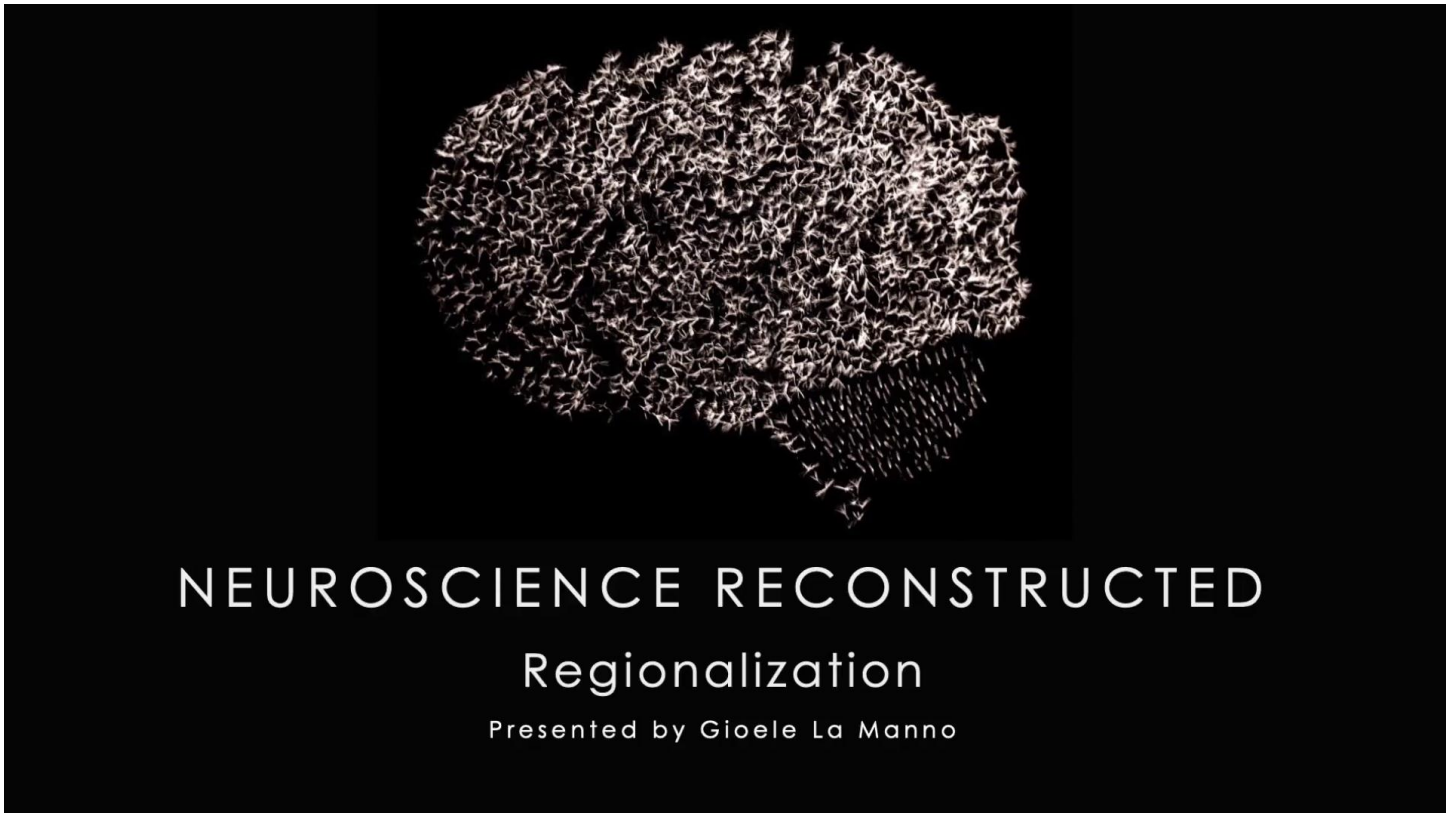

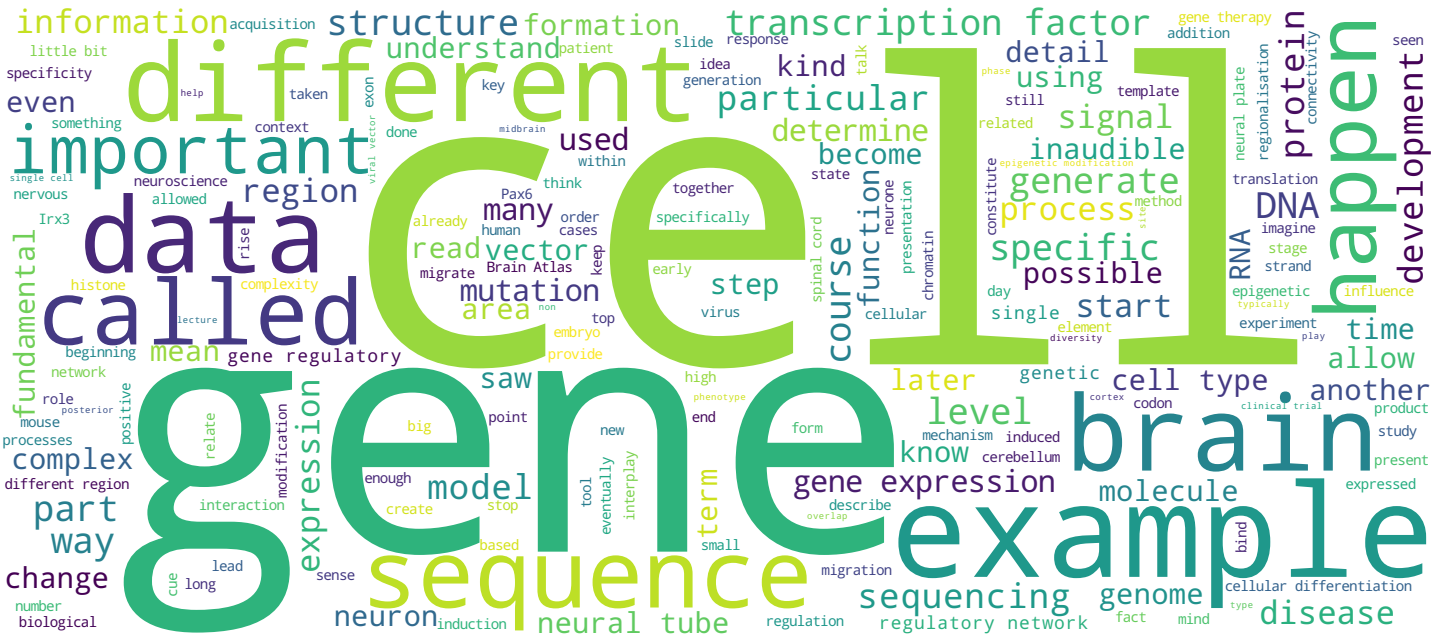

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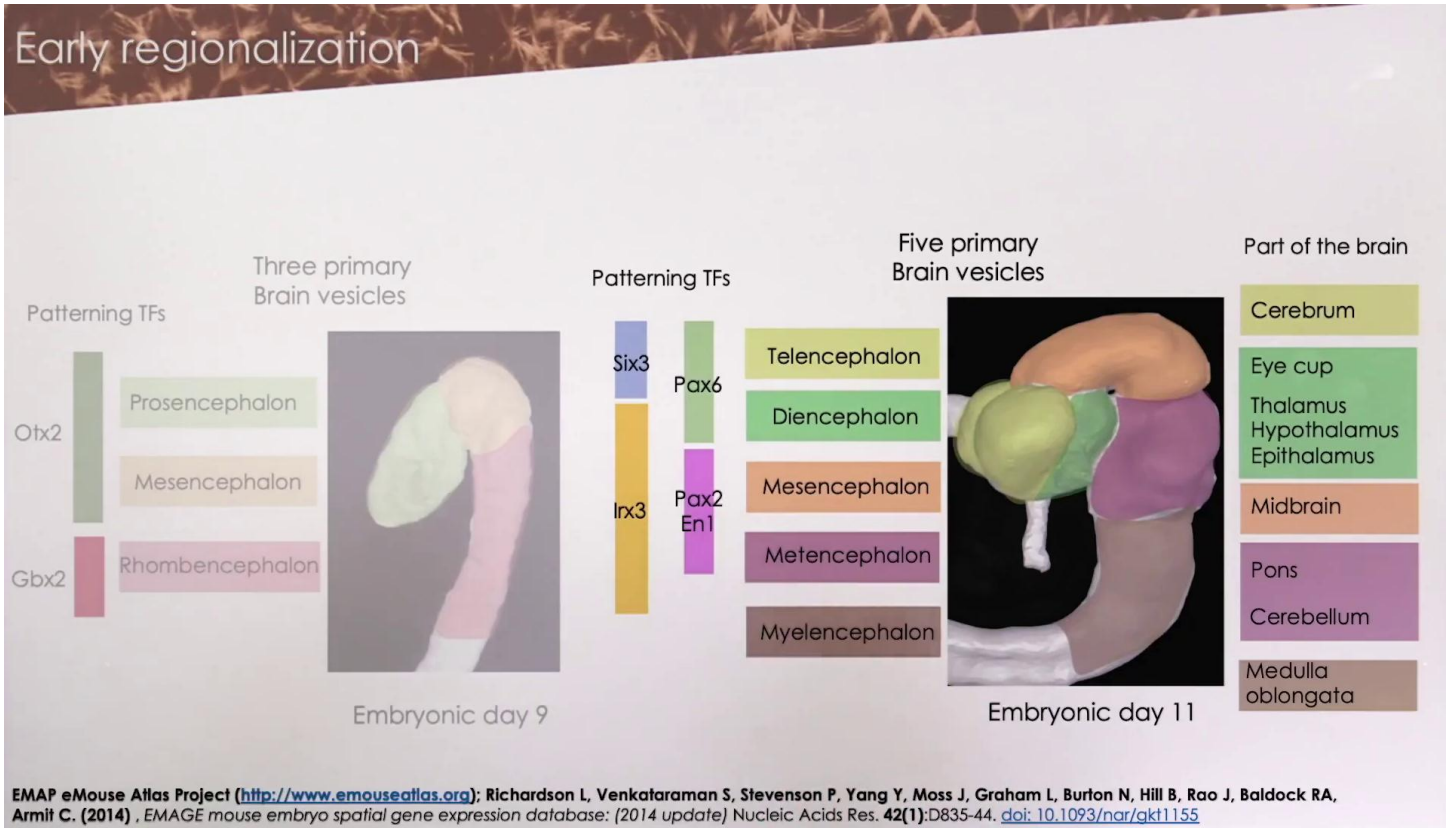
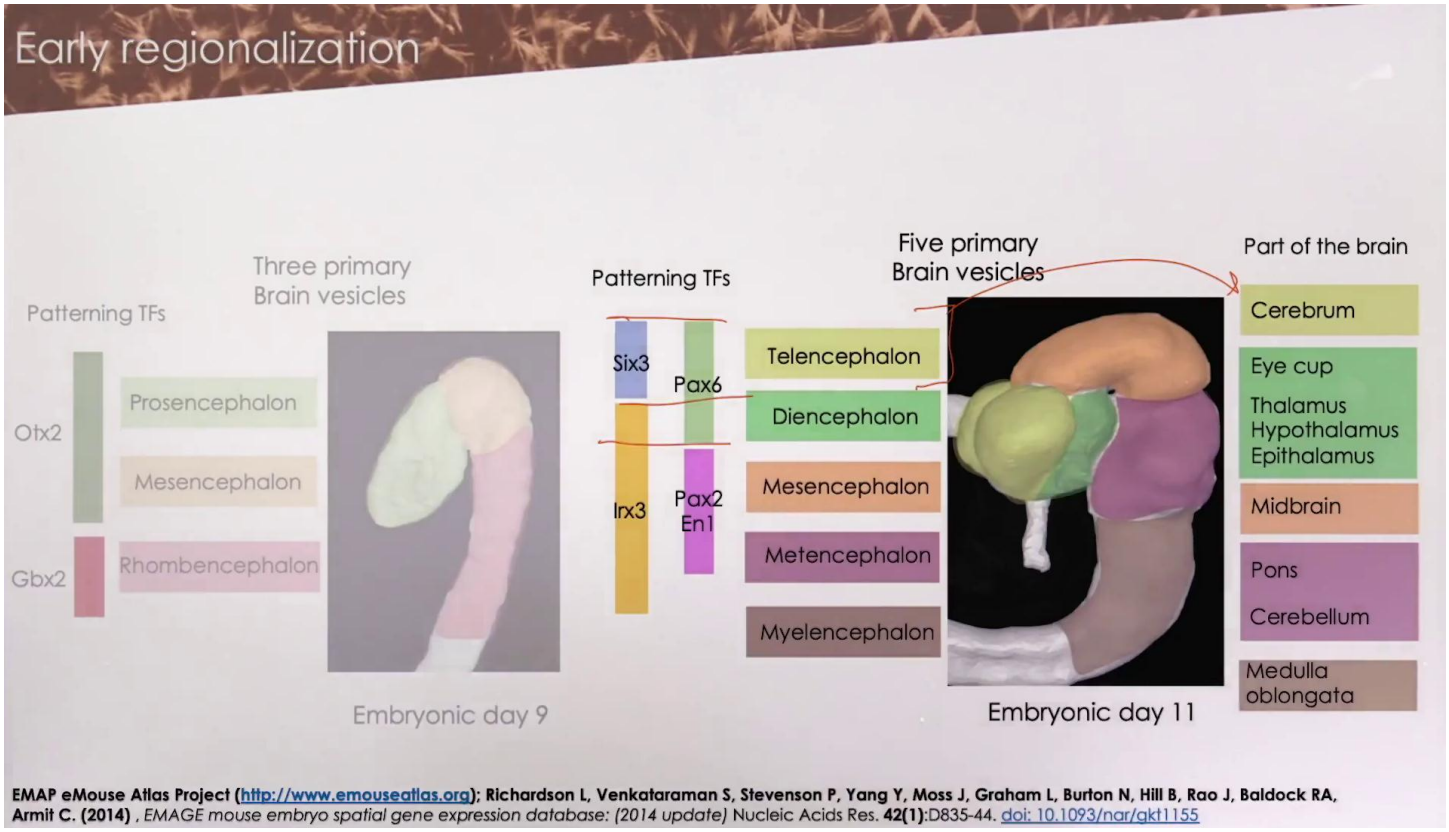


Let's now see some examples of this. What are the patterning transcription factors that characterise this regionalisation and deconstitute the response of these cues provided by early cues and then by secondary organisers. For example, the very early definition of domains that express Otx2 and Gbx2, two mutually repressive transcription factor, generate the first fundamental distinction between the prosencephalon, mesencephalon, basically forebrain and midbrain, and the rhombencephalon, the hindbrain that you can see here in this 3D rendering E9. Those transcription factors there are expressed in different regions, in combination with further cues, then generate an encoding of a regionalisation that is modified as what you can see later on in Embryonic day 11, where we have now other subscription factor kicked in, Pax6 defining the areas of the telencephalon, diencephalon, Pax2 and the engrailed defined region of the mesencephalon metencephalon, and the specificity and definition of finer area is allowed by the overlap of Pax6 and Pax2 and engrail single with other transcription factors like Six3 and Irx3.

Notes

Summary

0m 05s



This combinatorial encoding will make so that cells that are positive to two singles like Six3 and Pax6 will be specified to particular destiny while the ones that are in the segment that is positive for Pax6 and Irx3 will generate another segment, for example, some cells of diencephalon. Those different areas that are part by this transcription factor will then be specifically committed to generate only neurons in [inaudible 00:02:06] for a particular part of the brain. Of course, the party is Pax6 Six3 positive will generate areas of the cerebellum, of the eye cup and then part of the diencephalon we generate the thalamus, hypothalamus, and epithalamus. Encephalic segments are, of course, the mid brain and so on. We have neon brain, the pons, and the cerebellum. Finally, we get to the medulla oblongata or even more posteriorly to the spinal cord. This is an important overarching theme, defining area by the expression of a specific transcription factor. It actually doesn't stop at day 11. It actually becomes more complex with the interplay of organisers, and it generates explicit anatomical diversity and complexity of the brain.

Notes

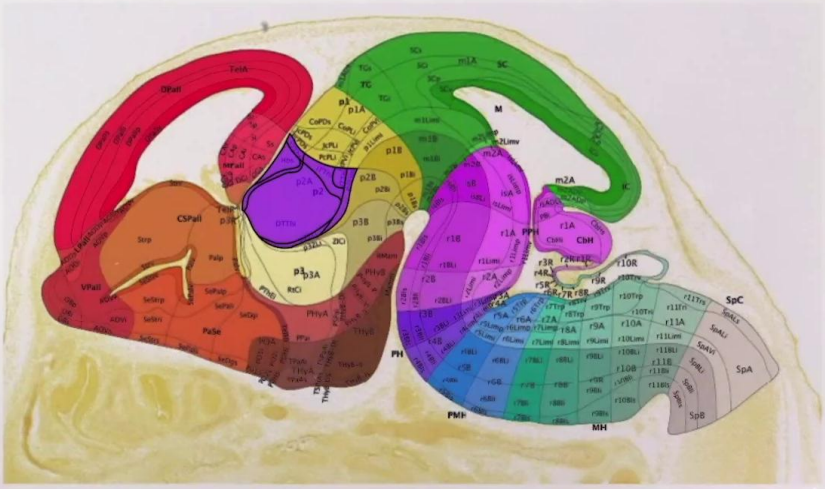
Summary

1m 36s

Regionalization

Further finer regionalizations

- Specific complex story for each region
- Complex anatomy
- Availability of gene expression/anatomical atlases to study and interpret those process correctly



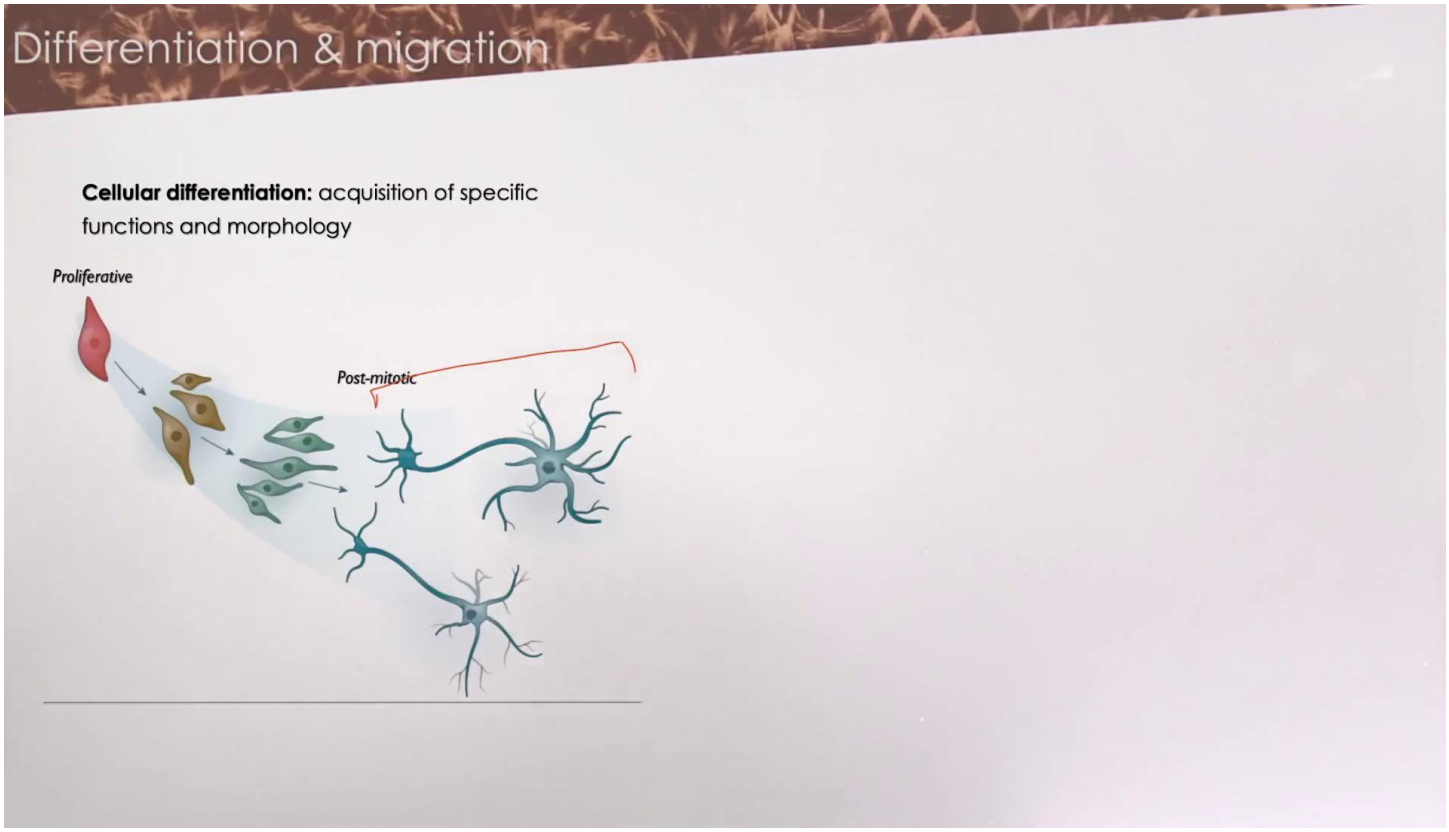
Allen Brain Atlas – Mouse (https://mouse.brain-map.org/);
Lein, E.S. et al. (2007) Genome-wide atlas of gene expression in the adult mouse brain, Nature 445: 168-176. doi:10.1038/nature05453

For example, if you look now at a much later towards the end of development this anatomically annotated section that is taken from the Allen Brain Atlas of the Mouse, you see that many more regions and subregions of the brain needs to be defined. Of course, every single one has its own story in terms of which genes are involved and which interplay is allowed to happen. This has been, for many of these cases, there have been studies that characterise specific genes and the fact they're knocked out so their elimination to determine to the formation of cerebellum might be impaired, if one gene is removed or is mutated. Overall, we're not going to go in details as long as this is achieved. But it's important to keep in mind that after this initial originalisation that is relatively easy to describe, we need to go region by region and address how this complex anatomy and specificity of cell type gets constituted, becoming a more complex but extremely interesting topic.

Notes

Summary

2m 58s

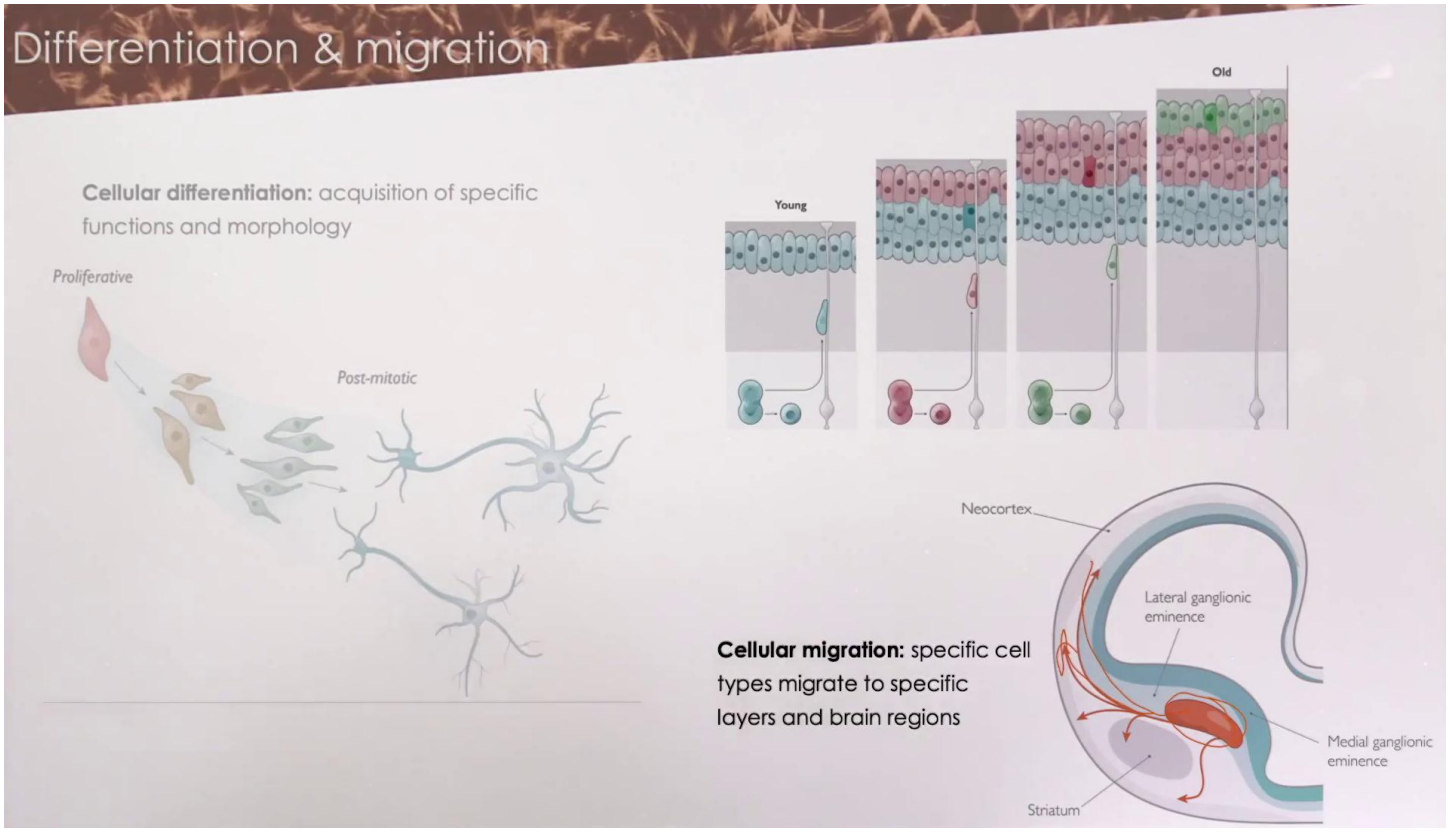


Well, we're not going to go into details about what happens in specific regions. It's important to keep in mind the overarching processes that will happen be specific to different regions. One is cellular differentiation. We have mentioned this different times during the presentation. Just note, to define it a little bit more specifically, we mean with cellular differentiation, the acquisition in a cascade to specific genospression profile that determine a change in acquisition of function and morphology from cells. At the beginning, we expect their development that we see to have proliferative cells, so-called neuros themselves. We have seen that they get induced. This induction that we saw, they will trigger a sequence of genospression waves that will gradually change the phenotype of those cells and will definitely and finally lead them to the specific morphology that is important for them to play a specific role in physiology. But cell differentiation is not enough to generate the complexity, and the structure, and connectivity of the brain.

Notes

Summary

4m 13s



Other important processes need to happen. One central one that you are going to hear about in the next lecture is cell migration. Cells need to migrate in different contexts. One kind of migration is encountered during the translation of cells from the ventricular zone. We saw the part of the neural tube that is more proliferative and addition to the ventricle to a more distal part. This is what happens and generates the certification of the cortex. But then also other kind of migration that relates to specific types that are born in one area of the brain, the medial ganglionic eminence, and then they migrate in other regions from the one they were originated from so that they constitute in this differnt region particular networks. They enrich the local heterogeneity, and they allow the formation of more complex networks. With this slide, thank you for your attention, and I hope you enjoyed the further presentation that we'll go more in depth from cellular differentiation and migration. Thank you.

Notes

Summary

5m 39s