Rubric for von Willebrand disease

Genetic Disease 3-Part Assignment – worth 15% of overall Course Grade!
(Rubric sums to 100 points)
(Groups of 2 - 3)

- Use Google Docs to work on all parts of this assignment as a group – you must invite your instructor to be a group member on the document. This allows your instructor access ongoing work and will be used if there are any questions regarding group member contributions. Instructions on how to use Google Docs are on the course home page (http://blc.arizona.edu/courses/181lab/) via the References and Writing link.
- Save final documents for each part of the assignment as a .doc or .docx and submit to the D2L drop box for the separate assignment. Put all of your net ids in the file name as well as GenDisPart 1. Example: netID1_netID2_netID3_GenDis1.doc. INVITING YOUR INSTRUCTOR TO THE GOOGLE DOC DOES NOT COUNT AS TURNING IT IN.
- Fill out a group evaluation at the end of completing each part of the assignment. Make sure that these are included in the final documents you turn in. Parts 1 & 2 of the assignment are a group assignment: everyone is expected to contribute equally and respond to other group members’ inquires about the ongoing work in a timely way. Work submitted individually for parts 1 & 2 does not meet the requirements of the assignment and will receive a zero.
- Parts 1 & 2 will be done as a rough draft, revised and then turned in as a final draft. The rough draft will contribute 30% and the final draft 70% to the overall score on parts 1 & 2.
- Part 3 will be done INDIVIDUALLY and students will not be given the opportunity for revisions for that part.

Information page to assist you in this work:
https://thinkbio.guru/3D_Directory/|Genetic_Diseases.html

Part 1: Introduction to your Genetic Disease (25 points):

General description
a.) How many suffer from the disease? Any particular groups/geography?
b.) Did you come across any other names for the disease, gene or protein? If so, list them 1 – 3 of them.
c.) What are the symptoms (if applicable - both long and short term)?
d.) The genetic disease you are investigating is the result of a protein not doing its job or doing its job incorrectly. What does the protein involved in your genetic disease do when functioning normally? Be SPECIFIC with your answer. Any technical terms, jargon or medical vocabulary should be accompanied by an explanation or definition not containing technical terms. Your explanation should make sense to a high school student. ***Make sure you carefully examine the resources provided for your specific genetic disease in the Information page link https://thinkbio.guru/3D_Directory/|Genetic_Diseases.html***
e.) Explain how the decreased function of the protein gives rise to the symptoms of the disease. Your explanation to the extent possible, should have all the linkages between the failure of the protein and symptoms of the disease. Again, any scientific jargon, technical terms etc. must be explained.
f.) What are the treatments for the disease? How do treatments for the disease (if any) alleviate the symptoms? You should integrate your answer from part (d).
Your mutation

g.) Use the amino acid changes provided for your disease in the Information page link (https://thinkbio.guru/3D_Directory/Genetic_Diseases.html) to find what the initial and resulting amino acids are. Based on the identity of the original and changed amino acids, what codon changed to what? Keep in mind that an amino acid may have many different codons, so please specify all of the codons for the original and changed amino acid. Use your codon table to deduce the codon changes necessary to go from the initial to resulting amino acid. Remember, the fewer the number of changes, the more likely it is to have been the case.

h.) What are the properties of the wild type (initial) amino acid? (Properties include: charge, shape, size and flexibility, features unique to the amino acid {i.e. the ability of histidine to respond to pH values typically found in the body, etc.}) Specify its 3-letter abbreviation.

i.) What are the properties of the mutant (resulting) amino acid? Specify its 3-letter abbreviation.

j.) How similar/different is the mutant amino acid from the wild-type?

Source Evaluation

k.) For each of the above questions - What are your sources for the information?

Include a formal MLA format citation for each source (this includes a parenthetical citation in the text of your answers such as this one: (1) which is dereferenced at the end of this document). Here is a link with general MLA instructions: http://owl.english.purdue.edu/owl/resource/747/08/

For each source, write a sentence or two explaining:

1.) What information you got from this source

2.) How reliable you consider the source. i.e. brief description of who hosts the website, how recent the information is, any possible bias the website hosts may have and the site itself as well as any references (if any) the site uses.

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Expectation</th>
<th>Loss of credit if:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sufferers (1)</td>
<td>Meaningful explanation of how widespread the disease is</td>
<td>Inaccurate or incomplete information.</td>
</tr>
<tr>
<td></td>
<td>Accurate commentary on distribution</td>
<td></td>
</tr>
<tr>
<td>Symptoms (1)</td>
<td>Easy-to-understand, clear and complete</td>
<td><strong>Unexplained technical terms</strong>; not presented in everyday, non-medical English.</td>
</tr>
<tr>
<td>Normal function of protein (3)</td>
<td>A non-technical description of the role the protein normally plays in cells.</td>
<td><strong>Unexplained technical terms</strong>; not presented in everyday, non-medical English. <em>Specific</em> role of the protein not described.</td>
</tr>
<tr>
<td>Explanation concerning how symptoms arise (3)</td>
<td>Explanation of why the absence of the protein or its misbehavior results in the genetic disease.</td>
<td><strong>Unexplained technical terms</strong>; not presented in everyday, non-medical English.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Incomplete logical chain.</td>
</tr>
<tr>
<td>Treatment Category</td>
<td>Description</td>
<td>Evaluation</td>
</tr>
<tr>
<td>------------------------------------</td>
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</tr>
<tr>
<td>Treatments (3)</td>
<td>A non-technical description of the treatments and why they work.</td>
<td>Unexplained technical terms; not presented in everyday, non-medical English. Missing an explanation/conjecture about why treatments work, or why it is unknown as to why they work.</td>
</tr>
<tr>
<td>Codon change (3)</td>
<td>Specific codon change and source of information, or deduced possible changes based on amino acid change</td>
<td>Incorrect or not possible based on sequence; invokes more changes than required</td>
</tr>
<tr>
<td>Amino acid change (3)</td>
<td>Correct; includes amino acid name and 3-letter representation Properties of both briefly stated and compared</td>
<td>Needlessly wordy; technical terms not defined (none are required)</td>
</tr>
<tr>
<td>Source evaluation (7)</td>
<td>Clear, complete information on where you found out what you learned. Thoughtful consideration of reliability of the source (and whether it is what it claims to be)</td>
<td>Evaluation overly trusting; original source(s) not cited in MLA format. Parenthetical, in-text citation is missing. Information retrieved from source not summarized. Reliability of source not evaluated.</td>
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</tbody>
</table>
**Part 2: Structural Analysis of the actual mutation in your Genetic Disease (35 points)**

*Information page to assist you in this work:* [https://thinkbio.guru/3D_Directory/Genetic_Diseases.html](https://thinkbio.guru/3D_Directory/Genetic_Diseases.html)

**Click on your disease and follow the link for the 3D STRUCTURE GUIDE to find the structure you need to analyze for Part 2.**

**Based on your own, original analysis of the structure provided in the link above, NOT research you do online.** Research should only be done to supplement your analysis (to clarify small points). Loss of credit will result if your analysis is a repeat of outside research rather than conclusions based on your thinking.

Consider the following questions (some may be more/less relevant depending on your structure):

**READ ALL INSTRUCTIONS on the webpage BEFORE you start answering these questions!!!**

a.) Is the protein a monomer? (a monomer= 1 protein chain, and has a beginning and an end). Or are there multiple subunits?

b.) Some proteins will have binding partners or binding site components that are distinct from the protein itself (ex. A heme or a DNA strand). Looking at Von Willebrand, do you notice any partners/components that are obviously separate from the amino acid chains?

c.) Estimate relative percentages of alpha helix, beta sheet and loops in your protein’s secondary structure. Where is your mutation relative to these structural elements? (Is it on an alpha helix, beta sheet, or ‘loop’ that goes in between?)

d.) Where are the hydrophobic/hydrophilic residues concentrated? Where does your mutation fall relative to these clusters and to the inside/outside of the protein? Try viewing your protein in the “spacefilled” mode to see this. Keep in mind the scale, the size of atoms, and consider, would water really be able to interact with that amino acid?

e.) Consider replacing the wild type amino acid that is shown with the one found in the mutant: what do you hypothesize changes when the amino acid (side chain) is changed?
   - What are the properties of the wild type amino acid? (Review from part 2.a)
   - What amino acids and/or other molecules is that wild type amino acid interacting with? You can visualize this by clicking on ‘Neighbors’. (Hold the mouse over each amino acid – the three-letter abbreviation for that aa will appear)
   - What are the properties of the amino acid(s) the wild type amino acid is interacting with?
   - What are the properties of the mutant amino acid?
   - Are there any special characteristics that the wildtype has that the mutant does not.
   - Based on the properties of the mutant amino acid vs. the wild type amino acid, would the mutant amino acid be able to interact with the surrounding amino acids in the same way? Would the mutant amino acid have an impact on the structure of the protein (this could be overall structure, or just part of the structure.) Justify your answer.

f.) What do you hypothesize is going wrong with the protein’s ability to function properly? How do the changes in structure/interactions you mentioned in part (e) lead to some of the symptoms of this disease? Make sure you refer back to the protein’s normal function described in part 1.
<table>
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</table>
| Structural analysis (15) | Questions above all correctly addressed | - Analysis not based on tools provided  
- Omissions, inaccuracies  
- Extensive use of outside resources used to complete the analysis (the majority of this should be your own, original work) |

| Hypothesis about change (20) | A thoughtful and thorough hypothesis based on the information provided by direct observation | - Does not take into account available information; implausible; shallow  
- Extensive use of outside resources used to complete the analysis (the majority of this should be your own, original work) |

<table>
<thead>
<tr>
<th>Group Member</th>
<th>Specific Tasks (leave blank if all shared)</th>
<th>Overall % of Total Effort (sum of ALL should = 100)</th>
<th>Additional Comments (Include special effort or failure to participate)</th>
</tr>
</thead>
</table>
Part 3: Structural Analysis of a hypothetical mutation for your Genetic Disease (40 points)

What if your Genetic Disease was caused by a different amino acid change? For Part 3 you will work INDIVIDUALLY, to compare an additional hypothetical (not actually characterized in humans) mutation to the wild type.
- This part of the project will give you a chance to apply what you learned from part 2 to a new scenario.
- You may find it useful to make reference to your graded part 2 as you complete this part.
- You will follow the link called ‘von Willebrand factor hypothetical mutant’ on the information page that you have been using for the previous parts of this project under the von Willebrand disease link:

a.) What codon changed to what? Use the amino acid changes provided for your disease in the Information page link above to find what the initial (wild type) and HYPOTHETICAL resulting amino acids are. Use your codon table to deduce the codon changes necessary to go from the initial to resulting amino acid. Remember, the fewer the number of changes, the more likely it is to have been the case.

b.) What are the properties of the wild type (initial) amino acid? (Properties include: charge, shape, size and flexibility, features unique to the amino acid {i.e. the ability of histidine to respond to pH values typically found in the body, etc.})

c.) What are the properties of the hypothetical mutant (resulting) amino acid?

d.) How similar/different is the mutant amino acid from the wild-type?

e.) Is the hypothetical mutation on an alpha helix, beta sheet, or ‘loop’ that goes in between?

f.) Is the hypothetical mutation on the inside or the outside of the protein? Is the hypothetical mutation surrounded primarily by hydrophilic or hydrophobic residues?

g.) Consider replacing the wild type amino acid that is shown with the one found in the hypothetical mutant:
   - What are the properties of the wild type amino acid? (Review from earlier in the document)
   - What amino acids does that wild type amino acid interact with? You can visualize this by clicking ‘Neighbors’.
   - What are the properties of the amino acid(s) the wild type amino acid is interacting with?
   - What are the properties of the hypothetical mutant amino acid?
   - Based on the properties of the hypothetical mutant amino acid vs. the wild type amino acid, would it be able to interact with the surrounding amino acids in the same way? Justify your answer.

h.) Based on the previous question, hypothesize why a protein bearing the altered amino acid would fail to form, be unstable, or be unable to perform its function. How do the changes in structure/interactions you mentioned in part (g) lead to some of the symptoms of this disease?

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|--------------------------|------------------------------------------|----------------------------------------------------------------------------------|
| Hypothesis about change (20) | A thoughtful and thorough hypothesis based on the information provided by direct observation | - Does not take into account available information; implausible; shallow  
- Extensive use of outside resources used to complete the analysis (the majority of this should be your own, original work) |