Lecture #2
Tissue Organization

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Biological Scales
Tissue Classifications

• Epithelial Tissue
  – Tightly packed continuous cell sheets. Serve as linings and barriers. Outer layer of skin; inside of mouth, stomach, and intestines; linings of organs.

• Connective Tissue
  – Support and structure. Fewer cells, largely extracellular matrix. Inner layer of skin, tendons, ligaments, cartilage, bone, fat, blood.

• Muscle Tissue
  – Optimized for contraction.

• Neural Tissue
  – Neurons and glial cells. Brain, spinal cord, peripheral nerves.
Organs Consist of Multiple Tissues
Epithelial Sheets

- Simple
- Stratified
- Columnar
- Cuboidal
- Squamous

Free surface

Basal lamina

Connective tissue

Figure 20-18 Essential Cell Biology 3/e © Garland Science 2010
Epithelial Sheets: Junctions

<table>
<thead>
<tr>
<th>name</th>
<th>function</th>
</tr>
</thead>
<tbody>
<tr>
<td>tight junction</td>
<td>seals neighboring cells together in an epithelial sheet to prevent leakage of molecules between them</td>
</tr>
<tr>
<td>adherens junction</td>
<td>joins an actin bundle in one cell to a similar bundle in a neighboring cell</td>
</tr>
<tr>
<td>desmosome</td>
<td>joins the intermediate filaments in one cell to those in a neighbor</td>
</tr>
<tr>
<td>gap junction</td>
<td>forms channels that allow small water-soluble molecules, including ions, to pass from cell to cell</td>
</tr>
<tr>
<td>hemidesmosome</td>
<td>anchors intermediate filaments in a cell to the basal lamina</td>
</tr>
</tbody>
</table>

Figure 20-22 Essential Cell Biology 3/e (© Garland Science 2010)
Tight Junctions

Figure 20-23 Essential Cell Biology 3/e © Garland Science 2010
Adherens Junctions

Figure 20-24 Essential Cell Biology 3/e (© Garland Science 2010)

Figure 20-25 Essential Cell Biology 3/e (© Garland Science 2010)
Connective Tissues

Collagen provides tensile strength

Fibroblasts secrete and reorganize collagen

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Figure 20-10 Essential Cell Biology 3/e (© Garland Science 2010)
Connective Tissues:
Proteoglycans provide compressive strength

Glycosaminoglycans (GAGs)

Hyaluronan molecule
Keratan sulfate
Chondroitin sulfate
Core protein
Link proteins
Aggrecan aggregate

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Muscle Tissue

- Desmosome
- Gap junction
- T-tubule
- Sarcoplasmic reticulum
- Intercalated disc
- Cardiac myofibril
Neural Tissue

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- Microglia
- Neuron
- Astrocyte
- Capillary
- Oligodendrocyte
- Myelinated axon
- Myelin sheath (cut)
- Ependymal cells
- Ventricle of brain
Structure / Function of Tissues

• Overall tissue / organ function depends on microscopic structure of "functional units"
• Subtle changes in microstructure can greatly affect organ function
Figure 1. Rates of protein secretion, determined from collected culture media by ELISA. Albumin (A), transferrin (B), and fibrinogen (C) secretion rates were significantly higher for the sandwich system as compared to the single-gel culture. Error bars represent standard deviation of four repeated measurements from a batch of cells.
A cell and its communication with other body parts
How are tissue structures formed?
A Tissue-Like Printed Material

Gabriel Villar, Alexander D. Graham, Hagan Bayley*

Living cells communicate and cooperate to produce the emergent properties of tissues. Synthetic mimics of cells, such as liposomes, are typically incapable of cooperation and therefore cannot readily display sophisticated collective behavior. We printed tens of thousands of picoliter aqueous droplets that become joined by single lipid bilayers to form a cohesive material with cooperating compartments. Three-dimensional structures can be built with heterologous droplets in software-defined arrangements. The droplet networks can be functionalized with membrane proteins; for example, to allow rapid electrical communication along a specific path. The networks can also be programmed by osmolarity gradients to fold into otherwise unattainable designed structures. Printed droplet networks might be interfaced with tissues, used as tissue engineering substrates, or developed as mimics of living tissue.

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Liposomes as Model Cells/Tissues?

**A Tissue-Like Printed Material**

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Liposomes as Model Cells/Tissues?

High osmolarity

Low osmolarity

Osmosis

What will happen?
Liposomes as Model Cells/Tissues?

What will happen?

What will happen?
Liposomes as Model Cells/Tissues?

What will happen?

http://www.sciencemag.org/content/suppl/2013/04/04/340.6128.48.DC1/1229495s1.mov
Liposomes as Model Cells/Tissues?

What will happen?

What are the defining characteristics of this model system?
Liposomes as Model Cells/Tissues?

What will happen?

Less pronounced variations in osmolarity between cells...
Are there other differences that could lead to such assembly mechanisms?
History of cell sorting

• 1955 Townes and Holftreter
• dissociated cells reconstruct structures in amphibian neurula
• always same pattern
• mimic events in vivo
• sorting vs invasion is of fundamental importance in tissue engineering
Work of Adhesion

- Example: two liquids such as oil and water
- Interfacial energy at the surface corresponds to the surface tension, $\gamma_{O/W}$
- Work required to inject air at the interface

\[ W_{O/W} = \gamma_{O/A} + \gamma_{W/A} - \gamma_{O/W} \]

\[ W_{O/O} = \gamma_{O/A} + \gamma_{A/O} - \gamma_{O/O} \]
\[ \gamma_{O/O} = 0 \]
\[ W_{O/O} = 2 \gamma_{O/A} \]
Work of Adhesion

- Example: two liquids such as oil and water
- Interfacial energy at the surface corresponds to the surface tension, $\gamma_{O/W}$
- Work required to inject air at the interface
  
  $$W_{O/W} = \gamma_{O/A} + \gamma_{W/A} - \gamma_{O/W}$$

- Steinberg model to predict sorting behavior
- Cells that express high levels of cell-adhesion molecules will have a large work of adhesion; low levels will have small work of adhesion
Tissue Sorting

- Dissociated cells reaggregate
- Sorting properties analogous to molecules in liquid solution
- Relative cohesion affinity (a-a, b-b, a-b) dictates sorting behavior

\[
\begin{align*}
W_{aa} & > W_{ab} \geq W_{bb} \\
W_{ab} & \leq \frac{W_{aa} + W_{bb}}{2}
\end{align*}
\]

(A) Sorting

\[
\begin{align*}
W_{aa} & \leq W_{ab} > W_{bb} \\
W_{ab} & \geq \frac{W_{aa} + W_{bb}}{2}
\end{align*}
\]

(B) Random

\[
\begin{align*}
W_{aa} & \geq W_{bb} >> W_{ab} \\
W_{ab} & << \frac{W_{aa} + W_{bb}}{2}
\end{align*}
\]

(C) Separation

Palsson and Bhatia
Work of Adhesion in Cell Sorting

- To use chart:
  - Calculate \(W_a/W_b\) and locate it on x-axis
  - Read work of adhesion (Wab) on y-axis
  - The background shading at the intersection will indicate the distribution of \(a\) and \(b\)
- Examples: \(W_a = 3, W_b = 1\)
  - \(Wab = 2.1 \rightarrow \text{mix}\)
  - \(Wab = 1.5 \rightarrow \text{complete coverage of } a \text{ by } b\)
  - \(Wab = 0.5 \rightarrow \text{incomplete coverage of } a \text{ by } b\)
How to measure Surface Free Energy?

Surface Tension for a Liquid Droplet Between Two Parallel Plates

- assuming liquid does not adhere to the plates.
- Sigma is the interfacial tension between the droplet and its surrounding medium.
- F is the force (in dynes) of the upper compression plate.
- R1 and R2 are the two principle radii of curvature of the droplet's surface.
- \( \pi R_3^2 \) is the area of contact between the droplet and either of the compression plates.

\[
\sigma = \frac{F}{\pi R_3^2 \left( \frac{1}{R_1} + \frac{1}{R_2} \right)^{-1}}
\]
Surface Tension in Cell Spreading

- Spreading behavior of embryonic tissues is due to differences in surface tension
- Parallel plate tissue surface tensiometer
  - Continuously records both the force applied to a living tissue aggregate and that aggregate's profile as it attempts to restore its original spheroidal shape

- A spherical heart aggregate on the lower compression plate (A) and compressed for 3.5 hours (B). When released (C), it temporarily retains a flattening of the upper and lower surfaces, but behaving like a liquid, it eventually rounds up again after a few more hours (D, E).

Foty, 1996
Surface Tension in Embryonic Tissues

The five embryonic tissues in order of decreasing surface tension are:
1. Limb mesoderm from 3.5 d embryos
2. Eye pigment epithelium for 4.5 d embryos
3. Heart ventricles from 5 day embryos
4. Livers from 5 day embryos
5. Neural retinas from 6-day embryos

At the right is the final configuration arising when two of these tissues are placed in combination with each other. The limb mesoderm was found to have the highest surface tension, the neural retina the lowest.

Foty, 1996
Mechanisms of Cell-Cell adhesion?
Cell adhesion molecules such as Cadherins

Interactions between two regions of apposing N-cadherin proteins. The purple and yellow proteins represent the cadherins from two apposing cells. The green dots represent the positions occupied by calcium ions. The dashed white line represented the boundaries of the "cell adhesion zipper" formed by these interactions.

Shapiro, 1995
Self-organization is a dynamic and lineage-intrinsic property of mammary epithelial cells

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Contributed by Mina J. Bissell, Lawrence Berkeley National Laboratory, December 30, 2010 (sent for review December 6, 2010)

Loss of organization is a principle feature of cancers; therefore it is important to understand how normal adult multilineage tissues, such as bilayered secretory epithelia, establish and maintain their architectures. The self-organization process that drives heterogeneous mixtures of cells to form organized tissues is well studied in embryology and with mammalian cell lines that were abnormal or engineered. Here we used a micropatterning approach that confined cells to a cylindrical geometry combined with an algorithm to quantify changes of cellular distribution over time to measure the with primary materials and a paucity of tractable culture systems for maintaining cell types from normal adult tissues. To facilitate a quantitative understanding of those processes in an adult epithelial tissue, we used a robust cell culture system that enables culture of pre-stasis normal HMEC obtained from reduction mammaplasties for 40–60 population doublings while maintaining both the LEP and MEP lineages (12). Flow cytometry-enriched cells from both lineages were placed in arrays of micropatterned microwells, where their distributions were...