
NEUROSCIENCE RECONSTRUCTED
Gastrulation and patterning
Presented by Gioele La Manno


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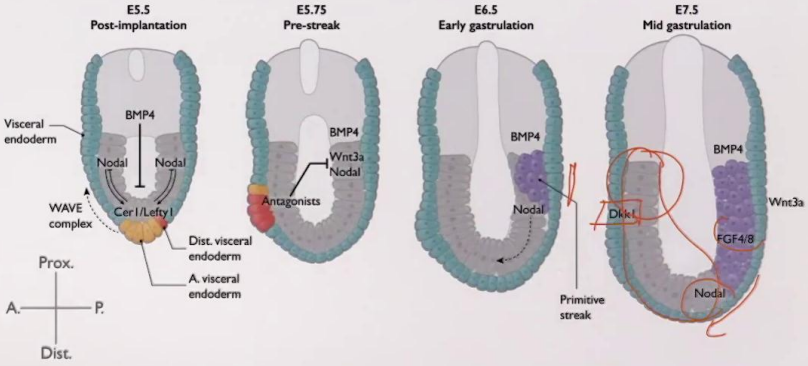
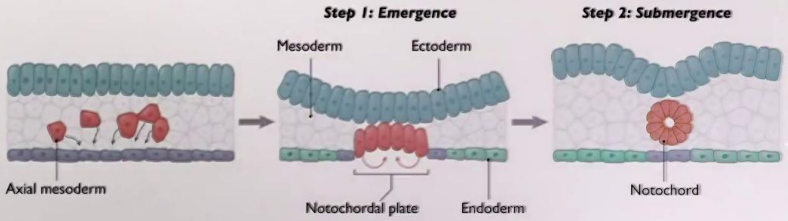
Gastrulation

Gastrulation is the starting point for nervous system development.

The gastrulation process has already:

- Broken symmetry defining AP and DV axes
- Defined the three embryonic germ layers
- Produced the notocord





Let's now look in more detail to gastrulation because this is the fundamental step that kickstarts the development of the nervous system. At gastrulation, as you can see in this slide, we have the initial determination of the embryonic sheath. We have the determination of the asymmetry of the embryo. In particular, we define basically anterior posterior pyridine with posterior signals like nodal, and winds, and FGF. They're signaled in the anterior part, this group of cells the anteriors lean in. They're going to be the anterior part, the head of the embryo, for example. They signal their plate. We see here indicated genes like DKK1 inhibit actually in the anterior part signals the posterior signals, nodal, FGF, and the winds, so that the anterior part free from this signal is specified to anterior plate. This generates the ectoderm, more generally the neuroectoderm, all the cells from which the neural tube, therefore, the central nervous system, is going to be generated, but also, actually the skin and the neural crest derivative. Let's look at how segregation of... How it happens that those cells of the neuroectoderm, segregate in different groups that have different roles and generate different organs and parts of the embryo.

Notes

Summary

0m 05s

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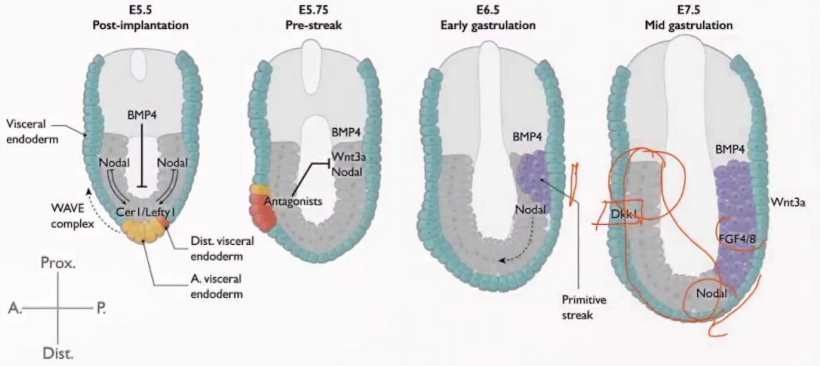
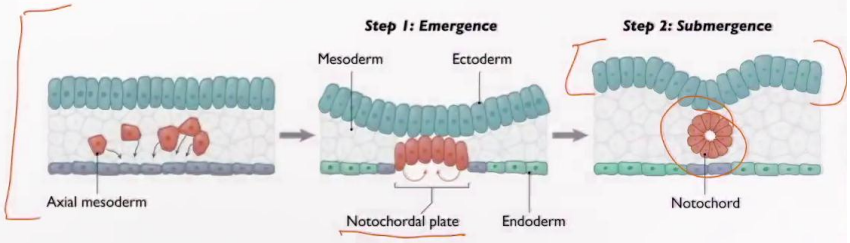


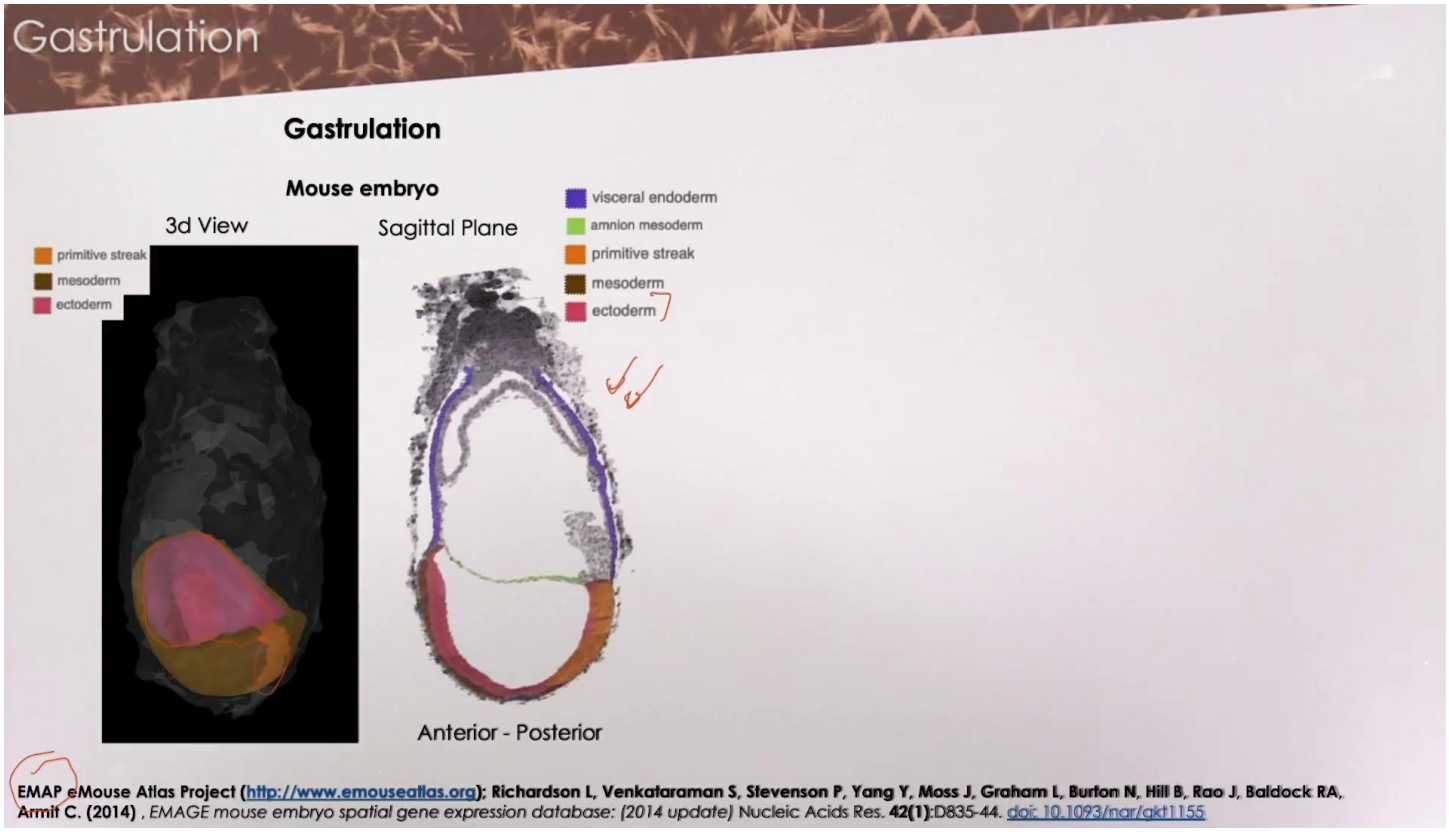


This happens through the induction, the fundamental event of the formation by this posterior mesoderm cells of the actual mesoderm. There are streams of mesodermal cells that move from the posterior part of the ventral part of the brain. They will then determine the formation of the notochordal plate and then the notochord. A fundamental organiser for the embryo, the notochord cells will secrete different ventralising signals that will induce the neuroectoderm to specify in different areas. Let's have a look.

Notes

Summary

1m 52s

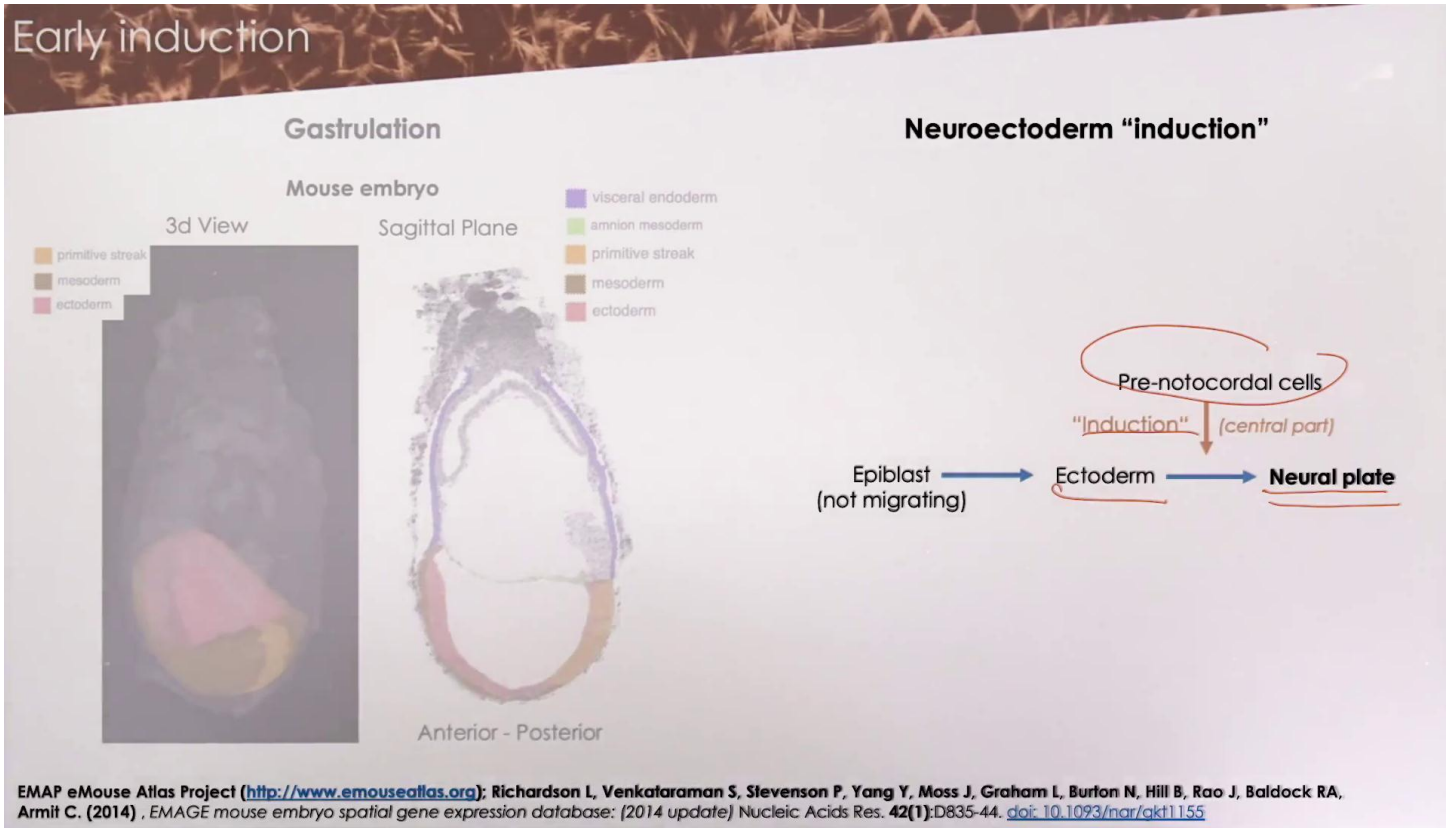


Illustrations are nice, but I want also in this occasion to shoot out to this particular resource, EMAP, eMouse Atlas Project, that you can find on the web, where you can get to see both in 3D and using a browser or histological section, everything digitised for you and browsable. You can see how the embryo looks at this point, think the understanding or the morphological relationship between this tissue out there of this embryonic sheaths or their plate and then the form with time, different structure of the day, for example, imagine how they, for example, fold, is very important to get a sense of how this movement of cells and notice changes in the embryo are concerted. For example, what you see here now in an unmutated saggital plane, is the logical slide and the 3D view, is the same areas that we were talking about in the previous slide. See the ectoderm that forms this sheet of cells that is presented dorsally on top of a layer of mesoderm that is present below. You see that the primitive streak, the fundamental organiser that is signaling, as we said, posterior signals, as we saw in the previous slide, is placed. This give a better understanding, I think, of how these structures are distributed in space, and I think it give a better sense of how this process happen.

Notes

Summary

2m 37s

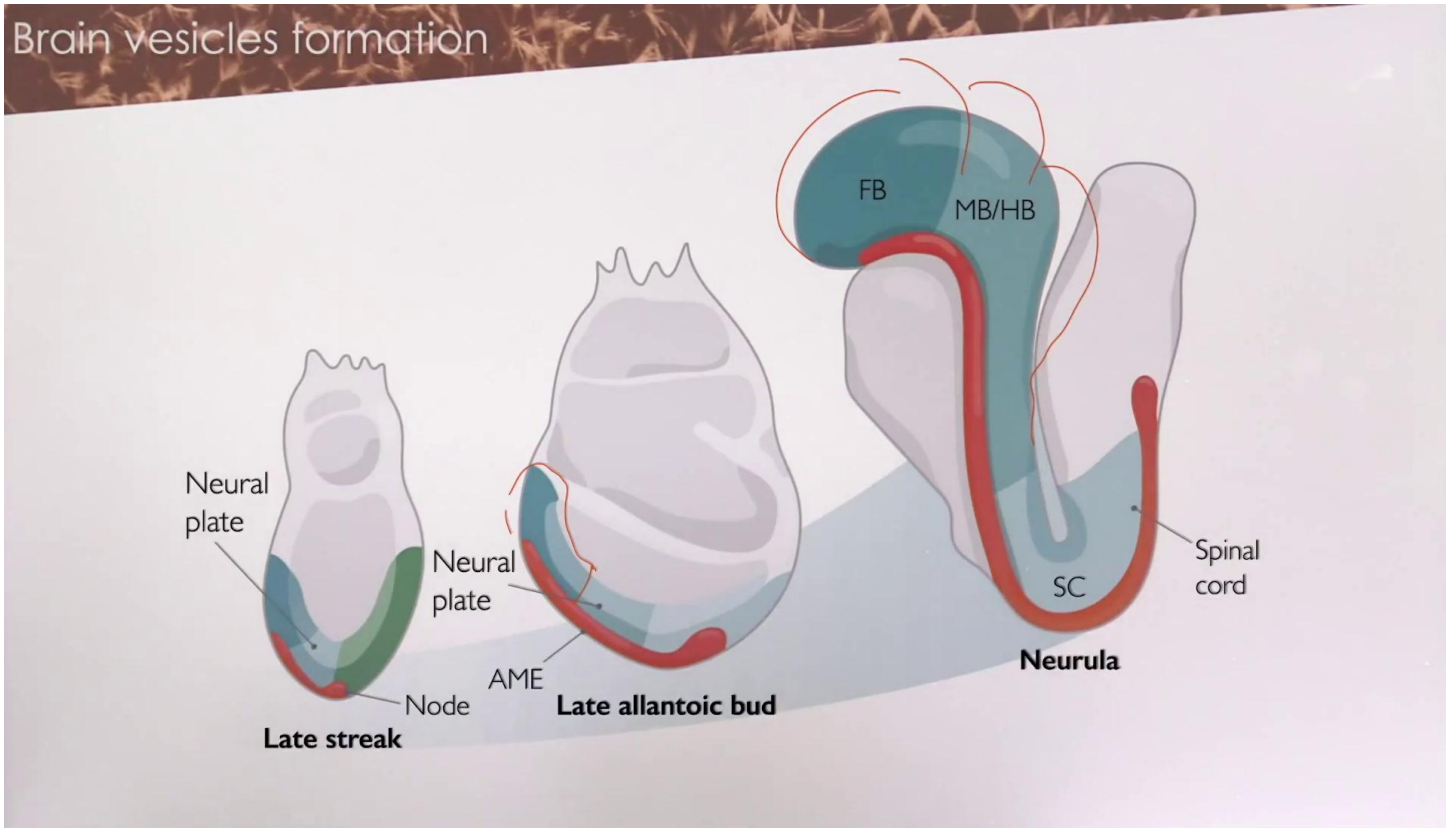


Let's go back to this idea of how the ectoderm is induced into neural plate. We said before that notochordal, pre-notochordal cells are important in determining an induction. Induction is here in quotation marks because it's actually interesting to note that the neural plate is the default plate in a sense of the ectoderm. If you take just ectoderm, and you leave it differentiate, you don't give it a posterior signal like FGF and the winds, if those morphogens are not given as an input to the self, they will just progress to become neural plate. The action of notochordal cells, it's pre-notochordal cells, is actually the one of inhibiting, not only trying to ventralise the sonic expression, but to inhibit a set of other signals that would eventually determine also either the more posterior phase or more lateral phase. This is important. Let's see how this happens a little bit more.

Notes

Summary

4m 16s

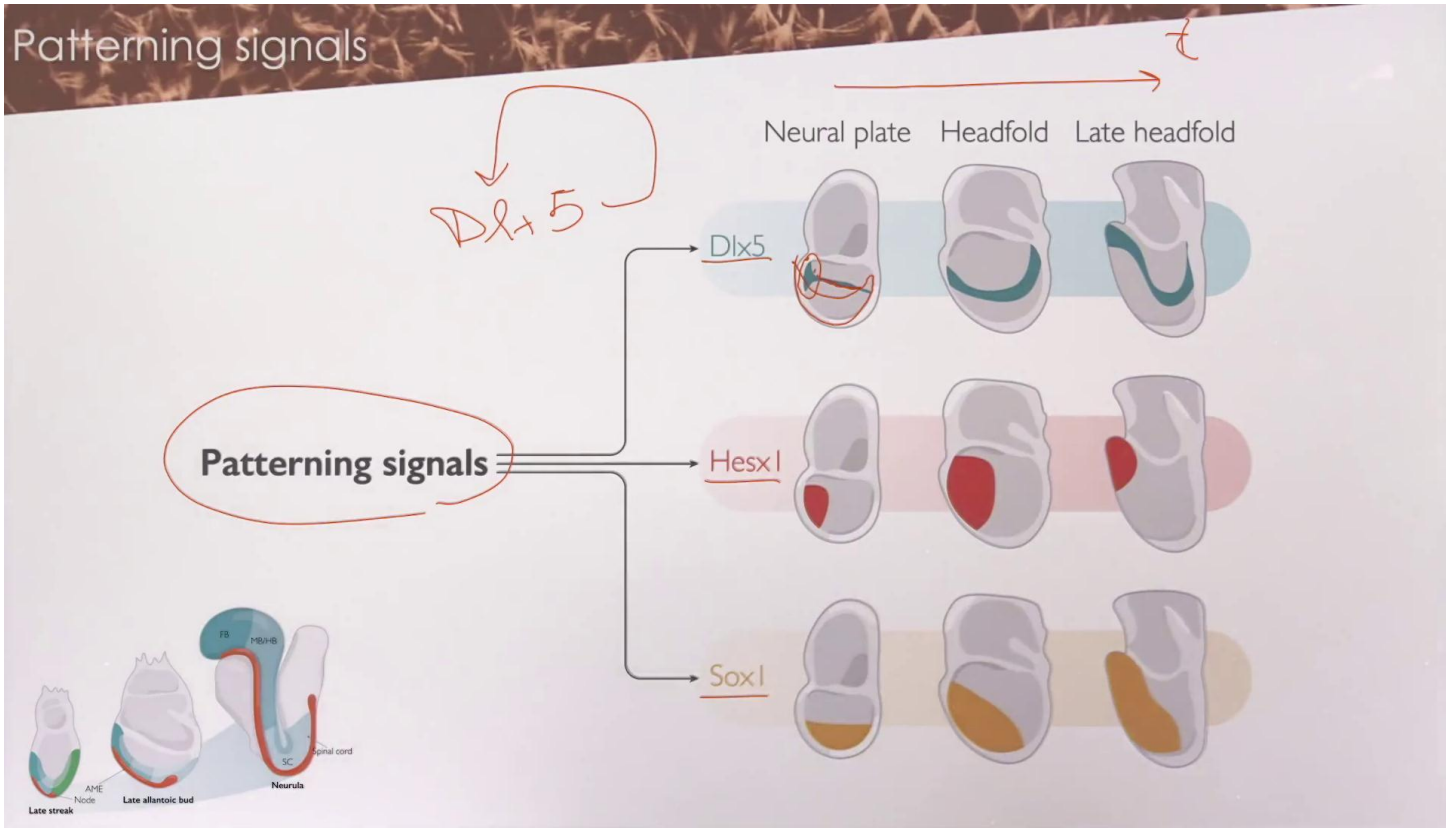


We need to remember that despite, we, of course, try to schematise this process, they happen and overlap in time and up in a concerted way. For example, already at the very early time in neurulation, there starts to be the definition of an interior posterior symmetry. The same signals that were used to determine the general interior posterior axis of the embryo during gastrulation are actually affecting those cells while they're being induced to become the neural plate. Even though the formation, as you see in this slide, the physical formation of the different vesicle, the forebrain, the midbrain, the hindbrain, and then, of course, more dorsally, the spinal cord from the neural tube are going to happen really only later. Already at this point, however, cells have made changes in their gene expression that will lead them eventually to generate this more microscopic process that we will see later in development. Again, sheathof cells will be regionalised. At inspection, I mean, a morphological inspection, they will look pretty much the same. We don't see at this point any fundamental difference. But if we then, with molecular techniques, we try to probe the expression of particular genes, in particular transcription factors that we said are important for the activation, transactivation of other genes and for general DNA networks, we get to see situations like this.

Notes

Summary

5m 29s

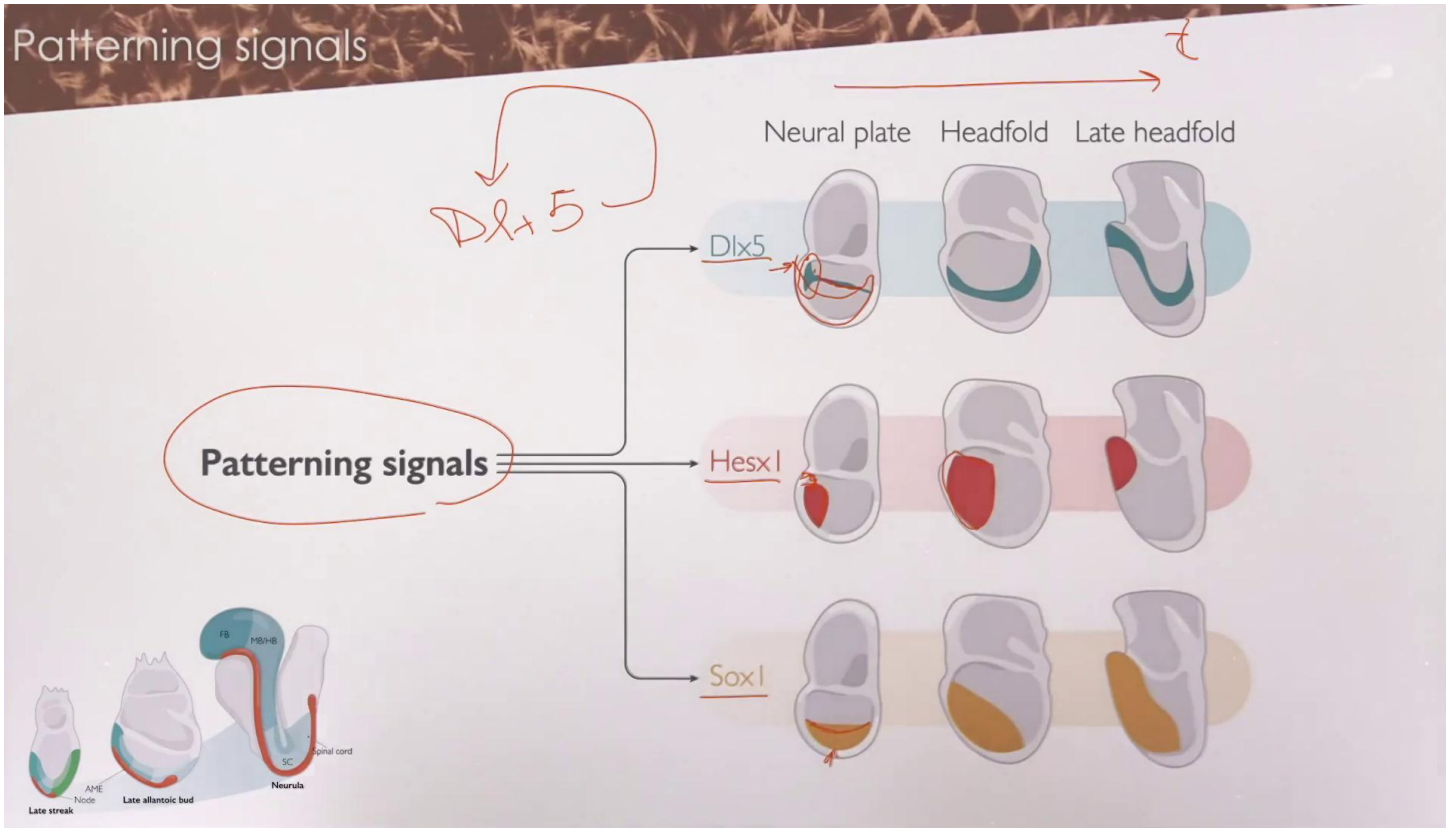


Now here, I'm showing in time from left to right, different, very close stages of gastrulation, post-gastrulation embryo. We call them neural plate stage, headfold, and late headfold, if we want to give them names. If we probe the expression, we ask which cells in this structure express some fundamental transcription factor, for example, Dlx1, Fx1, and Sox1. We actually can identify already territories of cells that express this gene. This, of course, has been determined by the pattern in signal that have been present during gastrulation to an earlier stages. They are already present very early. They are maintained by, for example, self-regulation. Very often, the transcription factors have self-regulatory loops to activate themselves. In this way, they can maintain a level of expression starting, for example, for initial learning induction. As you can see, the different transcription factor are localised in different areas, and some of them are overlapping. They're not necessarily mutually exclusive. You see Dlx, for example, is present in this interior area and then more, it proceeds naturally. Again, we're looking at the neural plate here. You need to imagine it. You saw in 3D in the previous slides.

Notes

Summary

7m 02s

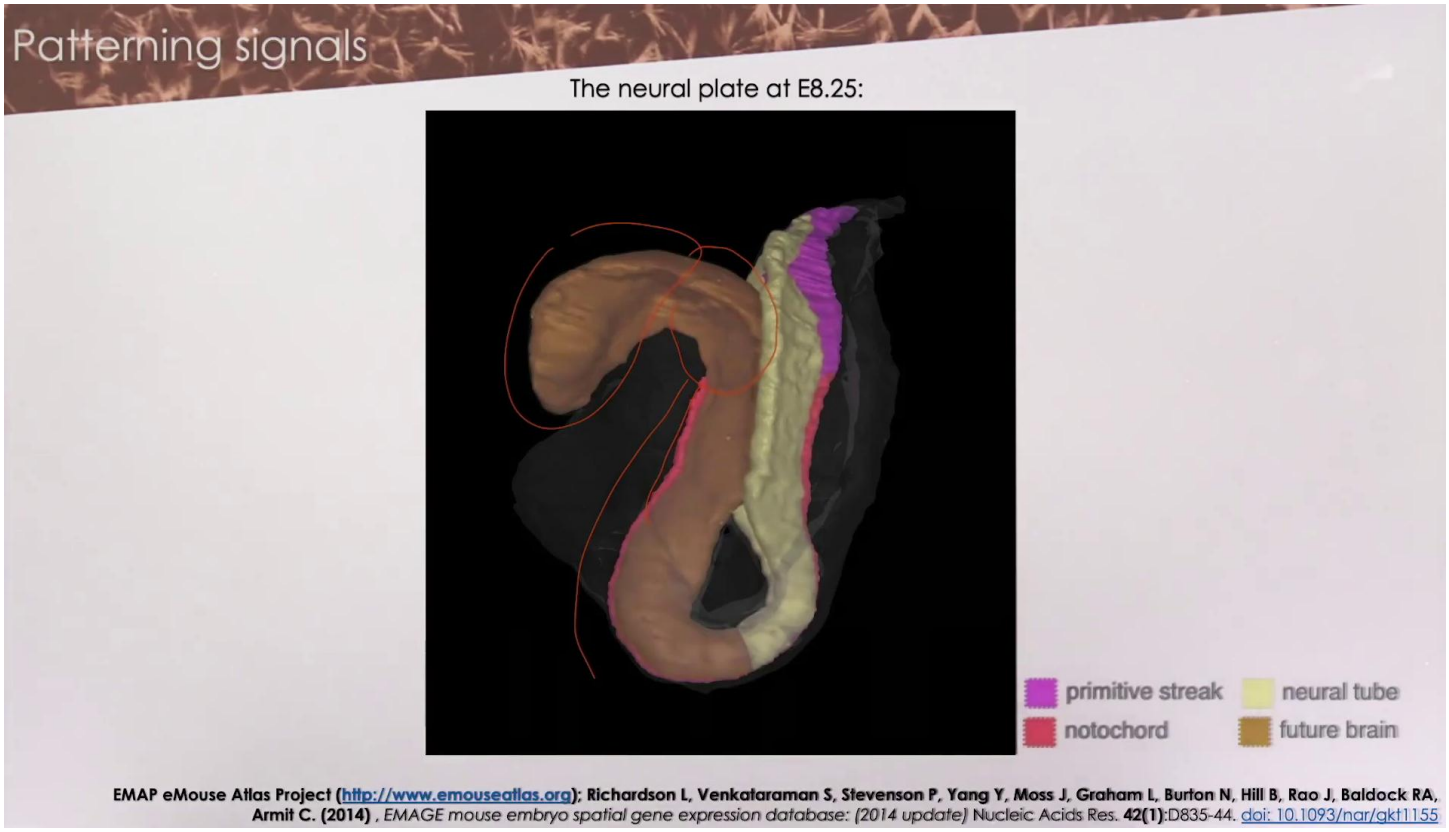


We're just looking at the saggital section here. Sx1 is a little bit more posterior. It's missing from this more interior part where, for example, Dlx is. Then if we see this expression of a gene like Sox1, we see that even more posterior, it continues more posterior in the area that will give rise to to the spinal cord, for example. Then you see while the embryo is growing, the domain that is positive, the adeno cells that express that particular transcription factor is maintained. But of course, a company that change in shape and morphology and the movements of the cells, for example, neural tube closure and the formation of the vesicles. This is another perspective. Now, we have been seeing before this transcription factor rise inside the cell. Now, we are looking at the distribution of the transcription factors across the entire cell population in different areas of the brain and across time. The combination of this information and coded by the overlap of transcription factor is going to tell exactly cells how to behave and in what cell type to differentiate and which structure to form.

Notes

Summary

8m 37s



Now, I wanted to show you at the stage of E8.25, so stage of the late headfold, how does actually the neural plate look, since, of course, the reality is a little bit sometimes different from the simplification of the illustration. I think, again, I suggest this resource to go and browse the different regions and the different neurulation both in 3D and using sections. Here you see the notochord that, as we said, is providing, ventralising signal from below to the neural tube. You can start to distinguish the areas, for example, the forebrain, the midbrain, the hindbrain, and then finally the part that will give rise to the spinal cord.

Notes

Summary

9m 55s