Neurodevelopment – Q & A by H.J.

Questions	Answers
Neural Crest derivatives	Schwann cells Autonomic neurons Gut neurons DRG Pia + Arachnoid
Anencephaly	Failure of neural tube to close (rostrally)
Spina Bifida	Failure of neural tube to close (caudally) Part of meninges protrudes through spinal cord.
Hox Genes	Similar to homeotic regulator genes in drosophilia. "Master Genes" Conserved region called *Homeobox* Includes emx and otx
Otx abnormality	Get epilepsy.
emx abnormality	Get schizencephaly
What determines pattern of hox gene expression?	Gradient of retinoic acid Produced by Hensen's node Gradient in ant-post creates hox expression in hindbrain
Where is the floor plate?	Ventral midline
What are the regions around the floor plate?	Adjacent = motoneurons Dorsal = interneurons Most dorsal = neural crest
What is BMP	Bone Morphogenetic Protein → single molecule that influences different tissues.
What induces ventral spinal cord characteristics?	Notochord. Thus if notochord transplant, get 2 floor plates and 2 mononeurons
What happens if notochord is removed from the embryo?	Floor plate and motoneurons fail to form
What is the floor plate and motoneurons induced by?	Product of Sonic Hedgehog (why does Nicholls leave out the R in moto**r** neurons? And why is it one word?)
What does Sonic Hedgehod induce?	Floor plate Motoneurons Serotonigeric neurons in ant. hindbrain Dopaminergic neurons in post. hindbrain

Notes:

	Oculomotor neurons in ant. midbrain
What does BMP induce?	Specification of cells in dorsal horn
What about retinoic acid?	Specifiy longitudinal gradients
Order of development	Sonic hedgehog specifies a ventral phenotype. Particular characteristics determined by previous history of tissue.
How is tissue initially restricted?	First by the anterior-posterior position (Hox Gene)
And further restricted by…	Dorso-ventral position (sonic hedgehog)

Main Point: Formation of forebrain and midbrain and spinal cord is by anteroposterior, dorsoventral and local patterning by induction of specific transcription factors.\

Cell Proliferation and Migration

Questions	Answers
How do the cells proliferate?	Grow radially. Nucleus migrates to inner (ventricular) surface. Pial end detaches. Cell divides Nuclei of daughters migrate to outer surface and reattach
Where would you find the younger neurons?	They migrate past the older ones.
Which ones are the largest?	Older ones.
Which neurons regenerate?	Olfactory. So smell can recover after injury
With whom do neurons share a common progenitor?	Glial cells
How do neurons move from ventricular to pial surfaces?	Via radial glial cells.
What are some neuronal migration proteins?	Astrotatin Integrin
What happens in a reeler mouse?	No reeler gene, so old neurons on outside, younger ones on inside.
What group of cells can migrate even without these radial glial cells?	GnRH – moves into CNS from olefactory epithelium.

Notes:

Kallmann's syndrome	In males – migration of GnRH fails to occur. - no smell and no normal sex dev't
What is the key to migration in PNS?	The substate. Eg. Neural cells migrate along laminin marked pathways

Maturation and Axon Outgrowth

Questions	Answers
What can influence maturation?	Environment – can shape output of cells (change their NT depending on env.)
What is LIF?	Leukemia inhibitory factor Can change the phenotype of crest cells
How to the axons grow?	Filopodia smell out substrates and choose direction. Can also clear out pathway and change substrate. Also have diffusible molecules which can attact the growing axon.
What is netrin?	In spinal cord. Used to direct axons.
What is laminin?	Present along pathways Synthesized by schwann cells after injury. If remove laminin (eg. Via Ab) then no neurite extension and outgrowth.

Myelin

Questions	Answers
What myelinates in PNS and CNS	PNS – Schwann Cells CNS – oligodendryocyes
Trembler mouse	No myelin. But if take sciatic nerve from normal mouse, then myelinates normally.
Significance of PMP-22	Aka. Peripheral myelin protein. Essential for layers of Schwann cell membranes to wrap and seal themselves around developing axons.
Who makes PMP-22?	Schwann cells make it and break it down. If neurons present, then Schwann won't break it down so it can be used.
Charcot Marie Tooth Disease	PMP-22 not normal Peripheral myelin fails to form Gly → Asp

Notes:

NGF

Questions	Answers
What happens if put leg on back of frog.	Nerves from CNS attracted to leg.
What causes growth?	NGF! Duh. In male mouse salivary glands.
What happens if remove NGF?	Ab against NGF in newborn mice prevents sympth. From dev't. So: req in dev't and survival.
Is parasymph affected by NGF?	Nope
What about sensory?	Needs NGF.
Ok, so what does the lack of NGF affect?	SYMPH & SENSORY →Required during a *critical period*
Where is NGF transported to?	Cell soma
What does it do there?	Regulates synth of norE via: 1. tyrosine hydroxylase 2. dopamine b-hydroxylase
What happens if NGF transport is impaired?	Level of these enz decreases!
How is it transported?	Anterograde AND retrograde

Neutrophins

Questions	Answers
What is BDNF?	Brain-derived neutrotrophic factor. Promotes survival of DRG neurons in culture. Rescues neurons in vivo if dying.
What happens early in devt before sensory neurons innervate targets?	The neurons req BDNF or NT3 for proliferation, differentiation and survival.
Who provides this stuff?	The neurons themselves (early on) and mesenchyme.
What about when they reach their targets?	Use NGF from the target.
How do they bind?	Low affinity neutrophin receptors.
What is TRK?	Has NGF receptor. (high affinity)

Notes:

How do they work?	Three pathways: 1. PLC 2. PI3K 3. MAP Kinase
What happens to cells that lack high affinity recepts?	Triggers cell death?
What type of NT do the NGF cells use in the CNS?	Ach
Where are they and what do they innervate?	In basal forebrain and innervate hippocampus (learning/memory)
What happens if u infuse NGF in old wrinkly rats?	Increased cholingeric cells, but still wrinkly.
What about the ability to learn the way through a maze?	Inc. performance in spatial memory.
What do cells in the hippocampus require for survival.	BDNF or NT-3
What does BDNF do?	Influences RGC branching and remodeling Dendritic growth of cortical neurons Formation of ocular dominance columns in V1.
What candles bundling of neurons into fascicles.	N-CAMs (Neural Cell Adhesion Molecules) → causes neurons to stick together
How are Ach receptors arranged before innervation in sketelal muscle?	Randomly.
…After innervation?	Focused at synaptic endplate.
What causes these receptors to aggregate?	Agrin
What releases agrin?	The nerve
In terms of cell death, what is a hypothesis on apoptosis and motor axon dev't?	Cells might compete for NGF. So if they don't get to where they are going, they don't get NGF and then they die by mean of apoptosis.
How are muscles fibers innervated in dev't?	Multiple axons innervate 1 motor fibre.
What about in mature muscles?	1 axon – 1 muscle fiber
What causes the change?	Competition between motoneurons. Elimination mediated by muscle fiber.

Notes:

How do neurons choose the 'right' target?	Chemical match during dev't (visual system)
How do they sort themselves out?	On the anterior-posterior axis. Preference based on repulsive interactions.
What is Eph (ephrin) series of TK?	Blocks fibers coming from posterior. (Highest conc in posterior). Keeps each fiber on the right track (repulsive interaction)
Where else do you find ephrin?	On temporally located ganglion cells (vs. nasally located ganglion cdells)
Is this hard-wired then?	Nope. Electrical activity can shape the mapping.

Regeneration and Repair

Questions	Answers
What happens to denervated nerves?	Distal portion degenerates Become supersensitive to transmitters Sprouts and forms new synapses
Are fetal / neonatal neurons able to re-establish connections if cut?	Yep
What about adult neurons in PNS?	Yes, but not as specific as neonatal. Little intrinsic ability to navigate to appropriate target.
What about adult CNS?	If they can reach the target, then yes, but usually cant go far because of astrocyte proteins.

Visual System and Critical Periods

Questions	Answers
Can visual influence affect cortical connections?	Stupid question!!
When is it most important?	During a critical period! (neuroplastic changes occur best here) It then becomes more 'fixed'.
What are some examples of neuroplasticity in the visual system?	Ocular dominance columns seen by EEG, 2DG uptake, etc.
What happens if an eye is lost in infancy	Then you don't see the unique columns
What happens if lost in adult?	Nothing

Notes:

What does a translucent monocular occluder or lid sutre do in the first few months of life?	Same thing.. Dramatic shrinkage of terminals
What is this correlated with?	Reduction of binocularly driven neurons when sutured (shift towards ipsi)
What does this suggest about astigmatisms or congenital squints (strabismus)?	You gotta correct 'em early or you're f******.
What happens to a Barn Owl if you put a prism over its eyes at birth?	The inf. colliculus changes to accommodate for the fact that the world is shifted.. This allows the sound mapping to correlate with visual input.
How much the the auditory receptor fields move by?	The same amount that the prism switched the visual input.
What happens to thalidomide babies?	Secondarily affect bone growth to give flippers instead of fullsize limbs.
What happens to albinos?	Frequent miswiring of retinogeniculate connections.
Are there any more questions in this Q&A?	Yes, one more.
What is the main theme and take home message?	**There are many innate properties of neurons, as well as important interactions between them that are crucial to the dev't of normal function.**

Notes: