**How Are Skeletal Muscles Formed? November 4, 2016**

**POSSIBILITY ONE)** Start with masses of stem cells; Signal those cells at locations where stem cells should differentiate into muscle cells. (How to cause these muscle cells to orient their axes parallel to the proper directions.)

("Note that cells of many muscles have oblique orientations: "pennate" vs. "palmate")

In other words, those stem cells located where bones need to be get signaled to stimulate "turning on" (transcription) those combinations of genes which will cause them to become bone cells.

**POSSIBILITY TWO)** Cells that are already committed to become muscle cells aggregate into masses along the sides of developing leg skeleton.

These aggregations of muscle cells then attach to their proper "origin" and "insertion' locations on bone surfaces.

These attachments signal the masses of muscle cells to split into biceps, triceps, deltoid, gastrocnemius, interosseous, etc. etc. that anatomy students have to memorize.

**POSSIBILITY THREE)** Cells at future attachment sites exert pulling forces on collagen fibers and muscle cells, lining them up between origins and insertions.

 **III A)** Pulling forces result from skeletal elongation?

 **III B)** Pulling forces are produced by traction (which also produces crawling by cells) of cells at the locations on the skeletal surfaces, where origins and insertions should form.

**POSSIBILITY FOUR)**  Chemotactic or haptotactic gradients of some molecules are secreted and diffuse outward from bone surfaces at locations where muscles will later be physically attached to bones (i.e. the future "origins" and "insertions")

Crawling muscle cells home in toward these attractant secretion sites, and develop strong attachments to them.

**POSSIBILITY FIVE)** Perhaps muscle cells aggregate into elongate masses before they enter the limb, and find their attachment sites ("origins" and "insertions") after, and independently of their arrangement into their anatomical shapes develop.

**PLEASE INVENT POSSIBILITY SIX, SEVEN, ETC, And experiments to detect and distinguish which of these processes actually occur.**

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**Some experiments:**

**a)** Dissecting early bones from embryos and culturing them in collagen gels results in

collagen becoming stretched to cells and to bones, and compressed & aligned where tendons and ligaments should form.

**b)** If you dissect out pieces of skeletal muscle, from any part of the body, and put them in the collagen gels with embryonic leg bones,, then the muscle cells physically rearrange and reorient to form anatomically real-looking muscles, attached to bone surfaces at correct (?) origin and insertion points. (This experiment should be tried with cardiac muscle cells: Would heart cells get incorporated and aligned among and along the biceps, pectorals?

**c)** Grim & other Czech researchers discovered that entirely different, non-muscle differentiated cell types get rearranged within developing chicken embryos, and (somehow!?) become shaped and attached to the skeleton as exact replicas of specific muscles (i.e except that these muscle-like structures contain no muscle cells, and are not contractile. These researchers concluded that "Positional Information" signals cause shaping and attachments of cells, independently of what cell type they differentiate into.

d) Bruce Carlson inserted surgical sponges (non-living, flexible plastic [?] meshes) into legs of frogs at times of muscle regeneration. Some kind of pulling forces attached these artificial "sponges" to the skeletal attachment sites where the ends of the gastrocnemius are normally attached.

In other words, both embryonic and regenerating tissues contain patterns of some kind of pulling forces that will "correctly" reshape and realign not just skeletal muscle cells, but other (any?) differentiated cells into realistic facsimiles of specific skeletal muscles, and can even rearrange non-living surgical "sponges" into the shapes and attachment points of the gastrocnemius, and perhaps other muscles.