

## Problem Set 6

(Due: April 10<sup>th</sup> 5:00 PM)

1. Insulin is a protein hormone that is secreted by the pancreas. The different parts of this question will explore some aspects of the production, structure, and function of insulin. Refer to this image to answer these questions: [https://upload.wikimedia.org/wikipedia/commons/1/18/Insulin\\_path.svg](https://upload.wikimedia.org/wikipedia/commons/1/18/Insulin_path.svg). You can also use this table of amino acids to help you figure out what the single letter codes mean. <http://www.sigmaaldrich.com/life-science/metabolomics/learning-center/amino-acid-reference-chart.html>
  - a. Insulin is synthesized by on the ribosome as a protein that contains and extra sequence at the N-terminus that allows it to be sent to the endoplasmic reticulum (or the ER – this is a part of the cell). Examine the sequence of this signal peptide (in red in the image).
    - i. What do you notice about the chemical properties of most of the amino acids?
    - ii. What is the name of the transporter that allows insulin to move into the ER?
  - b. In the image, you should note that once insulin gets into the ER, it is folded and oxidized. This occurs as it is anchored to the lipid bilayer.
    - i. What part of insulin favorably inserts itself into the bilayer?
    - ii. You may notice that the membrane embedded region contains an arginine (r) and a glutamic acid (d). Under normal conditions, what is the charge on each of these amino acids? Based on this, how do you think that these amino acids are able to be part of a transmembrane peptide?
    - iii. The “oxidation” part of this step refers to cysteine side chains getting oxidized. What happens when cysteine gets oxidized? How do you think this affects the stability of the insulin structure?
    - iv. Once inside the secretory vesicle, the protein chain is broken in two places by enzymes that catalyze hydrolysis reactions.
      1. These enzymes recognize specific amino acid sequence (show in dark blue in the image). What do these recognition sequences have in common?
      2. Draw the peptide bond that is formed between arginine and glycine (the target of the PC2 enzyme).
      3. Show the mechanism for this hydrolysis reaction (this is the 3 step process that we learned earlier in the term).
2. Once insulin is secreted into the blood, it seeks out insulin receptors.
  - a. Describe how the insulin receptor works.
  - b. Clearly explain how an enzyme inside a cell might be able to “sense” insulin binding to the outside of the cell.
  - c. Type 2 diabetes is marked by the development of insulin resistance. What does this mean and why is it important?
3. Epinephrine (aka adrenalin) is a hormone that is secreted by adrenal glands. It functions in a very similar way as glucagon and has a very similar physiological effect.
  - a. Using any combination of words and images, describe how epinephrine can stimulate energy (ATP) production in cells.
  - b. Look up the structure of epinephrine.
    - i. Which amino acid does it most closely resemble?
    - ii. Predict how the epinephrine receptor recognizes and binds to epinephrine.