

Research identifies presence of neuron-producing stem cells in meninges

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A multidisciplinary research, conceived by Dr. Francesco Bifari, Department of Medical Biotechnology and Translational Medicine, University of Milan, Italy and Dr. Ilaria Decimo University of Verona, Italy, found that meninges - the protective membranes that enclose the brain - contain a pool of neural stem cells. These stem cells are able to produce new brain neurons after birth. These findings, published in the leading scientific journal *Cell Stem Cell*, highlight the importance of meningeal tissue as well as of meningeal-resident neural stem cells in the development of innovative therapies for neurodegenerative diseases such as brain damage or Alzheimer.

This work is the result of an international collaboration that included the University of Milan, Italy, the University of Verona, Italy, the Vesalius Research Center, VIB, Leuven, Belgium, the German Cancer Research Center (DKFZ), Heidelberg, Germany, the Antwerp University, Belgium and the Brain Mind Institute, Swiss Federal Institute of Technology, Lausanne, Switzerland.

New neurons are added in the cortex after birth

Only a few decades ago, it was thought that no new neurons were added to the brain after childhood. This dogma has changed, with researchers finding more and more evidence that the brain is capable of healing and regenerating in adulthood, thanks to the presence of stem cells. However, neuronal stem cells were generally believed to only reside within the brain tissue, not in the membranes surrounding it.

Meninges: from protective membrane to neuron-producing stem cells niche

So far, meninges have been considered mostly as a merely protective membrane covering the brain. On the other hand, before this discovery, neural precursors - or stem cells that give rise to neurons - have been only described inside rare regions of brain tissue. This study considers the generation of brain neurons from an entirely new perspective. Thanks to a multidisciplinary approach that included novel top-notch techniques, this research identifies the presence in meninges of neuron-producing stem cells. These stem cells are generated during the embryonic period. After birth, these cells migrate from the meninges to the brain and then differentiate into functional and integrated neurons.

The finding of the presence of neuron-producing stem cells in meninges opens new perspectives for the development of new drugs for neurodegenerative diseases. "The next step - comment the first authors Dr. Bifari and Dr. Decimo - will be the understanding of the role of these meningeal resident neural stem cells in those conditions where the neural tissue is damaged such as brain and spinal cord injury, multiple sclerosis and Alzheimer disease.

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[**Scientists discover neuron-producing stem cells in the membranes covering the brain**](#)

Possible implications for brain regeneration?

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Summary:

Unexpected cells have been found in the protective membranes that enclose the brain, the so called meninges. These 'neural progenitors' -- or stem cells that differentiate into different kinds of neurons -- are produced during embryonic development. These findings show that the neural progenitors found in the meninges produce new neurons after birth -- highlighting the importance of meningeal tissue as well as these cells' potential in the development of new therapies for brain damage or neurodegeneration.

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In a cross-domain study directed by professor Peter Carmeliet (VIB -- KU Leuven), researchers discovered unexpected cells in the protective membranes that enclose the brain, the so called meninges. These 'neural progenitors' -- or stem cells that differentiate into different kinds of neurons -- are produced during embryonic development. These findings show that the neural progenitors found in the meninges produce new neurons after birth -- highlighting the importance of meningeal tissue as well as these cells' potential in the development of new therapies for brain damage or neurodegeneration. A paper highlighting the results was published in the leading scientific journal *Cell Stem Cell*.

Scientists' understanding of brain plasticity, or the ability of the brain to grow, develop, recover from injuries and adapt to changing conditions throughout our lives, has been greatly broadened in recent years. Before the discoveries of the last few decades, neurologists once thought that the brain became 'static' after childhood. This dogma has changed, with researchers finding more and more evidence that the brain is capable of healing and regenerating in adulthood, thanks to the presence of stem cells. However, neuronal stem cells were generally believed to only reside within the brain tissue, not in the membranes surrounding it.

The meninges: unappreciated no more: Believed in the past to serve a mainly protective function to dampen mechanical shocks, the meninges have been historically underappreciated by science as having neurological importance in its own right. The data gathered by the team challenges the current idea that neural precursors -- or stem cells that give rise to neurons -- can only be found inside actual brain tissue.

Prof. Peter Carmeliet (VIB-KU Leuven): "The neuronal stems cells that we discovered inside the meninges differentiate to full neurons, electrically-active and functionally integrated into the neuronal circuit. To show that the stem cells reside in the meninges, we used the extremely powerful single-cell RNA sequencing technique, a very novel top-notch technique, capable of identifying the (complex gene expression signature) nature of individual cells in a previously unsurpassed manner, a première at VIB."

Following up on future research avenues: When it comes to future leads for this discovery, the scientists also see possibilities for translation into clinical application, though future work is required.

Prof. Peter Carmeliet (VIB-KU Leuven): "An intriguing question is whether these neuronal stem cells in the meninges could lead to better therapies for brain damage or neurodegeneration. However, answering this question would require a better understanding of the molecular mechanisms that regulate the differentiation of these stem cells. How are these meningeal stem cells activated to become different kinds of neurons? Can we therapeutically 'hijack' their regeneration potential to restore dying neurons in, for example, Alzheimer's Disease, Parkinson's Disease, amyotrophic lateral sclerosis (ALS), and other neurodegenerative disorders? Also, can we isolate these neurogenic progenitors from the meninges at birth and use them for later transplantation? These findings open up very exciting research opportunities for the future."

Unique funding opportunities: Moving into uncharted territory is high risk, and can offer high gain, but securing funding for such type of research is challenging. However, Carmeliet's discoveries were made possible to a large extent by funding through "Opening the Future: pioneering without boundaries," a recently created Mecenat Funding Campaign for funding of high risk brain research but with potential for breakthrough discoveries, started up by the KU Leuven in 2013 and unique in Flanders.

Prof. Peter Carmeliet (VIB-KU Leuven): "Being able to use such non-conventional funding channels is of utmost importance to break new boundaries in research. This unique Mecenat funding initiative by the KU Leuven is innovative and boundary-breaking by itself. Our entire team is enormously grateful for the opportunities it has created for our investigations."

Story Source:

Materials provided by **VIB - Flanders Interuniversity Institute for Biotechnology**. Note: Content may be edited for style and length.

Journal Reference:

1. Bifari et al. **Neurogenic Radial Glia-like Cells in Meninges Migrate and Differentiate into Functionally Integrated Neurons in the Neonatal Cortex**. *Cell Stem Cell*, November 2016 DOI: [10.1016/j.stem.2016.10.020](https://doi.org/10.1016/j.stem.2016.10.020)

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