Protein tenascin-C important in retinal blood flow disorders

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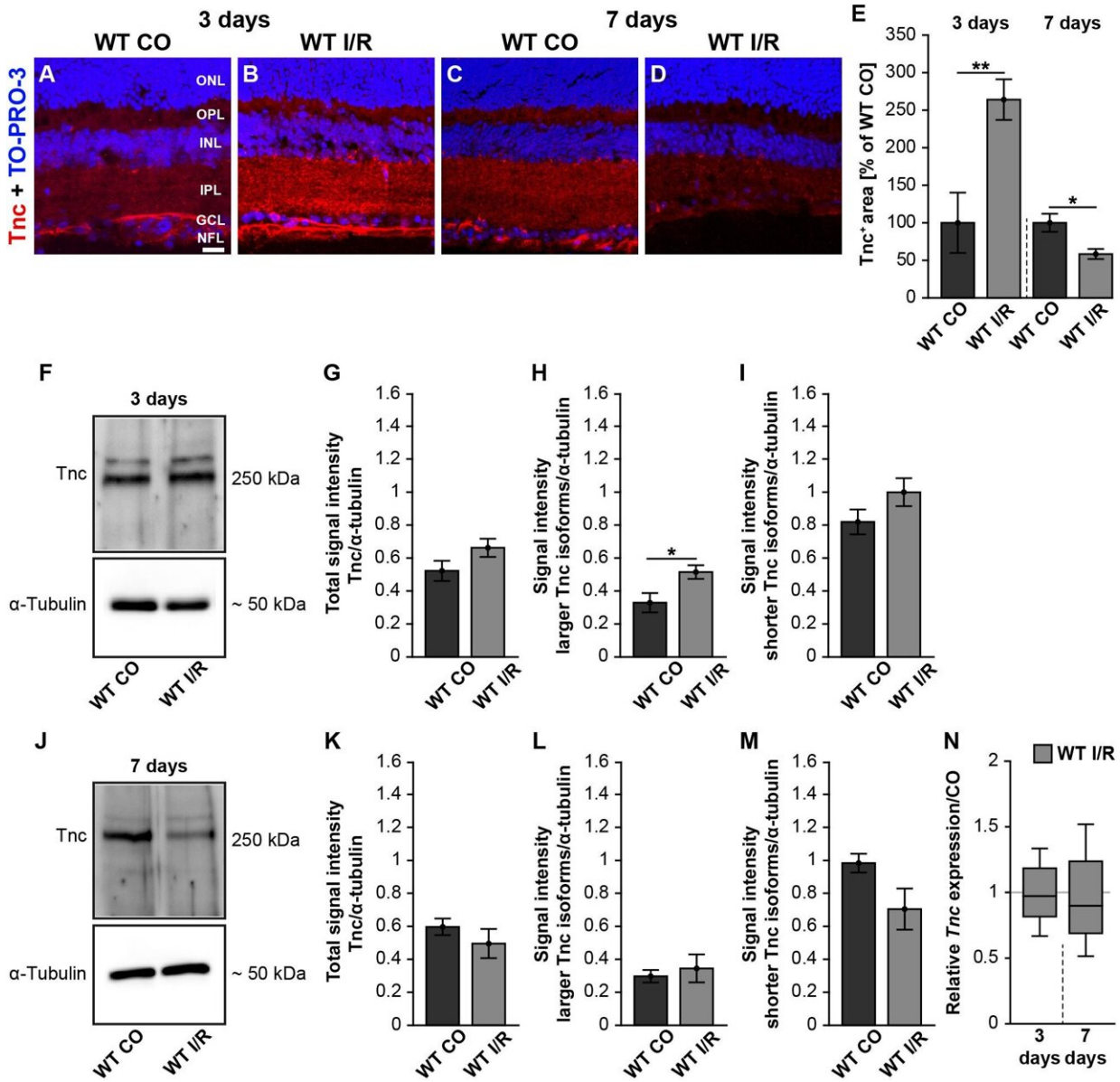

Figure 1. Early induction of Tnc in the ischemic WT retina. (A–D) Images of Tnc stained retinal cross-sections from control and ischemic WT groups at 3 and 7 days. Immunohistochemistry revealed a Tnc signal in the IPL and OPL as well as in the NFL (red). Cell nuclei were counterstained with TO-PRO-3 (blue). (E) Tnc+ staining area was significantly increased at 3 days, indicating an early induction of Tnc after ischemic injury. However, a significantly reduced Tnc staining could be demonstrated at 7 days. The WT CO group was set to 100%. (F–I) Consistently, relative protein quantification showed a significant upregulation of larger Tnc isoforms at 3 days after I/R. (J–M) Comparable Tnc protein levels were observed after 7 days. (N) No differences of the Tnc mRNA expression were noted at both points in time after ischemia. Data were analyzed via Student t-test and presented as mean ± standard error mean (SEM) in panels (E,G–I,K–M). For RT-qPCR, groups were compared using the pairwise fixed reallocation and randomization test in panel (N). These data are shown as median ± quartile ± minimum/maximum. *p Frontiers in Neuroscience (2021). DOI: 10.3389/fnins.2021.642176

Many eye diseases are associated with a restricted blood supply, known as ischaemia, which can lead to blindness. The role of the protein tenascin-C, an extracellular matrix component, in retinal ischaemia was investigated in mice by researchers from Ruhr-Universität Bochum (RUB). They showed that tenascin-C plays a crucial role in damaging the cells responsible for vision following ischaemia. The results were published online by the team in the journal *Frontiers in Neuroscience* on 20 May 2021.

As part of the research, the team around Dr. Susanne Wiemann and Dr. Jacqueline Reinhard from the Department of Cell Morphology and Molecular Neurobiology at RUB collaborated with Professor Stephanie Joachim's research group from the Experimental Eye Research Institute at the University Eye Clinic in Bochum.

Tenascin-C after retinal ischaemia

Ischaemia occurs due to an interruption in the supply of blood and nutrients to the retina—similar to a stroke. This causes the cells responsible for vision to die, which can lead to impaired vision or even blindness. The research team showed in mice that retinal cells express increased levels of tenascin-C at a very early stage following ischaemia. The quantity of the protein then gradually reduces again as the damage to the retina progresses. "Tenascin-C could therefore be a biomarker for the early detection of ischaemic eye conditions," says Jacqueline Reinhard.

Improved retinal function in mice without tenascin-C following ischaemia

The researchers also conducted electroretinogram analyses, allowing them to measure the electrical signal flow of the retina after a light stimulus. They thus showed that retinal ischaemia impairs the function of certain cell types in the retina: both the rod-photoreceptors and the bipolar cells, which are involved in downstream visual processing.

In genetically modified mice, who were unable to form tenascin-C, the cells responsible for vision in the retina functioned considerably better following ischaemic damage than those in control animals, who had tenascin-C. In addition, fewer photoreceptors died without tenascin-C after ischaemia.

Possible changes between the neuron contact points

The researchers also demonstrated elevated levels of the vesicular glutamate transporter vGlut1 in the ischaemic retina. "These could be linked to impaired synaptic signal transmission between the cells and

contribute to cell death as a result of retinal ischaemia. Tenascin-C could be an important modulator here," assumes Jacqueline Reinhard. "Based on this knowledge, future therapy approaches could be developed to improve the treatment of ischaemia."

More information: Susanne Wiemann et al, Knock-Out of Tenascin-C Ameliorates Ischemia-Induced Rod-Photoreceptor Degeneration and Retinal Dysfunction, *Frontiers in Neuroscience* (2021). DOI: 10.3389/fnins.2021.642176

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