

# FULL SPEAKER BIOGRAPHY and ABSTRACT

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Pierre Vanderhaeghen is a group leader of the Belgian FNRS, at University of Brussels, Belgium. His lab focuses on the mechanisms of development and evolution of the cerebral cortex, from the differentiation of neural progenitors to the formation of cortical networks. They combine and integrate molecular and cellular approaches, including pluripotent stem cell technology, mouse transgenics, and human neuroembryology.

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## **Corticopoiesis in a dish: intrinsic mechanisms of neuronal specification from pluripotent stem cells**

The mechanisms that control the development of the cerebral cortex remain poorly understood, but the identification and characterization of factors capable of (re)specifying cortical neurons has important implications for our understanding of brain diseases, and in the context of neural repair.

Embryonic stem (ES) and other pluripotent stem cells constitute a promising tool to study neural development, as well as for the modelling of human diseases. Recently we have found that embryonic stem cells, cultured without any morphogen $\nabla$ , recapitulate in vitro the major milestones of cortical development, leading to the sequential generation of a diverse repertoire of pyramidal neurons that display most salient features of genuine cortical neurons.

When grafted into the cerebral cortex of mouse neonates, these neurons develop patterns of axonal projections corresponding to a wide range of cortical layers, but also to highly specific cortical areas, in particular visual and limbic areas, thereby demonstrating that the identity of a cortical area can be specified without any influence from the brain.

The combination of in vitro manipulation and grafting experiments in embryonic, neonatal and adult brain indicate that, while the specific fate of ES-derived cortical progenitors can be changed in vitro depending on the cellular and molecular context, their identity remains stable following grafting, thereby allowing the generation of highly stereotyped and specific axonal projection patterns.

Overall our data shed new light on the mechanisms of neuronal specification, and may have important implications for the rational design of brain repair by cell replacement.

### **What is the central hypothesis of my presentation?**

The main mechanisms of development of the cerebral cortex can be recapitulated in vitro from pluripotent stem cells.

### **What is the most important observation I will discuss?**

We will describe a mechanism by which embryonic stem cells, cultured without any morphogens, recapitulate in vitro the major milestones of cortical development, leading to the coordinated generation of a diverse repertoire of cortical neurons that can connect with the brain in a layer-specific and area-specific pattern.

### **What is the translational significance?**

ES cell-based corticogenesis constitutes an innovative tool for pharmaceutical research, which may be used to model brain diseases and for drug screening, and constitutes an attractive alternative to animal experimentation. In the long run, cortical neurons generated in vitro could be used also in the perspective of brain repair, for many diseases striking cortical neurons.