Neural cell categories

- After the ectodermal tissue has folded into the neural tube, another series of signaling interactions determine the type of neural cell to which it gives rise.
- Many of these neural signals have been characterized as GROWTH FACTORS.
- The mature nervous system contains a vast array of cell types, which can be divided into two main categories:
  - the neurons, primarily responsible for signaling,
  - and supporting cells called glial cells.

Growth factors are proteins that bind to receptors on the cell surface, with the primary result of activating cellular proliferation and/or differentiation. Many growth factors are quite versatile, stimulating cellular division in numerous different cell types; while others are specific to a particular cell-type.

<table>
<thead>
<tr>
<th>Growth Factors</th>
<th>Factor Principal Source</th>
<th>Primary Activity</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet-Derived Growth Factor (PDGF)</td>
<td>platelets, endothelial cells, placenta</td>
<td>promotes proliferation of connective tissue, glial and smooth muscle cells</td>
<td>no catalytic protein kinase, 3 distinct dimer forms: AA, AB and BB</td>
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<tr>
<td>Epidermal Growth Factor (EGF)</td>
<td>submaxillary gland, Buckner gland</td>
<td>promotes proliferation of endothelial, glial and epithelial cells</td>
<td></td>
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<tr>
<td>TGF-α</td>
<td>lung cancer transformed cells</td>
<td>may be involved in normal wound healing</td>
<td>related to EGF</td>
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<tr>
<td>TGF-β</td>
<td>wide range of cells; protein is associated with the ECM</td>
<td>promotes proliferation of many cells; inhibits some star cells; induces mesenchyme to form in early embryos</td>
<td>at least 18 family members, 4 distinct receptors</td>
</tr>
<tr>
<td>Nerve Growth Factor (NGF)</td>
<td>parasympathetic ganglia, sympathetic ganglia, and dorsal root ganglia</td>
<td>promotes neurite outgrowth and neural cell survival</td>
<td>several related proteins that stimulate acetylcholine receptors, Wnt, Notch, and IGF</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>kidney</td>
<td>promotes proliferation and differentiation of erythroblasts</td>
<td></td>
</tr>
<tr>
<td>Transforming Growth Factor-β (TGF-β)</td>
<td>activated T&amp; cells (T-helper) and natural killer (NK) cells</td>
<td>inhibits fibroblast growth factor, platelet-derived growth factor, and epidermal growth factor production; promotes wound healing; inhibits angiogenesis and lymphocyte proliferation</td>
<td>at least 100 different family members</td>
</tr>
<tr>
<td>Insulin-like Growth Factor I (IGF-I)</td>
<td>primary liver</td>
<td>promote proliferation of many cell types</td>
<td>related to IGF-II and proinsulin</td>
</tr>
<tr>
<td>IGF-II</td>
<td>variety of cells</td>
<td>promote proliferation of many cell types; primarily of fetal origin</td>
<td>related to IGF-I and proinsulin</td>
</tr>
</tbody>
</table>
Researchers are finding that the destiny of neural tissue depends on a number of factors, including growth factors and where the position of the pluripotent or multi-potent cells are located when they receive the signal.

- For example, a key factor in spinal cord development is a secreted protein called sonic hedgehog that is similar to a signaling protein found in flies.

- The protein, initially secreted from mesodermal tissue lying beneath the developing spinal cord, marks young neural cells that are directly adjacent to become a specialized class of glial cells.

- Cells further away are exposed to lower concentrations of sonic hedgehog protein, and they become the motor neurons that control muscles.

- An even lower concentration promotes the formation of interneurons that relay messages to other neurons, not muscles.
Cell Cycle and neuron generation

- Neurons of the cerebral cortex are generated in the ventricular zone of the neural tube, an epithelial layer of stem cells that lines the lateral ventricles.
- Once they have left the cell cycle, the neurons migrate (on glial cells) out of the VZ to form the cortical plate (gray matter for the cortex).
- On the cortical plate, neurons become organized into well defined layers.

As the brain develops, neurons migrate from the inner surface to form the outer layers. Left: Immature neurons use fibers from cells called glia as highways to carry them to their destinations. Right: A single neuron, shown about 2,500 times its actual size, moves on a glial fiber. (10⁻⁶ m/hr)

Illustration by Lydia Kibiuk, Copyright © 1995 Lydia Kibiuk.

Improper migration leads to diseases including childhood epilepsy, mental retardation, lack of sense of smell and possibly many others.

Hiroshima/Nagasaki Effects
Timing of Cell Differentiation

- Remarkably, the final position of the neuron is correlated exactly to its birthdate
- Cells leaving later migrate past the older neurons (in deeper cortical layers) to the outermost cortex.
- The layering of the cortex is thus an inside-first outside-last layering.

Axon guidance mechanisms

- Axonal growth is led by growth cones
  - Filopodia (growing from axons) are able to sense the environment ahead for chemical markers and cues.
  - Mechanisms are fairly old in evolutionary terms.
- Intermediate chemical markers
  - Guideposts studied in invertebrates
- Short and long range cues
  - Short range chemo-attraction and chemo-repulsion
  - Long range chemo-attraction and chemo-repulsion
- Gradient effects
Axons locate their target tissues by using chemical attractants (blue) and repellants (orange) located around or on the surface of guide cells. Left: An axon begins to grow toward target tissue. Guide cells 1 and 3 secrete attractants that cause the axon to grow toward them, while guide cell 2 secretes a repellant. Surfaces of guide cells and target tissues also display attractant molecules (blue) and repellant molecules (orange). Right: A day later, the axon has grown around only guide cells 1 and 3.
Sir John Carew Eccles (January 27, 1903 – May 2, 1997) was an Australian neurophysiologist who won the 1963 Nobel Prize in Physiology or Medicine for his work on the synapse. He shared the prize with Andrew Fielding Huxley and Alan Lloyd Hodgkin. Eccles was the recipient of many honors, including a knighthood in 1958. In 1963, he was named “Australian of the Year.” His research contributed significantly to knowledge of the neurophysiological processes by which thought is processed, and in unraveling the complexities of the human brain.