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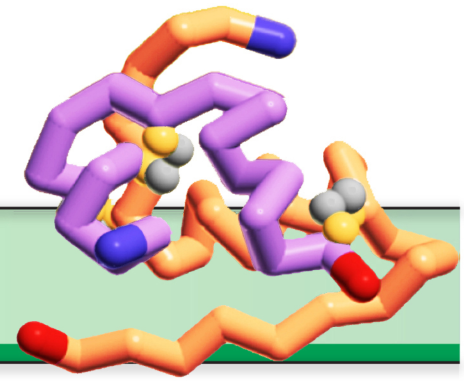

Exploring Further

Function of the C-Peptide Activity

Purpose

- Explore the function of the C-peptide within the insulin gene
- Learn how the concentration of molecules impacts their ability to interact
- Consider some of the issues involved in drug design

Preparation

- Create protein notecards by folding 3” x 5” index cards in half, two for each student, plus a few extras. (Exact size of notecards isn’t crucial.)
- On the inside flap of each notecard, write a molecule name.

  - For each group of approximately 12 students, include 1 notecard with **A-Chain** and 1 notecard with **B-Chain**.
  - The rest of the notecards should contain the names of other molecules found in the cell – pick ones the students know – some examples include: hemoglobin, starch, glycogen, DNA, phospholipid, water, RNA, ribosome – the exact number of each of these is not critical.
  - For activity 2, make notecards labeled **C-peptide** – to equal the number of copies of A-Chain and B-Chain.
  - For activity 3, make a second set of notecards – one for each student – with equal numbers labeled **A-Chain** and **B-Chain**.
  - Notecards can be made for permanent use by printing on cardstock, laminating and cutting the cards. Eight cards can be made from a single sheet of paper.

Activity 1 – Find Your Partner

1. This activity, in conjunction with activity 2, suggests a function for the C-peptide in assisting the A and B-Chains in interacting within the context of all the other molecules within the cell.

2. Pass out one notecard to each student, instructing them to keep the identity of their molecule hidden from everyone else.

   a. 1 A-Chain and 1 B-Chain for approximately every 12 students

   b. Mixture of other molecules on remaining notecards

3. Tell students that they represent various molecules within the cell. They are to move around the room, randomly encountering other students. (Review the concept of Brownian motion.)

4. Note the time, and tell students to start.

5. When two students encounter each other, they should quietly disclose the contents of their notecards to each other.

   a. If one of the students contains the A-Chain, and the other contains the B-Chain, they should link arms, call out, “insulin,” and continue moving around the room, encountering other students.

   b. If students can’t form insulin (A-Chain only, B-Chain only, or neither A or B-Chains), no action is taken. They move on, continuing to encounter other students.

6. When all insulin molecules have been formed (based on the number of A and B-Chains that were initially handed out), note the time. Have students remain standing for activity 2.

Activity 2 – Matchmaker, Matchmaker

1. This activity demonstrates a role for the C-Peptide in assisting the A and B-Chains in interacting.

2. All students keep their cards from activity 1, with the following exception: swap out a C-Peptide for one of the non-insulin proteins, with the total number of C-Peptides equal to the number of insulin molecules formed in activity 1.

3. Each C-Peptide should link arms with an A-Chain and a B-Chain.

4. Repeat activity 1, noting the start and stop times. Expect the activity to take less time, since the A and B-Chains are connected by the C-Peptide and should therefore find each other faster.

5. Following the activity, guide a discussion about the possible roles of the C-Peptide:

   a. One possible role of the C-Peptide is to help the two chains find each other in the crowded cell environment.

   b. Another possible role is that the C-Peptide is necessary for the correct folding of the protein.

Function of the C-Peptide Activity (continued)

c. How might we determine which of the possibilities is the correct one?

d. You may choose to have students read this Chemical and Engineering News Article, *Insulin*, http://pubs.acs.org/cen/coverstory/83/8325/8325insulin.html describing the historical background of the use of insulin for treating diabetes, isolation, genetic engineering. Thayer, Ann, Oct. 25, 2004. Insulin. Chemical & Engineering News: 59

This article describes initial experiments to genetically engineer human insulin – which, due to federal regulations, required that only INACTIVE proteins could be synthesized. Mixing purified A and B-Chains produced active insulin. With changed regulations, genetically engineered human insulin currently is made as a (B-Chain – C-Peptide – A-Chain) construct, because it only requires one synthesis and purification instead of two.

Activity 3 – Increasing the Odds

1. This activity models what happens in genetic engineering, when the two chains are mixed in vivo (in the absence of all other molecules).

2. Provide each student with a new notecard.

a. Half the notecards should say chain A.

b. Half the notecards should say chain B.

3. Repeat activity 1, noting the start and stop times. It may be useful to stop the process before EVERY insulin is formed.

4. Have students calculate the number of insulin molecules folded per minute from activities 1-3, then discuss the differences in the rate of insulin formation in the three different scenarios.

a. You will expect to find the formation rate to be the slowest in activity 1, where A and B-Chains must interact in the mixture of all the other molecules within the cell.

b. Activity 2 demonstrates the value of the C-Peptide in bringing the A and B-Chains together in the crowded cell environment.

c. Activity 3 demonstrates that when equal concentrations of purified A and B-Chains are mixed together, they can easily interact and form active insulin.