Neural stem cells in the mice embryo lines the ventricles: In two populations, lateral ganglionic eminence and medial ganglionic eminence. CNS have two surfaces: ventricular surface lining the ventricles, and pial surface facing the externa.

Neuroepithelial cells are cells that lines the ventricles froming the ventricular zone.
Radial glia are cells giving rise to adult neurons and glia, with cell bodies remaining in the VZ but process extending to the pial surface.

- Two modes of migration:
  - Radial migration: from ventricular surface to the pial surface
  - Tangential migration: horizontally within a specific zone.
- Two types of neurons and their mode of migration
  - Projection neuron (purkinje), excitatory, radial migration in the more dorsa cortical zone
  - Interneurons, inhibitory, tangial migration from the subcortical zone: lateral ganglionic eminence and medial gnaglionic eminence to the cortical zone, where they then undergoes radial migration.

- Early developmental stage neuronal migration: process attached to pial surface, somal translocation only.
- Later developmental stage migration consist of 4 stages:
  - Bipolar stage: neurons move out of the ventricular zone into the subventricular zone
  - Multipolar stage: neurons move into the subventricular/intermediate zone, tangential migration possible.
  - Process extension stage: neurons extend process towards the ventricular surface, soma movement possible
  - Locomotion stage: neurons move along the radial glia, eventually settle in cortical plate, other zones disappear.
    - Consist of process extension followed by soma translocation, cyclic action
    - **Confocal microscopy** imaging shows the leading process is rich in microtubule.
    - Swelling is formed in the distal axon, cage-like microtubule structure pulls centrosome into the swelling. Centrosome causes nucleus translocation, pulling the nucleus into the swelling as well, retraction of the trailing process.

Signalling pathways underlying neuronal migration:

- Lis1, NUDEL, Dynein
  - Lis1, NUDEL, Dynein form complex on microtubule, couples nucleus and centrosome allows migration
  - **RNAi of Lis1: lack od radial migration**
  - Defect in this complex result in lissencephaly, lack of sulcus, smooth brain

- Double coated (Dcx), double coated like (Dclk)
  - Microtubule binding proteins stabilising microtubule, promote polymerisation, involved in nucleus-centrosome coupling.
  - **RNAi of DCX produce similar effect as inhibition of Lis1**
  - Defect in this complex also induce lissencephaly.

- Extrinsic signalling: Reelin - ApoER2/VLDLR - Dab1 - SFK
  - Reeling (ligand) - ApoER2/VLDLR (receptor) - Dab1 (adaptor) - SFK (phosphorylase), regulate downstream microtubule assembly.
  - **Reelin mutants shows** inverted layer arrangement in the cortex

- Tangential migration of interneurons:
  - **GFP labelled graft traced in vivo to show migration path**
  - **Nkx2.1-Cre allow fluorescent tagging of neurons once Nkx2.1 is transiently expressed**. Confocal fluorescent microscopy shows Nkx2,1-Cre expressing cells are interneurons. Also shows MGE and LGE are sources of interneurons
  - Interneurons enter the cortical zone in subventricular zone stream and marginal zone stream.
  - Radial migration of interneurons: cyclic process with a branched leading process
    - Extension of leading process and branching process, formation of swelling
    - Centrosome translocation into the swelling
    - Nucleokinesis, movement of nucleus into the swelling, trailing process retraction.
  - Signalling: Cxcl12(ligand) - Cxcr4/Cxcr7 (Recrptors):
    - Cxcl12 is expressed in the marginal and subventricular zone guides migration of interneurons.
    - **KO Mutants of Cxcr4/7 enter cortical plate prematurely, imaged with ISH.**

Other cells can also affect migration of purkinje and interneurons, such as blood vessel endothelials, oligodendrocytes, microglia etc

Experiments showing influence of blood vessel on neuronal migration:

Transgenic mice shows genetically altered vascular network lead to increases in interneuron migration

Imaged with ISH, qPCR and immunohistochemistry, organ slices, microscopy imaging in vitro

Induced by factors released by blood vessel cells such as SPARC or VEGFA. Other candidates can be tested using RNA sequencing

Defects in neuronal migration can lead to diseases such as epilepsy intellectual disability, delay in development.