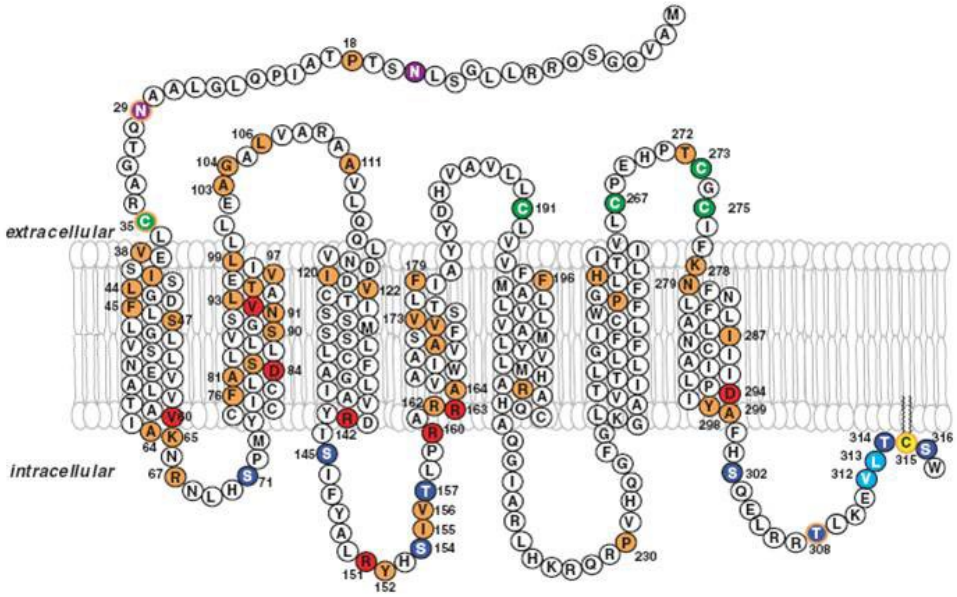
Module 2: Cells and Division

Review Activity



During module 4 on evolution, we will spend several classes examining the evolutionary significance of fur colour in a certain group of mice from the Sonoran desert in the South-Western United States. To prepare for this module, in the review activities for the first 3 modules we will be examining the molecular, cellular, and genetic basis for mouse coat colour.

In the review activity for unit 1, you examined the MC1R molecule displayed above. MC1R is a transmembrane receptor protein involved in a typical cell communication pathway. What organelles in the cell could conceivably play a role in producing the MC1R molecule and directing it to the appropriate location within the membrane of the cell? For each organelle you list, describe what it would actually do.

Nucleus: House the DNA which has the instructions for producing MC1R, produce the mRNA working copy of this gene.

Ribosomes: Translate the mRNA of MC1R into the actual protein.

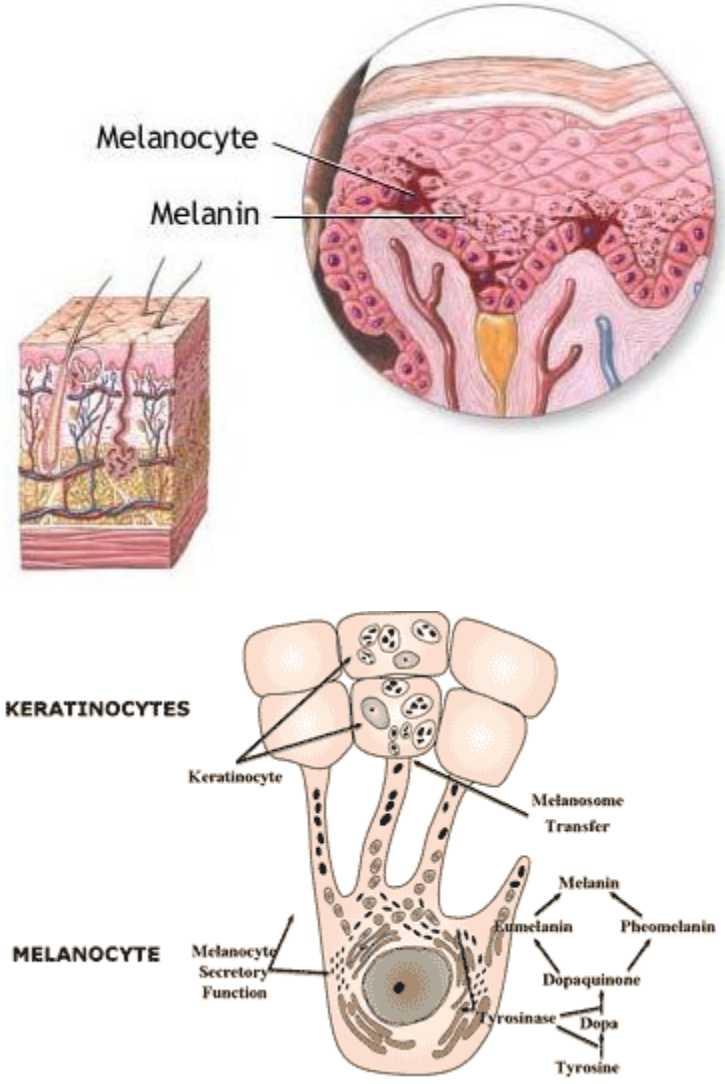
RER: Site for protein synthesis using ribosomes; modify and process the protein to help it towards taking its final shape.

Golgi: Modify and process the protein further, package and embed it in a vesicle membrane for shipping.

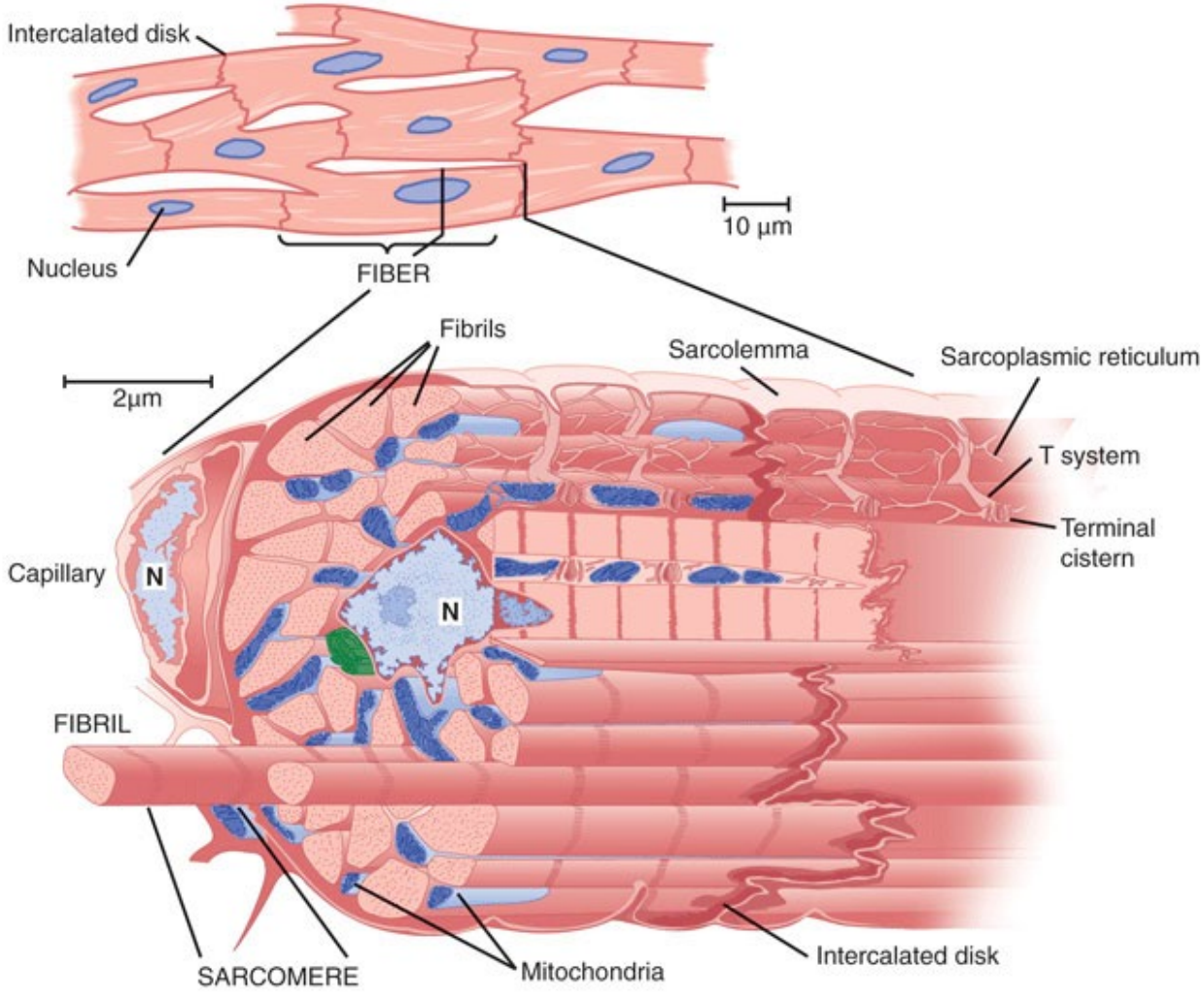
Vesicle: Move the molecule to the plasma membrane, fuse with the membrane, inserting MC1R into its final location.

Use information on three different types of cells from the following paragraphs and images in order to answer the subsequent questions.

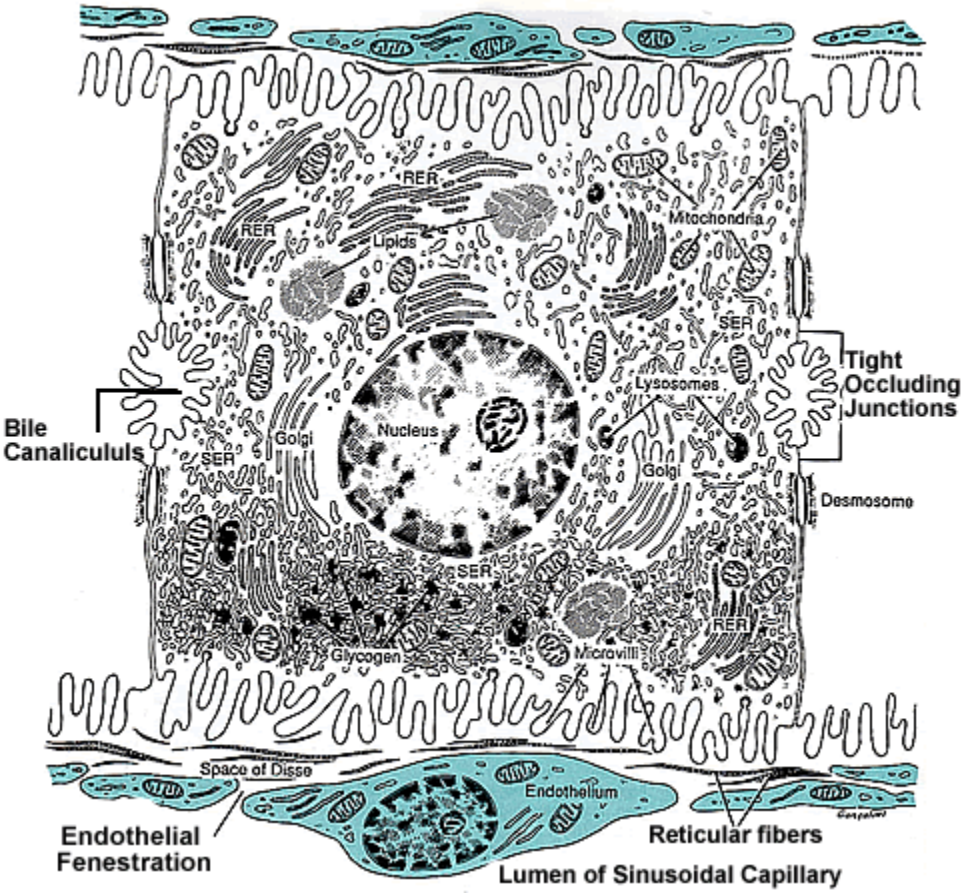
MC1R is found in the cell membrane of melanocytes, which are cells located in the bottom layer of the skin's epidermis, as well as several other locations in the body. The primary function of melanocytes is to produce the pigment melanin (a molecule based on the amino acid tyrosine, but which is **NOT** a protein), which they package in vesicles called melanosomes. These vesicles are then exported out of the melanocyte and into surrounding cells called keratinocytes, which eventually move from the lower part of the skin to the surface, resulting in pigment deposition near the skin's surface.



Below is an image of a cardiac myocyte, which is a heart muscle cell. These cells exhibit striations formed by alternating segments of thick and thin protein filaments, and their primary function is to move these filaments against each other to contract and relax (or expand) the shape of the cell.



Below is an image of a hepatocyte, which is a liver cell. Among many other things, liver cells function in the detoxification of waste products, drugs, and hormones.



Based on the functions of the three types of cells described in the preceding paragraphs (i.e., only consider the drug detox function for liver, and not the many other functions of liver cells), compare and contrast melanocytes, myocytes, and hepatocytes in terms of their organelle constituents. What types of organelles are melanocytes likely to have more of, and why? What about myocytes and hepatocytes?

The primary function of melanocytes is to produce melanin and ship it out of the cell. Melanin isn't a protein, so its synthesis does not take place in the RER. Instead, it is produced in specialized vesicles called melanosomes. However, like many vesicles in the cell (and almost all that are destined for export), these melanosomes are produced in the Gogli. Thus, one would expect melanocytes to have a higher than average amount of Golgi bodies, due to their function of exporting molecules from the cell.

Myocytes are all about movement, and movement takes energy. The energy currency for cells is a molecule called ATP, and ATP is produced from the oxidation of C-H bonds (from carbs and lipids) in mitochondria. Thus, one would expect myocytes to have more, and maybe many more mitochondria than average cells. Muscles are also very high in protein, due to the extensive networks of protein filaments. Therefore, muscle cells should contain a higher amount of RER for the production of all of these protein filaments.

As mentioned, hepatocytes have MANY functions, and they have lots of different organelles accomplishing these. However, for the stated purpose of detoxification of waste products, hormones, and drugs, hepatocytes require a large amount of SER, as this is the organelle which contains the enzymes necessary to accomplish these tasks. Thus, hepatocytes tend to be very high in SER.

A curious scientist decided to compare cardiac myocytes and hepatocytes to see which contained more mitochondria per unit volume. After controlling for size (hepatocytes are cuboidal with sides around 30 micrometers, while cardiac myocytes are tubular with lengths around 150 micrometers and diameters of 20 micrometers), the researcher produced the following results:

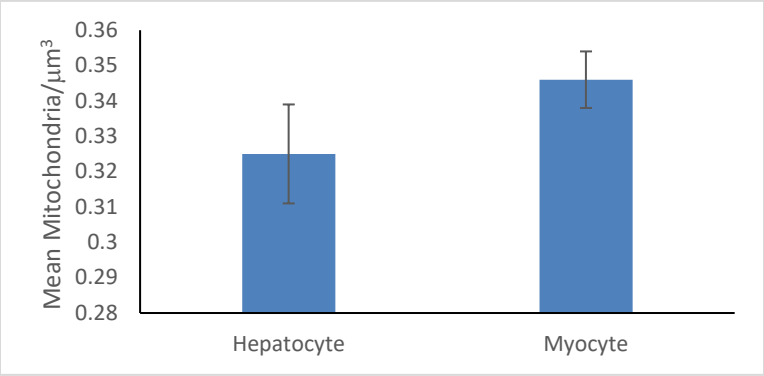
Hepatocyte:
Mean mitochondria: 0.325 mitchondria/μm^3
95% CI: 0.014

Myocyte:
Mean mitochondria: 0.346 mitchondria/μm^3
95% CI: 0.008

How would you statistically analyze these data? Which statistical test should you use, what kind of output would you expect, and what would you report in a paper?

Nominal independent variable, ratio dependent variable with repeated measures… should use a t-test to test hypothesis, comparing means to identify whether there is a statistically significant difference. Eyeballing it here, the two groups seem different but maybe not enough, so we might expect a p-value a little above 0.05, indicating that we might not be able to reject the null. In a paper you should report the p-value, the test statistic (t-stat), and the degrees of freedom (df).

How would you graphically represent these data? Draw a graph of what you present in a paper.



Suppose you performed the statistical test you indicated in the previous question and obtained a p-value of 0.16. What conclusions can you draw from this result?

While the means do appear different, the p-values are a little too high to comfortably reject the null hypothesis, which is that the type of cell has no effect on the number of mitochondria per unit volume. So, even though there does seem to be a suggestion that myocytes have more mitochondria than hepatocytes, this difference isn't statistically significant, and more research is required to either confirm or reject this hypothesis.

You are a cancer researcher who focuses on a specific type of eye cancer called retinoblastoma. From your years of research, you have a hypothesis that the retinal cancer cells may be dividing uncontrollably because they lack certain cell cycle control molecules that regular retinal cells possess. You now have technology which makes it possible to fuse two cells together to mix their cytoplasm, and these newly created 'double cells' remain viable long enough to identify changes in the nuclei associated with moving into a different stage of the cell cycle.

Armed with this technology, and with cultures of both rapidly dividing retinal cancer cells and slowly dividing (or essentially not dividing) normal retinal cells, design an experiment which could allow you to test your hypothesis.

Experimental design: Fuse a rapidly dividing cancer cell currently in the G1 stage with a slowly dividing normal cell currently in the G1 stage. There are molecules in the normal cell which prevent it from progressing into the S phase inappropriately; if these molecules are lacking in the cancer cell, fusing with the normal cell should introduce these molecules to the cancer cell and thus prevent it from proceeding to the S phase. Replicate procedure a significant number of times.

It is also important to control for effects of the process, i.e., to make sure that the process of fusing itself isn't somehow preventing the cancer cells from moving into the S phase. Thus, two cancer cells should be fused together using the same procedure (and the process replicated numerous times). If the process if having no effect, the cancer cells should quickly initiate the S phase.

Independent variable: Presence of control molecules (normal cells have them, cancer cells don't)

Dependent variable: Initiating the S phase (counts of cells that do this)

Control variables (at least 2): Any number of correct answers; similar environmental conditions for all tests, exactly the same procedure applied in treatment (fuse with normal cell) and control (fuse with cancer cell), same types of cells (retinal cells) from the same species, etc.

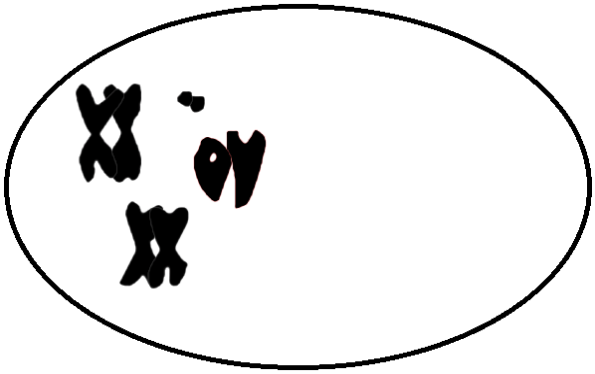
The hypothesis presented above suggests that a specific molecule in the cell should prevent the cell from progressing through the cell cycle. In this particular example, such a molecule does indeed exist, and it is called pRb, which stands for 'retinoblastoma protein'. When this molecule is present (and activated), a retinal cell will not proceed from G1 into the S phase. Employing basic Biology language encountered in this course, describe what pRb is, what it does, and how this particular molecule could be responsible for the results described above.

pRb belongs to a class of molecules known as tumour suppressors, because, no surprise, they prevent tumours from forming. They do this by accomplishing the everyday function of inhibiting a cell from progressing through the cell cycle. Specifically, they prevent cells from progressing from G1 into the S phase. They do this by binding to and inhibiting the function of

other protein molecules which whose job it is to direct the cell into the S phase. In other words, they are the brakes. To remove the brakes, certain signal molecules bind to and inhibit the function of pRb. When this happens, the cell cycle initiating molecules targeted by pRb are freed up to do their job, and the cell cycle progresses.

If, for whatever reason, pRb is not produced, is produced but is not folded properly, or is continuously bound to its own inhibitor molecules, it will not serve its function, which means it does not 'put the brakes' on the cell cycle, and the cell will continuously divide. The result would be a tumour, and cancer.

Using the internet, find *n* for *Drosophila melanogaster* and identify whether the species is haploid or diploid. Then, draw a primary spermatocyte cell for this species that is in late prophase I of meiosis I.



These are images of *Drosophila*'s actual chromosomes. The size and shape of the chromosomes don't actually matter for this answer. As long as you have a diploid cell with n=4, and homologous chromosomes paired up in tetrads, you're all good.

Make a rough sketch (i.e., just focus on the chromosomes) of all possible genetic gametes that could be produced by a *Drosophila* spermatocyte cell you just drew.

There are 16 answers for this, with every possible mix and match of the chromosomes above (within the constraints that each cell has 1 and only 1 of each of the homologs from above).

Which property of meiosis accounts for the production of the different potential gametes you just drew?

Independent assortment. There are four different tetrads made of homologous chromosomes, and each of these has two possible orientations on the metaphase plate. Thus, there are two orientations to the power of 4 different tetrads (or 2^4) possible different gamete combinations that could be produced.

Use the internet to research and describe the following human disorders. For each, be sure to identify the process which leads to the disorder.

Edward's Syndrome:

Trisomy 18, where an organism ends up with 3 of chromosome 18 due to a nondisjunction event during the meiotic production of gametes in one of their parents.

Symptoms:

http://en.wikipedia.org/wiki/Edwards_syndrome#Signs_and_symptoms

Klinefelter's Syndrome:

XXY, where an organism ends up with 2 of chromosome X as well as 1 Y. This occurs due to a nondisjunction event during the meiotic production of gametes in one of their parents (mom has an egg with 2 Xs, fertilized by a sperm with Y; Mom has an egg with X, fertilized by a sperm with XY).

Symptoms:

http://en.wikipedia.org/wiki/Klinefelter_syndrome#Signs_and_symptoms

Turner's Syndrome:

Monosomy X, where an organism ends up with only one sex chromosome (X). This occurs due to a nondisjunction event during the meiotic production of gametes in one of the parents (mom produces an egg with no X (both went into a polar body), fertilized by a sperm with X; mom produces an egg with X, fertilized by a sperm with no sex chromosome (both X and Y went into another sperm).

Symptoms:

http://en.wikipedia.org/wiki/Turner_syndrome#Signs_and_symptoms