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Biomaterials-Tissue Interactions

CONTENTS

TEXT: I. V. Yannas. *Tissue and Organ Regeneration in Adults.* New York: Springer, 2001.

Introduction.

How are biomaterials used?

Brief survey: from organs to cells.

How are biomaterials used?

Today's brief survey: from organ to cell

outline of survey

1. **Five Therapies for the Missing Organ**
   - **Examples of permanent implants**
   - **Examples of regenerated organs**
2. **Tissue and organ regeneration viewed as as processes of chemical synthesis.**
3. **What is the mechanism of organ regeneration?**
4. **Cell-matrix interactions.**
5. **The unit cell process.**

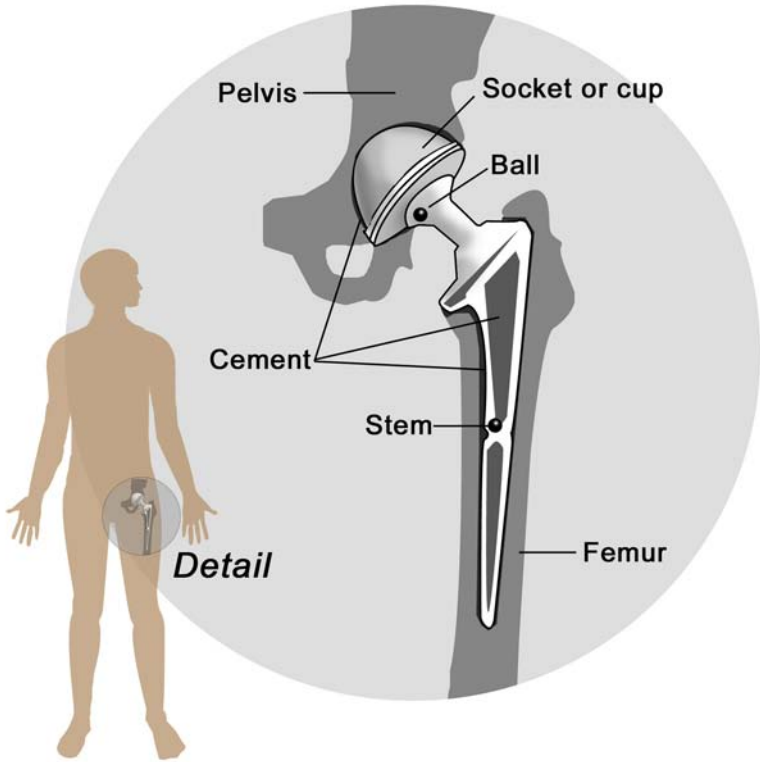
Five Therapies for the Missing Organ

1. Transplantation (e.g., kidney transplant, heart transplant, liver transplant)
2. Autografting (e.g., heart bypass, skin grafting).
3. Permanent implants (e.g., hip prosthesis, pacemaker, breast implant)
4. In vitro synthesis (e.g., epidermis)
5. In vivo synthesis or regeneration (e.g., skin, nerves, conjunctiva).

Remarks: Biomaterials are used in therapies #3, 4 and 5. Tissue engineering includes therapies #4 and 5.

Therapy # 3 :

Example of permanent implant



Another example of permanent implant

AbioCor™ Implantable Replacement Heart
(http://www.abiocor.com)

Two cases of massively burnt patients

1. **Six-year-old boy burned massively was treated in upper abdomen with own skin (meshed autograft) and in lower abdomen with template.**
2. **Middle-aged man burned in industrial fire, lost skin in right side of face was treated with template.**

Example of poor nerve regeneration

undegraded template inside nerve chamber

Image removed due to copyright considerations.

Example of good nerve regeneration

template inside nerve chamber degraded optimally

Image removed due to copyright considerations.

2. Tissue and Organ Regeneration viewed as as processes of chemical synthesis.

Ammonia synthesis (F. Haber)

$$3H_2 + N_2 \xrightarrow{T,\ P} 2NH_3$$

Reactants → Products

NOTE: stoichiometry of chemical equation expresses conservation of mass (Lavoisier)

Apply chemical symbolism and terminology to organ regeneration

- **Example of "reaction diagram":**

$$KC + DRT \rightarrow E \bullet BM \bullet RR \bullet D$$

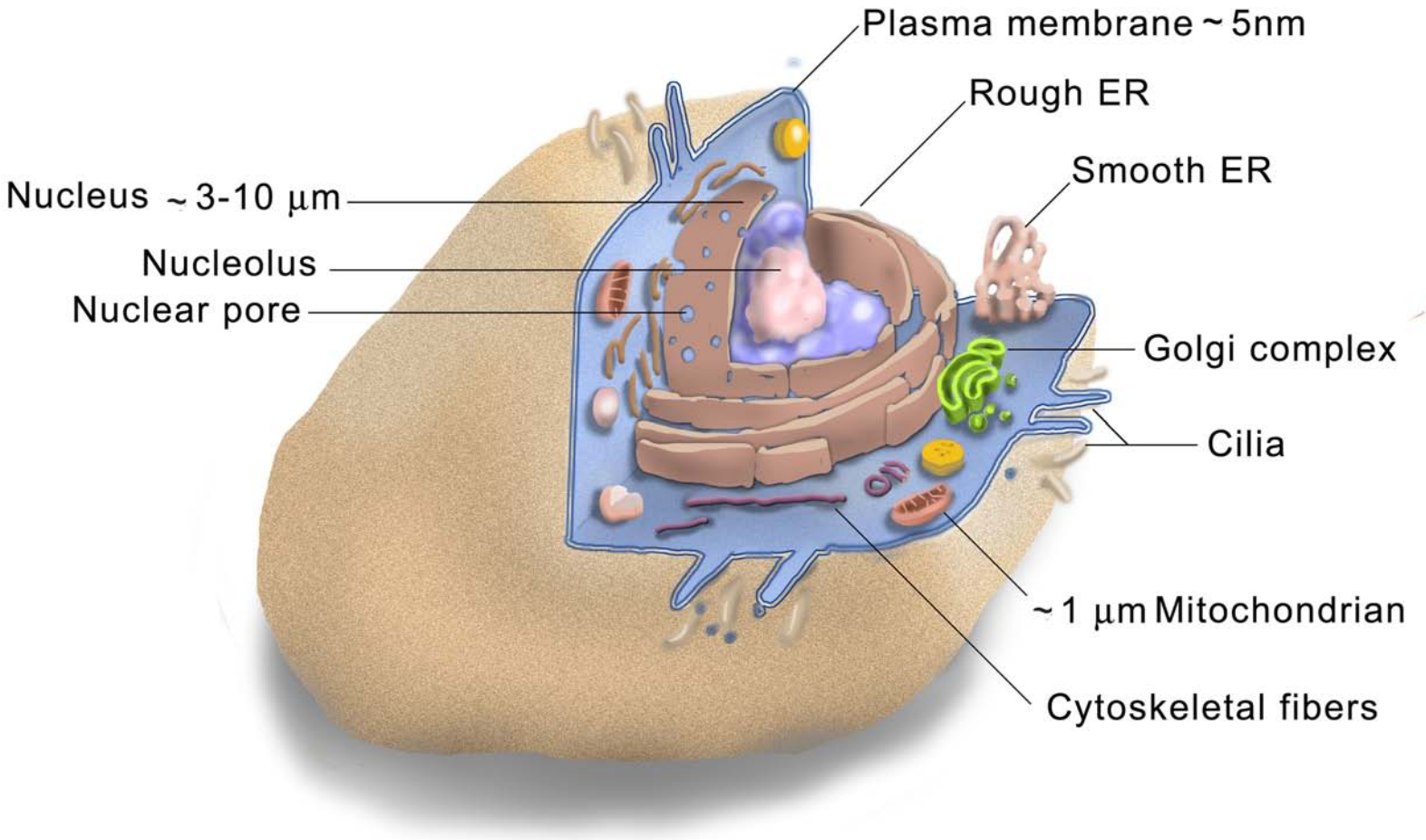
- **Reactants: cells, regulators, matrices**
- **Reactors: in vitro cell culture; in vivo (anatomical site)**
- **Products: either scar or regenerated tissue (or intermediate cases)**

3. What is the mechanism of organ regeneration?

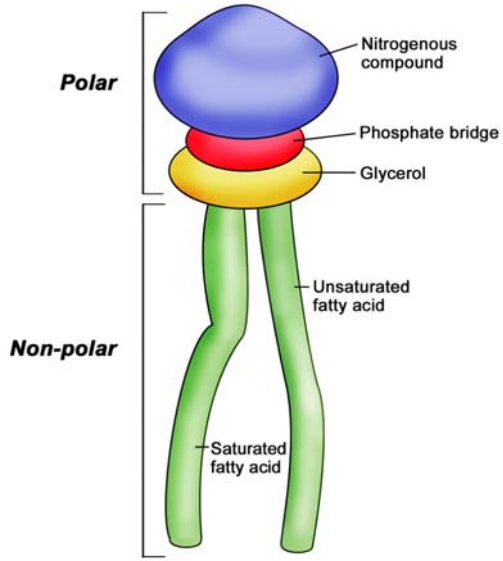
1. Data: There is an antagonistic relation between contraction of a wounded site and regeneration at that site.
2. Theory of induced regeneration: Blocking of contraction process leads to regeneration.
3. Contraction is mediated by cell-matrix interactions. Templates block these interactions.

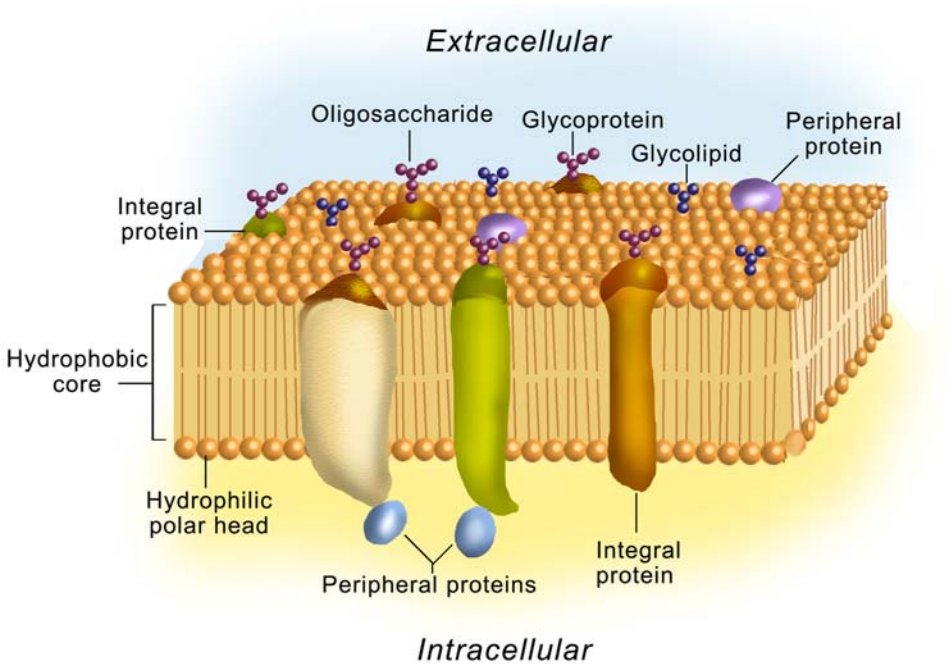
4. Cell-matrix interactions

A typified cell

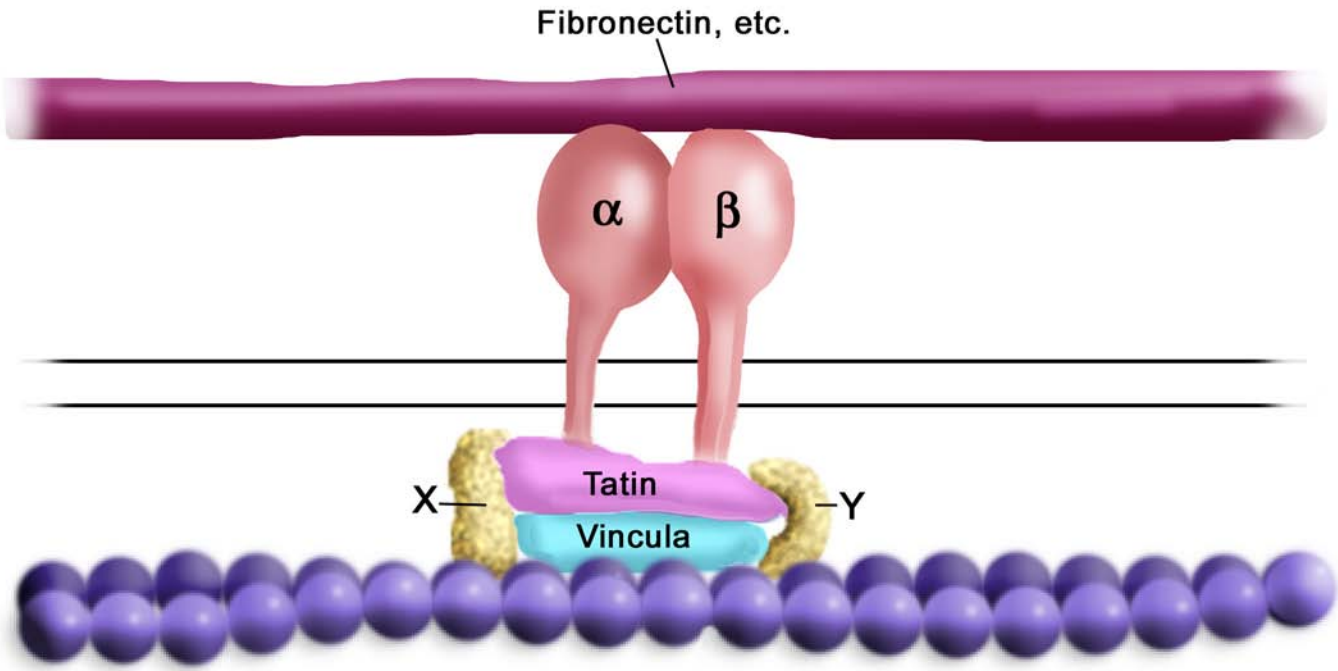


Cell membrane





Cell-matrix interaction through integrins

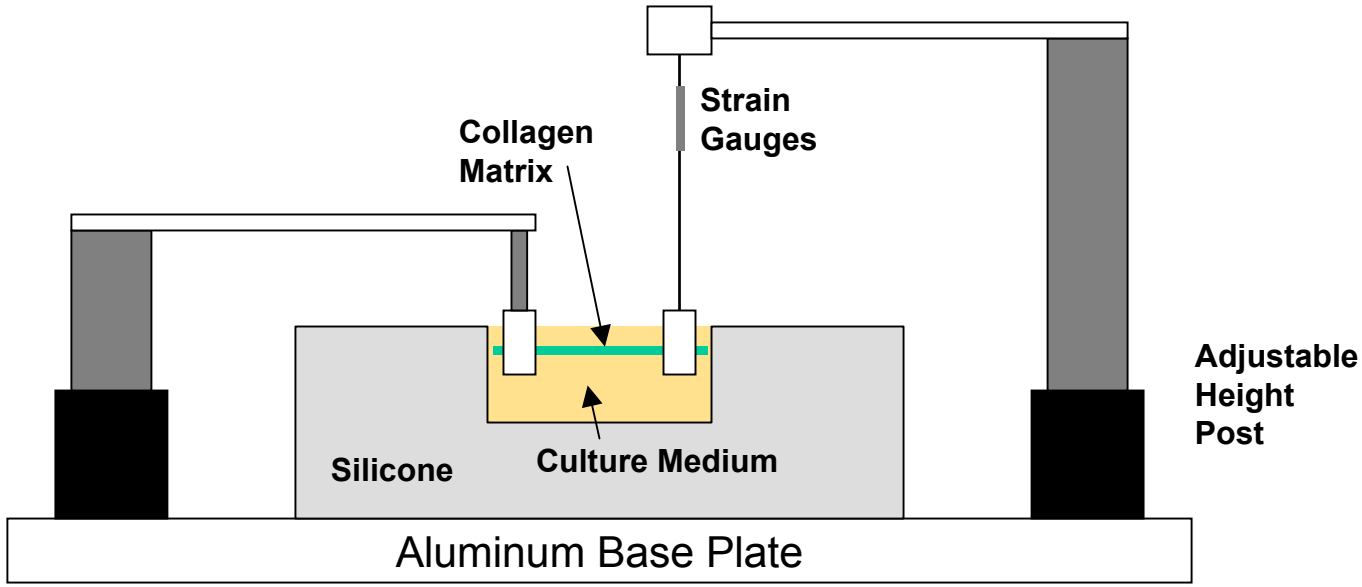


Live Cell Imaging

Freyman et al., 2001

Images removed due to copyright considerations.
See Freyman, T.M. et al. “Micromechanics of Fibroplast Contraction of a Collagen-GAG Matrix.” Experimental Cell Research 269: 140-153 (2001)

Modified cell force monitor



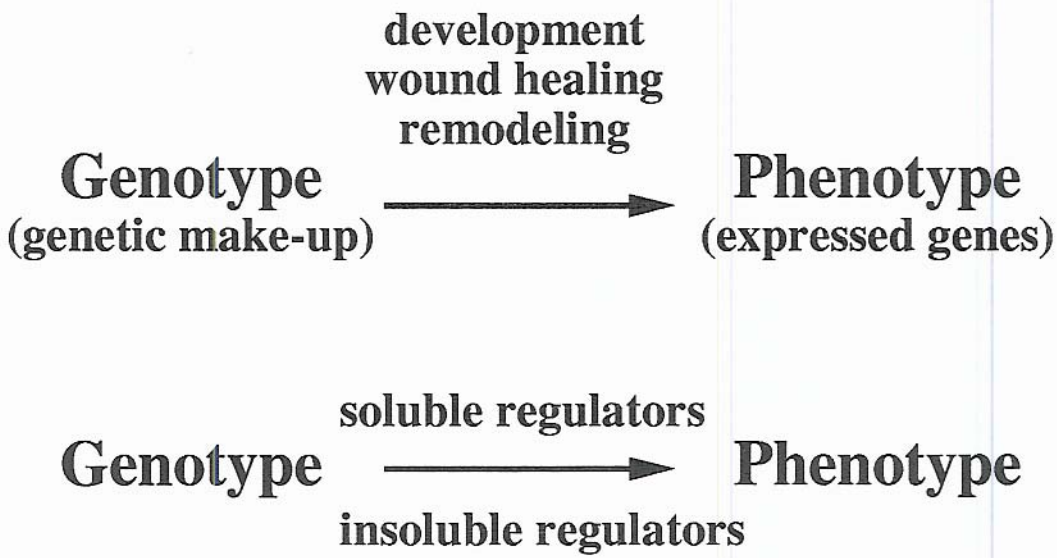
Use to study unit cell processes quantitatively

See Freyman et al., 2001

5. The unit cell process

- **Study cell function as if it comprises several distinct processes.**
- **Identify the critical unit cell process.**
- **Focus attention on controlling the critical process.**

Conditions for gene expression



Classic data: Cell-matrix interaction affects cell shape

1. Epithelial cell + plastic → Flattened cell

   Epithelial cell + collagen → Rounded cell

(Cytoplasmic structures, which control shape, are modulated by insoluble substrate.)

2. Endothelial cells + plastic → multilayered structures

   Endothelial cells + plastic + FGF → confluent monolayer

   Endothelial cells + plastic + FGF → ECM

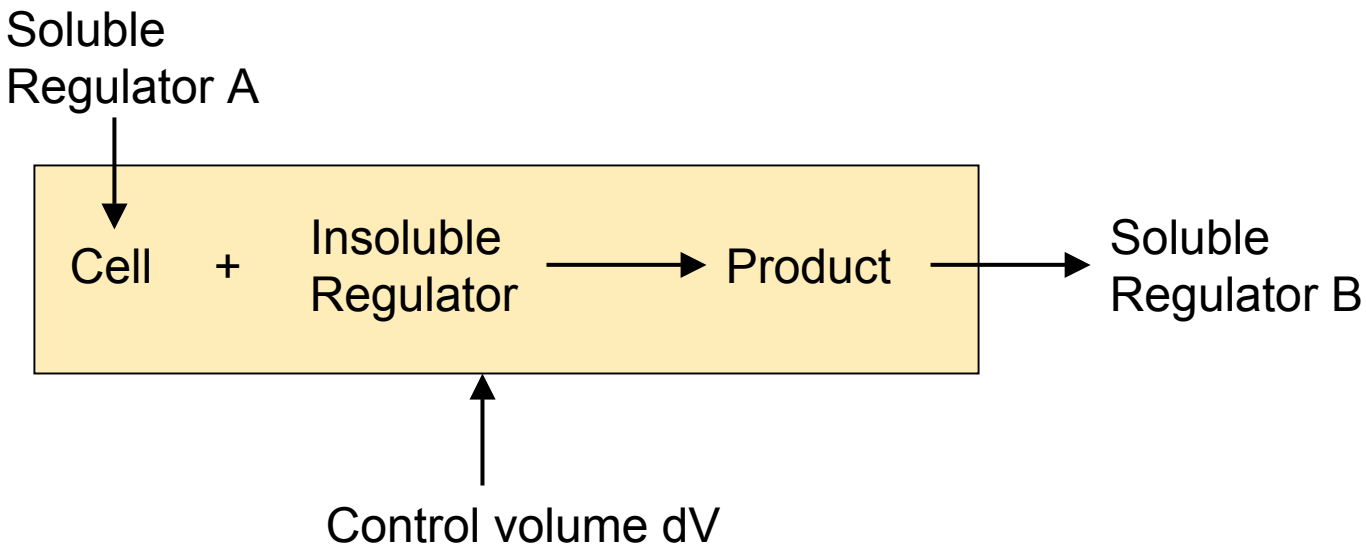
   Endothelial cells + ECM → confluent monolayer

   Endothelial cells + ECM → new ECM

(Loss of normal phenotypic properties in absence of regulator or in absence of ECM.)

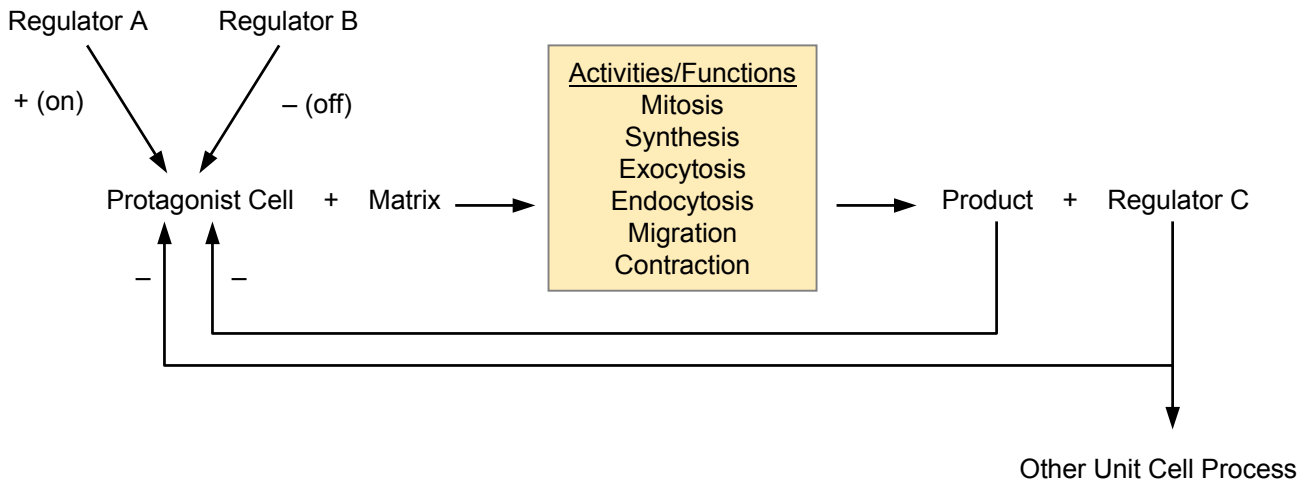
See D. Gospodarowiez et al., *Cancer Res.* **38**:4155 (1978).
S.C.G. Tseng et al., *J. Cell Biol.* **97**:803 (1983).

Definition of unit cell process

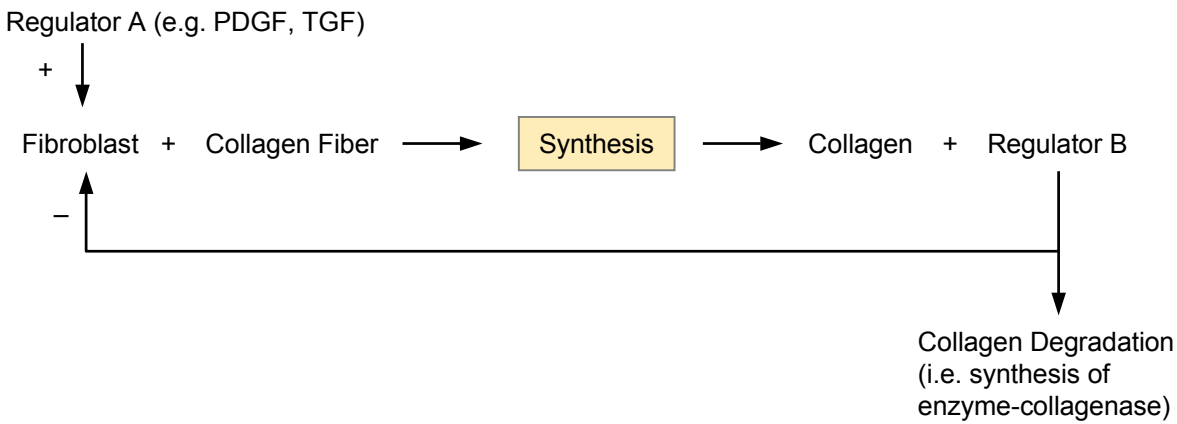


Unit cell process confined conceptually in a control volume dV

Various unit cell processes



Example: Collagen Synthesis



Properties of a unit cell process

Working Paradigm: Unit Cell Process

a) Describes a specific **cell-matrix interaction**. Usually it describes the induction of a specific phenotype of the **protagonist cell** by an insoluble **substrate**.

b) Confined conceptually in a **control volume** dV (Fig. 1.2).
Order of magnitude: 10x10x10 μm.

c) **Regulated by diffusible substances** which enter into and exit from control volume. These substances regulate the cell-matrix interaction. Also regulated by **mechanical forces** which act by deforming the matrix, thereby modulating the cell-matrix interaction.

d) The cell-matrix interaction is a highly specific process: the **cooperative configurational interaction** between ligand and receptor. Usually both ligand and receptor are macromolecules, each with a highly specific configuration.

e) Can be **reproducibly** demonstrated (or rejected) *in vitro*. **Falsifiability** of each model of cell-matrix interaction.

f) **Scale**: small enough to be reproduced *in vitro* and large enough to have significant physiological content.

g) Forms a conceptual bridge between ***in vitro and in vivo*** phenomena.