Did you perform bioenergetics experiments with the injured neurons? What major respiratory differences have you observed or would you expect to see?

Thank you very much for your presentation, very interesting research.

I was wondering if your lab is looking for other approaches other than the knockout of PTEN to stimulate regeneration. I think Prof. Bettina already asked about small molecules that could modulate PTEN activity in a more acute manner, but as you mentioned, for regeneration to happen you need the Schwann cells to be dedifferentiated. Is there any strategy regarding this aspect?

Thank you in advance, Professor Bernd

Dear Dr. Knöll,

thank you for the interesting talk. When a nerve suffer a lesion and the axon that it is cut, will the axon terminus be degratated? During the regeneration process, is the axon being connected or the neurons are actually regrowing e reconnecting with the the neurons before the lesion?

Thank you

1) The current treatment used for repairing damaged nerves is to surgically ligate one end to the other. When they are far apart, a nerve taken from another part of the body is used. Which nerves are used for this repair? Which nerve would not be inconvenient to be removed?

2) The left arm and hand are the ones who suffer nerve damage more often. However, most of the population is right-handed. Is there an explanation for this phenomenon?

3) Why did PTEN KO mice have more connective tissue between their nerves?

4) Since PTEN KO causes the presence of facial tumors in older mice, what would be a possible roundabout to apply PTEN KO for a possible nerve recovery treatment in older people?

Professor Bernd, thank you for your very interesting and didatics lecture! I have never studied this topic, but your explanation was very understandable. I heard about Phineas Cage who had his brain pierced by a metal bar and had a behavioral change. I want to know if there is any evidence that peripheral neuronal lesions are

capable of causing behavioral changes in addition to motor difficulties? Or do they cause any other physiological impact on the individual?

Is there a direct correlation between the nerve regeneration efficiency and the inflammatory process caused by macrophages recruited by the schwann cells?

It was not very clear to me what the influence of microglia and astrocytes on the signaling pathway of PTEN.

Using your experience, which would you say it is the most common molecular mechanism to neuronal injury? Altered Ca(2+) homeostasis, free radical formation, mitochondrial dysfunction, protease activation, altered gene expression, or inflammation?

How the PTEN signalling can be related to ageing diseases, mainly simptons linked to the Peripheral Nervous system? In addition, there's functional implications of the structural differences between nerves of PTEN KO and Wild type nerves?

After PTEN KO a decrease in inflammation around the injured nerve was noted due to lower recruitment of immune cells. Was it tested to induce sepsis in one of the animals with KO PTEN, through CLP for example, and compare their survival with WT?

Professor Knöll showed immunoassays targeting microglia and astrocytes. In my project, my main goal is to study the inflammatory pathway in microglia triggered by neuronal injury in Parkinson's disease model. I was wondering if there are any studies regarding the specific inflammatory pathways that can happen within these cell types in the experimental conditions presented. From what I have studied in Parkinson's disease, these inflammatory pathways are great pharmacological targets and can help attenuate the pro inflammatory responses. Maybe the same could be done for the injuries presented in the talk.

First, I would like to thank you for the excellent presentation and for your research; we can clearly see the importance and possibilities of application. Since we normally express PTEN, I would like to know, how does the regulation of our metabolism work to protect us from an excess of negative control that could suppress the proliferation of neuronal cells or conjunctive tissues?

There are data in the literature that demonstrate that the catalytic activity of PTEN can be modulated by reactive oxygen species (ROS) (Kitagishi & Matsuda, 2013).

How much is known about redox mechanisms involved with stimulation of axon regeneration after CNS injury in mice from reactions between PTEN and ROS? Can we think about better studying these mechanisms, especially involving ROS derived from the bicarbonate/CO_2 buffer possibly regulating PTEN activity? KITAGISHI, Yasuko; MATSUDA, Satoru. Redox regulation of tumor suppressor PTEN in cancer and aging. **International journal of molecular medicine**, v. 31, n. 3, p. 511-515, 2013.

A more broad question: To solve all life problems (or most of them) is simple a matter of knowing how to make another fully developed cell?

Why CNS neurons cannot be repaired the same way as PNS neurons? Wouldn't it be evolutively advantageous? And could Schwann cells be used to repair CNS neurons as a treatment for neuronal injury? Thank you for the excellent talk.

Thank you for the excellent talk, professor Knöll! You commented that PTEN deletion promotes the activation of Akt and mTOR signaling and then improves functional regeneration. Do you know if PTEN deletion could also have an influence on Schwann cells differentiation? Thank you!

I'd like to know if are there any studies on how the PTEN knockout could be related to cancer? Since PTEN is a tumour supressor gene, wouldn't its deletion induce a tumour formation?

Firstly, congratulations for this wonderful presentation.

In your presentation, your showed the relation between PTEN expression and regeneration of peripheral nerves. Is there any known relation between PTEN expression and regeneration/degeneration of the central nervous system? If so, is there any known relation between PTEN and the physiopathology of some neurodegenerative diseases such as Parkinson's or Alzheimer's?

Why was the main focus of the studies on the PTEN gene and not other tumor suppressor genes, such as p53 and Rb?

How the KO of PTEN affects the DNA repair of these shawnn cells? Does this cells acumule more double strand breaks and may have some apoptosis higher rates? Does it increase the chances of creating tumor cells?

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PTEN is known as a tumor suppressor gene, during your research with the KO
animals did you notice any kind of unexpected cell growth?
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Do you intend to verify PTEN deletion in the peripheric nervous system since its nerves are most common injured? In this case, what could be the effects analyzed in the mice?

What do you think would be the fastest way possible for these studies to directly help a patient?

Genetically, how neuronal regeneration could be modulated after an injury.

Thank you so much for your presentation, it was so good. I liked so much... I just have one question, in cellular level, is possible to cultivate cells with the disease or the KO gene for studies in vitro without using mice?

Why is the recovery of injured nerve cells very slow as compared to other cells of the body. Could stem cell therapy work for regeneration of dead nerve cells?

Thank you so much for the opportunity to see your work. Based on the need to circumvent tumor development in knockout PTEN models, I would like to know what your group thinks about testing PTEN inhibitors in compartmentalized cultures of neurons?

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The PTEN K.O. is an activator of mTORc that improved the regeneration of
injured nerves, but had a tumorigenic side effect...do you think...
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Is there any other physiological implications for the animal after motor neurons depletion?

Congratulations on the excellent lecture professor. The regeneration itself is a very complex process, you obtained very interesting results from stimulation and regenerations, would it be possible to obtain encouraging results in cases of more than multiple injuries?

Has a pro-survival effect mediated by PTEN modulation been observed in other types of injuries?

Professor Knoell! Thank you so much for the excellent talk! I was wondering, generally, younger organisms tend to have better tissue regeneration, does this also happen with the nervous tissue of mice? Could PTEN expression vary with aging?

First of all, I would like to thank you for sharing your work! Did your group study the neighborhood of the TSG? Or did some enrichment? To find pathways and targets that may have the potential to modulate regeneration and minimize or avoid harm?

In old and younger mice, the signaling pathway of PTEN is the same?

Is there a molecular strategy to make a PTEN transient silencing in mice just during the time of regeneration instead of a Knock-out?

Thank you.

You showed that when the pten is KOed there is a regeneration of the injured cells, having even a larger diameter than the uninjured control cells. Do you see any concerns about this increase?

Do you think the use of a drug that inhibits pten would be viable? Once tumor formation was observed.

How the depletion of phosphatase and tensin homologue (PTEN), a tumor supressor gene, affects axon regeneration in peripheral neuron injuty in knockout female mice for PTEN and and its influence in phenotype?

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When there is a transient inhibition of PTEN expression, is it still possible
recovery the neuronal injury?
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What are the mechanisms involved in nerve enlargement in view of PTEN depletion? Why does PTEN induce such a significant effect on mouse bristles?

In your opinion, why are there more cases of neuronal damage in males? Is there any difference between the injury recovery frameworks related to the individual's sex?

The anatomy os peripheral nerves in human and mouse is very similar. But this similarity extends to the molecular components of these cells in diferentes groups? For example, an antibody against Sox10, Oct6 or Zeb2 would work well and target specifically those proteins in peripheral nervers of both species (human and mouse)? In other words: how conserved are these proteins used as a markers of peripheral nerves?

Hello professor Bernd.

I'm complementing below my question made in the meeting chat:

Is there some research being made aiming to find a reversible inhibitor of PTEN that could be used to modulate the AKT pathway as a strategy to avoid tumor formation? That approach would be applicable as drug therapy to improve the results of treatment of nerve injuries in humans?

Are there other approaches that could increase activation of the p-Akt signaling pathway that doesn't involve PTEN that could also be explored to restore neuronal injuries?