2.785J/20.411J/3.97J/HST.523J

CELL-MATRIX MECHANICS

Homework #6

Response of the rotator cuff to injury.

The rotator cuff is a complex of tendons (principally comprised of fibroblast-like cells) that insert into the humeral bone that forms the shoulder joint (Fig. 1). Ruptures of this tendon complex are not uncommon (Fig. 1, white arrow). The following questions deal with findings made by researchers studying various aspects of the behavior of cells in the torn rotator cuff.

1. A common finding is that the ends of the cuff retract after rupture over a 3-6 week period, widening the gap between the torn ends. This may explain why these tears do not heal naturally (*i.e.*, the ends to not rejoin naturally). It has been observed that the gap between the ends widens to a point with time and then there is no additional retraction.
a) What could explain retraction of the ends of the ruptured tendon?
b) What connection might there be between the acute inflammation induced by the injury that resulted in the rupture of the tendon, and the retraction of the ends?
c) What explanation could you offer for the fact that the retraction of the ends occurs for a certain period (*e.g.*, 6 weeks) and then there is no additional retraction of the ends?
d) Assuming that an appropriate animal model exists for this condition what method would you use to directly test your answers?

2. One method of treatment of the torn cuff is to suture the ends together. Assume that the healing process involves the filling of the gap, reduced by suturing to about 2 mm, with reparative tissue. The researcher has conducted experiments to study the contractile behavior of cells in this reparative tissue with healing time. She has removed pieces of the reparative tissue from an experimental animal model after 2, 8, and 26 weeks for laboratory testing of the stress-strain behavior of the extracellular matrix (Fig. 2) and the contractile behavior. For the latter, she pulls the tissue to increasing lengths and excites the cells to contract using a chemical regulator, and measures the force (Fig. 3). She interprets the findings as showing that the contractile behavior of the cells decreases through the 26-week period of the experiment. Do you agree? Explain. Show on Fig. 3 how you arrived at your answer, and scan Fig. 3 to send with your answers.

3. What is the explanation at the molecular level for the contractile behavior of the reparative tissue in Fig. 3?

4. In order to investigate the contractile behavior of the reparative tissue cells, the researcher has isolated the cells for growth in culture.
a) Describe one *in vitro* assay that she could use to investigate the contractile behavior of the cells, other than the cell force monitor.
b) Note the principal limitation of the assay that you have proposed to use in (a).
c) In order to obtain enough cells to use in the *in vitro* assay in (a) she needs to allow time for the cells to grow in culture and then she needs to subculture them into additional culture dishes. How might this process of increasing the number of cells affect her contractile results?

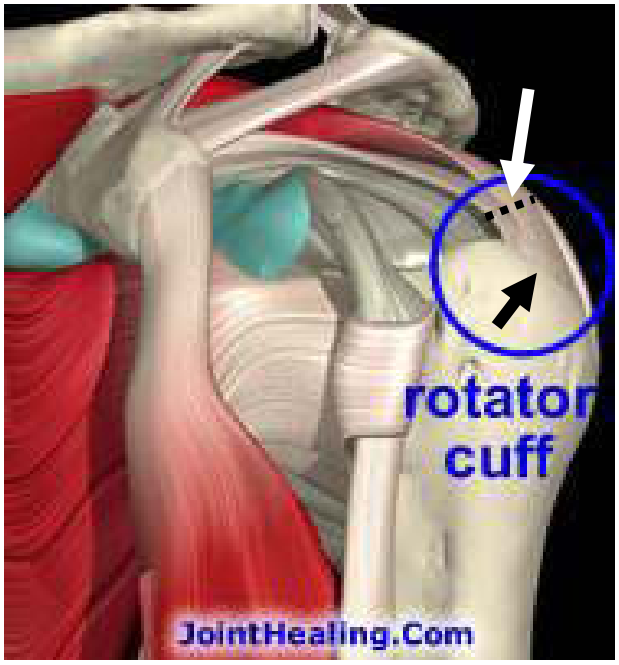

Fig. 1 Schematic showing the rotator cuff and the location of a tear in the tendon (dashed line; white arrow). The black arrow shows the insertion of the tendon into bone.

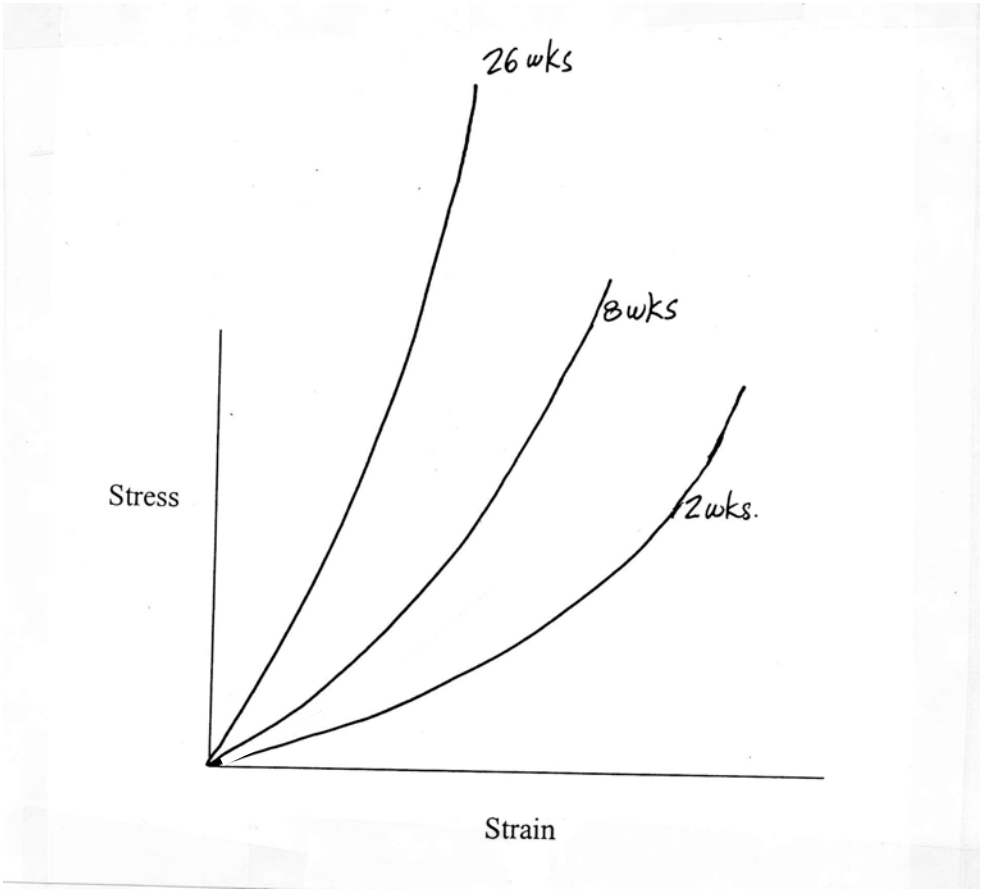

Fig. 2 Stress-strain curves for the reparative tissue.

Scan this sheet with your answer.

Name _____

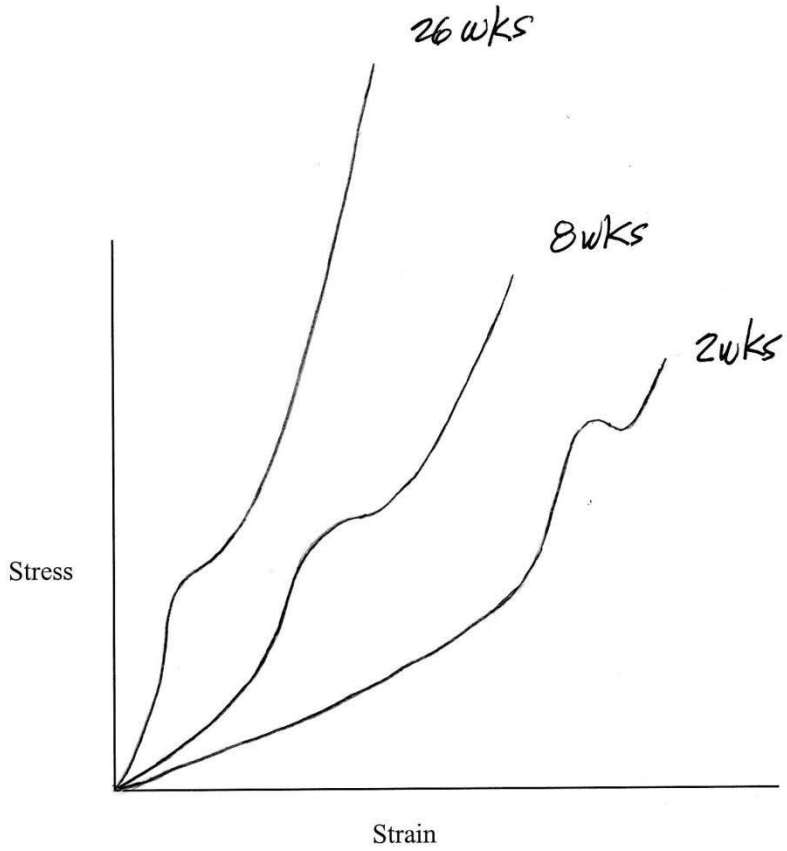

Fig. 3 Stress-strain curve for the reparative tissue in Fig. 2 when contraction is stimulated.

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