Developmental Neurobiology

Presented By: Javier Fierro Jr.
November 11th, 2014
Axon Growth is a Dynamic Process

http://video.mit.edu/watch/watching-neurons-grow-6353/
The Growth Cone

- F-actin bundle
- F-actin network
- Filopodium
- Lamellipodia-like veil
- Dynamic microtubule
- Stable microtubule
- Axon shaft

Legend:
- C domain
- T zone
- P domain
Motors Move the Growth Cone Forward

A Filopodia extend

B Microtubules from central core advance

C Cytoplasm collapses to create new segment of axon

A1 Filopodium contacts an adhesive substance

A2 Vesicle fusion adds membrane to leading edge of filopodium

A3 Actin polymerization pushes filopodium forward

New axon growth
How Does a Neuron Find Its Target?

Two Hypotheses

1. Axon Projections are Imprecise
   - Proper connections are worked out by electrical activities during early experience

2. Chemospecificity Model
   - Axons are directed to their precise targets by chemical signals that exist independent of experience
Chemospecificity Hypothesis

A Normal Optics

Field of view

Retina

Tectum

Connectivity

Action
Chemospecificity Hypothesis

https://www.youtube.com/watch?v=ypgplb-UBww
Chemospecificity Hypothesis

A Normal Optics

Field of view

Connectivity

A Normal Optics

B Inverted

Field of view

Connectivity

Action

A Normal Optics

B Inverted

Field of view

Connectivity

Action
Chemotaxis

A. Attractant
B. Repellent
C. Collapse
D. Growth permissive
Molecules Involved in Chemotaxis

Ligands
- Netrin
- Slit
- Semaphorin

Receptors
- UNC-40/DCC
- UNC-5
- SAX-3/ROBO
- Neuropilin
- Plexin

Responses
- Attraction
- Repulsion
- Repulsion
- Repulsion
Mechanisms for Changes in Sensitivity to Axon Guidance Cues

Roof Plate

Commissural neuron

Floor Plate

Netrin

Slit
Mechanisms for Changes in Sensitivity to Axon Guidance Cues
Guide Post Cells

https://www.youtube.com/watch?v=EeunJ9j2Ckw
Synaptogenesis

a) Synaptogenesis
Stabilization of contacts between neurons

Recruitment of specific presynaptic proteins
Adhesion molecules
Recruitment of specific postsynaptic proteins
Signalling to actin cytoskeleton

b) Mature synapse
Modulation of synaptic function
Induction of dendritic spine maturation
Receptor
Modulation of postsynaptic protein function
Activation of intracellular signalling
Cell Adhesion Molecules
Components of a Synapse

- Axon
- Dendrite
- Synaptic cleft
- Synaptic vesicles
- Active zone proteins
- Trans-synaptic adhesion molecules
- Postsynaptic density
- Receptors
Some Glutamatergic Synapses Can Mature Within 1 Hour
Proteins in the Postsynaptic Density

- Cytoskeleton/Actin: 12%
- Kinases/Phosphatases, and Regulators: 11%
- GTPases and Regulators: 8%
- Cell Adhesion: 7%
- Metabolism: 7%
- Receptors and Channels: 6%
- Scaffolds: 6%
- Translation: 6%
- Mitochondria: 6%
- Membrane Trafficking: 5%
- Motor Proteins: 4%
- Chaperones: 2%
- Cytoskeleton - Others: 4%
- Others: 4%
- GTPases and Regulators: 8%
- Kinases/Phosphatases, and Regulators: 11%
Axon Pruning/Synapse Elimination

Pruning is a key process that shapes the brains of young children

- Refines connections based on experience
  - Connections used regularly become stronger and more complex
  - Connections used rarely are considered non-essential, and eventually get pruned to increase efficiency
Zebrafish as a Model Organism to Study Development

https://www.youtube.com/watch?v=vDxjochBf2g
Zebrafish as a Model Organism to Study Development

https://www.youtube.com/watch?v=PHGh06h1DJc