B. Cell-Matrix Interactions

A. How cells pull onto and deform the matrix to which they attach themselves.

B. Cell-matrix interactions control the spontaneous closure of wounds in organs.

C. What happens when regeneration is induced?

B. Cell-matrix interactions control the spontaneous closure of wounds in organs.

1. Hypothesis: Regeneration requires selective blocking of contraction. Need for understanding of kinetics and mechanism of contraction (to be tested later).
2. Initiation of contractile force. Defect perimeter or center of skin defect?
3. Propagation of contraction. Do cells cooperate?
4. Termination of contraction. How does the contractile force die out?

2. Initiation of contractile force. Located at defect perimeter or uniformly distributed?

- Picture frame vs. uniform contractile field (UCF) hypotheses.
- Data in Fig. 9.2 (attached) show that the ECM analog that blocks contraction is effective at perimeter but not at center of defect.
- These data support the picture frame hypothesis.
- However, other data (Fig. 4.4) support the UCF hypothesis.

Spontaneously contracting dermis-free defect (10 d). Contractile cells stained brown. Two magnifications.

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Contraction of dermis-free defect blocked by DRT

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Brown, contractile cells. Blue-gray, porous DRT.

Effect of DRT location on contraction blocking

DRT is a biologic-ally active ECM analog

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See Figure 9.2 in Yannas, I. V. *Tissue and Organ Regeneration in Adults*. New York: Springer-Verlag, 2001.

3. Propagation of contraction. Do cells cooperate?

- **Cell cluster at edge of defect reaches thickness of about 100 μm at time of contraction initiation (Fig. 9.3, attached).**
- **Contraction is more vigorous when cell density inside pores is high (Fig. 10.4, attached).**

Cells (F) form cluster, thickness δ, located at edge of skin defect. δ increases after injury.

2 d post-injury

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See Figure 9.3 in [Yannas].

6 d post-injury

Compare two ECM analogs with different activity.

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See Table 10.1 in [Yannas].

Cell density high inside pores of ECM analog (analog B) that blocks contraction poorly

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See Figure 10.4 – top image in [Yannas].

Much lower cell density inside pores of ECM analog (DRT) that blocks contraction effectively

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See Figure 10.4 – bottom image in [Yannas].

4. Termination of contraction. How does the contractile force die out?

- Epidermal confluence? No, it precedes arrest of contraction by at least several days.
- Synthesis of basement membrane? Certain steps coincide roughly with arrest of contraction.
- Loss of traction in the stroma?
  - Ffibronectin depletion (“grip-to-slip”)
  - Granulation tissue critically degraded by collagenases.
  - Depletion of contractile fibroblasts (following sufficient synthesis of collagen or other inhibitory mechanism).
  - Dermis stretched up to high-stiffness region, resists deformation by contractile cells.

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See Figure 10.5 in [Yannas].

Contrac-tion arrest occurs clearly after epidermal confluence is reached at 19 d

Defect area closure using three proto-cols

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See Figure 8.1 in [Yannas].

Kinetics of defect area closure using three protocols

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See Figure 10.2 in [Yannas].

Conclusions

- **Closure of a defect in skin or a peripheral nerve appears to be initiated at the time of injury.**
- **Closure proceeds mainly by contraction, the engine of closure.**
- **It is probably terminated by a stromal mechanism that is associated with loss of cell traction and cancellation of the contractile force.**