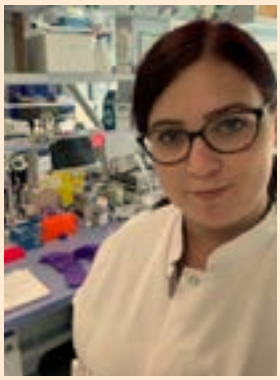
Meet the researcher

Sonja Fixemer



My job includes many hours and days at the fluorescence microscope where I analyse stained post-mortem brain slices.

At the end of my Bachelor's studies, I had a hard time deciding between a Master's in neuroscience or immunology. Both fields are immensely complex and captivating at the same time. I went for neuroscience in the end because what's more fascinating than studying the very organ that coordinates our entire body and is the *siège* of our mind and personality? I actually also bring aspects of immunology into my neuroscience research; after all, the brain has its own immune cells, which are called microglia.

Despite being less famous than their well-studied neighbours – i.e. nerve cells or neurons –, it's becoming increasingly clear that microglia play many different roles to keep our brain happy. Through constant surveillance and monitoring of the entire brain tissue, microglia detect any kind of change in homeostasis, including an invasion of pathogens, the presence of infected or dying cells and modified activity patterns of adjacent neurons.

Microglia are routinely in close contact with the neuronal connection points called synapses. They check if synapses are actively used; if not, they "clip them off". This helps the neuronal network to only maintain relevant synapses, which prevents an overexcitation of the neurons and also regulates neuroplasticity. This ability of the brain to form new connections is crucial for the learning process and to form new memories. In the event of a brain injury, the highly mobile microglia can be quickly recruited to the site of damage to clear harmful cell debris via an "eating and digesting" process called phagocytosis.

In my PhD research project, I'm investigating the role of microglia in the most common neurodegenerative disorder related to dementia: Alzheimer's Disease. More than 100 years ago, Prof. Alois Alzheimer himself noticed tiny cells (later identified as microglia) accumulating around the senile plaques, which are now known to be typically found in the brain of Alzheimer's patients. It seems that in the very early phase of the disease, microglia still have a beneficial role by phagocytosing ("eating") the toxic amyloid-β protein responsible for the build-up of senile plaques. However, there is increasing evidence that due to this chronic exposure, some microglia might lose their protective function or even develop a neurotoxic profile, thus actively contributing to neuronal loss. How and when microglia change their functional profile still remains unclear.

We don't have an "all or nothing" situation here; not all microglia seem to behave the same way and instead form subpopulations with different functional predispositions. Together with my supervisors Prof. Dr. Michel Mittelbronn, Prof. Dr. Alexander Skupin and Dr. David Bouvier, we aim to decipher the morphological and transcriptional profiles of microglia subpopulations and how they relate to the presence of Alzheimer-typical protein deposits. This will help provide new therapy research targets to either boost the protective microglia subpopulations or to suppress the neurotoxic cells in this still incurable disease.

We examine the post-mortem brains of Alzheimer patients and non-neurological diseased aged people provided by so-called brain banks. To work with human tissue is a great privilege because the more commonly used animal tissue doesn't simulate the complex aspects of Alzheimer's disease in humans. We focus on a precise part of the brain called the hippocampus, which plays an essential role in forming new memories and remembering previously acquired information. In Alzheimer's Disease, the hippocampus is particularly affected by neurodegeneration, resulting in memory loss, disorientation and the inability to form new long-term memories.

We use various high-tech microscopy techniques (including super-resolution and electron microscopy), AI-assisted image analysis tools and molecular biology techniques to understand how microglia profiles change in various hippocampal subregions of Alzheimer's patients compared to non-demented elderly people. In other words, a part of my job includes many hours and days at the fluorescence microscope where I analyse stained post-mortem brain slices. Sometimes I forget that I'm even looking at human brain cells; they look like carefully painted miniature artworks! As a young researcher, I'm excited to share my first results with the scientific community and the general public, and am happy to contribute to a better understanding of this devastating disease. ◆

Luxembourg-born Sonja Fixemer obtained her Bachelor's degree in Cell Biology (Biologie cellulaire et physiologie des organismes) and her Master's degree in Neuroscience (Neurosciences cellulaires et intégrées) at the University of Strasbourg. Sonja is currently in the third year of her doctoral studies at the University of Luxembourg. She conducts her research at the Luxembourg Centre for Systems Biomedicine (LCSB) and the Luxembourg Centre for Neuropathology (LCNP).