Dr Tamara Grigoryan of the Max Delbrück Center for Molecular Medicine outlines her investigations into the Schwann cell, a unique and understudied cell that only exists in the peripheral nervous system

# The Schwann cell understanding

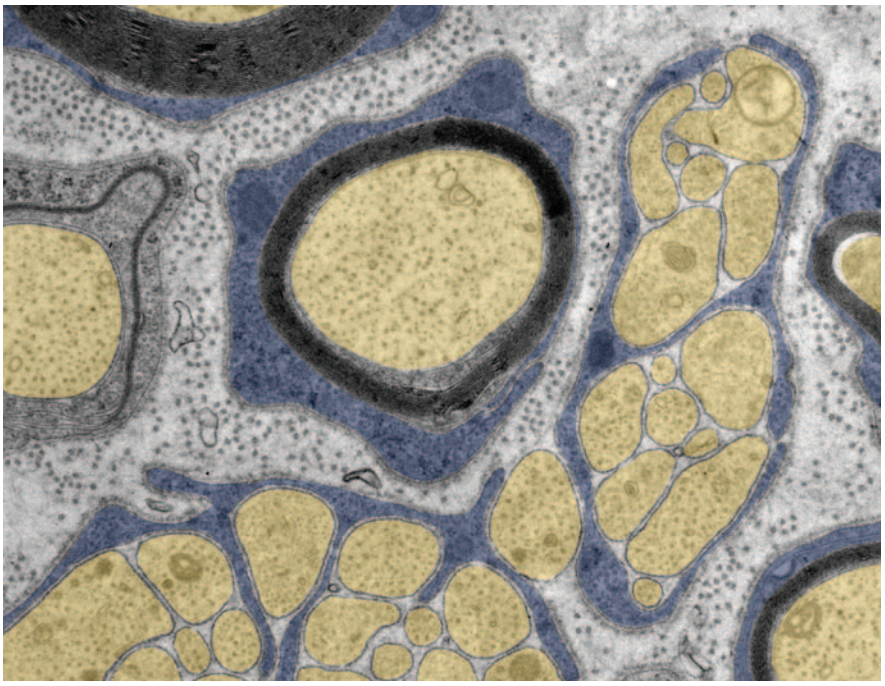
**DR Tamara Grigoryan from the research group of Professor Walter Birchmeier at the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch has gained new insights into the formation and differentiation of axons, through which nerve cells receive or transmit information. Axons can be myelinated (wrapped in a myelin sheath, which then allows for faster nerve impulse conduction) or non-myelinated (without a myelin sheath).**

**Grigoryan spoke to Horizon 2020 Projects about her experiments using transgenic mice and also highlighted the importance of encouraging more women to benefit from Horizon 2020 funding.**

**Dr Tamara Grigoryan**

### What is the background to your research and your main motivation to investigate axon myelination?

There are two main aspects to the project. The first aspect is the cell type that I am working on. It is a very specific cell type, the Schwann cell, which only exists in the peripheral nervous system (PNS). This cell type is named after its discoverer in the 19th Century. It does not occur in the central nervous system (brain and spinal cord). Schwann cells belong to the group of glial cells – one large group of cells in the nervous system, besides the neurons (nerve cells). It's a very understudied type of cells and has long been considered a passive bystander, mere 'glue' that kept together the nerve cells (hence the term 'glia').



**A cross-section though mouse nerve bundles. The nerve projections are false coloured in yellow, the Schwann cell cytoplasm – in blue, the layers of myelin – in black, around the nerve projection**

It is now known that glial cells, and their subtype the Schwann cells, are very major components of the nervous system, essential for the function of the nerve cells. The Schwann cells provide trophic support to the nerve cells and promote the conduction of signals along their projections (axons). Schwann cells surround the axon and form a myelin sheath, which insulates the nerve fibre similar to the plastic insulation of a power cable. This ensures that the nerve fibre can transfer an impulse or signal very fast.

Schwann cells are also responsible for the regeneration of the nerve, for example in trauma. If you cut your finger and damage a nerve, it will regenerate, regrow. Yet damaged nerve cells of the brain or spinal cord for the most part won't, because there are no Schwann cells in the central nervous system.

The second aspect to the project focuses on molecular mechanisms. We discovered that the development of Schwann cells is regulated by a certain signalling pathway, Wnt/β-catenin signalling. The researchers from the lab of Professor Walter Birchmeier in Berlin, where I come from, have been studying it for many years. Wnt/β-catenin signalling plays key roles in embryonic development, cell growth (proliferation), cell maturation or cell specialisation (differentiation) and in the regulation of stem cells, and, as the most recent work from the MDC now shows, even in the formation and differentiation of nerve fibres.

### How did you conduct your experiment and what were your research results?

Our research aimed to address the role of the Wnt signalling in the Schwann cells, and we did it by generating transgenic mouse models. We genetically manipulated the key component of the pathway, β-catenin, in such a way that we could over activate or downregulate Wnt signalling specifically in the Schwann cells and nowhere else in the mouse. We observed

abnormalities in a specific stage of a nerve fibre development in our transgenic mice.

At the beginning of their development in the embryo, the axons are grouped in bundles as an extension of a nerve cell, and surrounded by a Schwann cell. Around birth, the Schwann cell begins to sort out the thick axons from the bundle and to wrap them in a myelin sheath, an isolation layer, which is made of protein and fat. The thin axons are not sorted out; they remain bundled and do not receive a myelin sheath. Myelin is absolutely vital for the correct signal transduction transaction potential along the nerve.

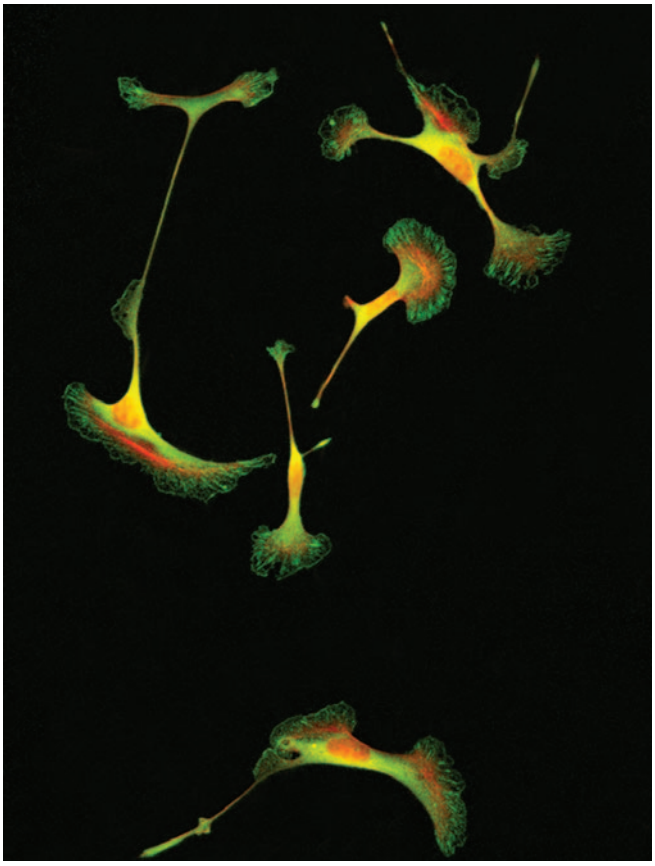
When we downregulated Wnt signalling, the Schwann cells failed to correctly sort out axons, and even the large axons remained bundled, without a myelin sheath. When we over activated the signalling pathway, the Schwann cells sorted axons faster, and they even started isolating the small nerve fibres, which also leads to the non-functioning of the signal transduction. It is only a certain size of nerve fibres, which is to be myelinated, that is, this process has to be very precisely regulated. In both cases, disrupted sorting and consequent myelination process lead to nerves cells not functioning properly.

### Are there many ways of overcoming the defects in the Schwann cells, or is that part of another investigation?

There are not many ways to manipulate Schwann cell functions. However, Wnt signalling can be manipulated by chemical activators or inhibitors of the pathway, which can potentially be used to correct the defects of Schwann cell development. We certainly hope that our findings will provide a deeper insight into the onset of developmental Schwann cell diseases, such as neuropathies.

### How do you see the results of the investigation benefitting future research?

It is the first time that Wnt signalling has been shown as a major player in the Schwann cell development myelination. Understanding the mechanisms of the Schwann cell development and myelination will allow us to address the questions of what goes wrong in disease and why, and to target the treatment more specifically. Dysregulated Wnt signalling often leads to the onset of cancer, which raises a question as to what is the role of Wnt in the Schwann cell derived cancers.



**RT4, a Schwann cell-derived line used in experiments, visualised with antibodies against different components of the cytoskeleton (red and green)**

### What are your thoughts on European research funding and how important do you consider Horizon 2020?

European funding is certainly very important. Not only because it is one of the largest research funding programmes, but also because it brings science in Europe beyond the national borders and promotes collaboration. The most important aspect of the H2020 programme in my opinion is that it is structured to connect the basic and applied sciences, industry and challenges in the society. Such an approach not only promotes ideas and discoveries but also, importantly, the practical application of those discoveries, and encourages the ideas to move from the lab bench to the market.

Promoting the equal gender opportunities for women in science is a priority for me. While more and more women are reaching senior levels in science, they often give up a scientific career, much more often than men, partially because the science world does not take into account the demands that having a family can place on women. I completely agree with astrophysicist Professor Jocelyn Bell Burnell, who in a recent interview, suggested that grants only offered to female-friendly laboratories would help change all this, because the "financial pressure works wonders where words don't".

HORIZON 2020

Dr Tamara Grigoryan
Max Delbrück Center for Molecular Medicine (MDC)
Berlin-Buch

BROWSE www.mdc-berlin.de