



# *Networking against neuroinflammation*

*The nEUROinflammation ITN Marie Curie network looks for new treatments for two diseases in which neuroinflammation is involved: stroke and multiple sclerosis (MS).*

TEXT **ULLA KALTIALA** PHOTO **RAIJA TÖRRÖNEN**



Natalia Kolosowska and Meike Keuters say that working as Early Stage Researchers in the nEUROinflammation network will open up invaluable opportunities and experiences.

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“What makes inflammation an important target for new stroke treatments is that it offers a wider therapeutic time-window than the standard fibrinolytic treatment, which must be started within 4.5 hours from the onset of the symptoms.”

“By affecting the inflammatory processes, we could reduce further damage and enhance recovery.”

There is a preventive aspect as well, because inflammation is present in many diseases, such as atherosclerosis or type 2 diabetes, which increase the risk of stroke and are associated with a worse outcome of stroke.

**THE MARIE CURIE** Initial Training Networks funded by the European Commission aim to enhance scientific excellence, innovations, cooperation with the industry, and researchers’ career prospects both in the academic and private sectors. The nEUROinflammation partners represent both sectors. The network offers doctoral training to 13 Early Stage Researchers, two of whom are doing their PhD work at UEF in Kuopio: **Meike Keuters** and **Natalia Kolosowska**.

Neuroinflammation can be initiated by various cues, including ischemia, injury and other inflammatory processes in the body. However, most immune cells are capable of both an adverse pro-inflammatory response and a protective anti-inflammatory one. A new way to treat neuroinflammation is to modulate the response in the anti-inflammatory direction.

**RESEARCHERS IN KUOPIO** have already been able to do this in mouse models of stroke, spinal cord injury and ALS by treating them with recombinant interleukin-33 (IL-33), a cytokine similar to that produced naturally in the body and involved in immune regulation. The treatment shifted the inflammatory response

in the neuroprotective anti-inflammatory direction, resulting in decreased lesion size and better functional outcomes.

**Paula Korhonen** recently presented the results in her doctoral thesis.

As part of her PhD project, Kolosowska has done further research on mice treated with IL-33, cooperating within the group led by Associate Professor **Tarja Malm**. “We have been able to identify miRNAs that are associated with the protective effect of IL-33 in stroke.”

MicroRNAs, or miRNAs, regulate gene expression in cells, and some of them are involved in regulating inflammation. Malm focuses especially on how miRNA levels are altered in stroke and how comorbidities and treatments affect them. An entirely new treatment approach would be to pack protective miRNAs in their natural vehicles, exosomes, to be transported into the brain to reduce inflammation.

Keuters started her PhD training at UEF in collaboration with Medeia Therapeutics, a biotechnology company which has since ceased to operate. Aranda Pharma continues their product development, and Keuters has been testing one of their drug candidate molecules under Koistinaho’s supervision.

The treatment targets a newly identified step in lipid peroxidation, a harmful process causing oxidative damage to cells in inflammation and stroke. “The novel molecule has proved very promising, reducing lipid peroxidation, lesion size and oedema as well as improving motor function.”

**BOTH KEUTERS**, who did her Master’s in experimental and medical neuroscience in Germany, and Kolosowska, who mastered in biotechnology in Poland, are pleased about their PhD posts. “The network offers great opportunities for training and creating research contacts, including summer schools and a secondment in another partner institution,” Keuters says.

“It’s exciting to take part in hot, emerging research, and working abroad is a nice experience,” Kolosowska adds.

Koistinaho and Malm say they had the opportunity to choose the ESR researchers from an abundance of good applicants both from top European research institutions and from outside the EU.

“It’s an advantage to work with talented and motivated doctoral students. Especially in my small newly-founded research group, it really makes a difference,” says Malm. ●

**“IN A WAY, THEY REPRESENT** the opposite ends of the spectrum of diseases involving neuroinflammation. MS has long been known as a strongly inflammatory autoimmune disease, whereas in acute stroke the role of inflammation has been discovered more recently. Now we know inflammatory processes are involved in practically all brain diseases,” says **Jari Koistinaho**, Professor of Pharmacology, whose molecular brain research group is one of the 13 partners in the network.

“We focus more on stroke, but new treatments that might be useful for both stroke and MS patients may be developed.”

**WHEN STROKE OCCURS**, the immediate damage is worsened by the following inflammation.