# GESINAS - ImmunoTools Award 2014

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## Lesion formation in Multiple Sclerosis: the switch from homeostasis to tissue damage

My research is directed towards the understanding of the pathological mechanisms underlying multiple sclerosis (MS) - a chronic neurological disease of the central nervous system. I have extensive experience in the field of Neuroimmunology including virology, pathology, immunology and neurosciences and have been instrumental in establishing novel research tools to develop new therapeutic approaches for MS. My commitment to MS extends to understanding the needs of people with MS by organizing interactions between patients and scientists. One of these events is called Meet The Scientist which is part of MS Life, a weekend in the UK for people affected by MS who can attend meetings, talks and chat with researchers and others, to learn exactly what we as research scientists do in the lab to help them fight the disease. For more details please see *www.mssociety.org.uk/ms-research/research-blog/2012/04/ms-life-2012-meet-scientists*. To facilitate this interaction and understanding I, with the help of many colleagues in the UK and the Netherlands have designed and executed the Charcot Tapestries; for more details please *http://multiple-sclerosis-research.blogspot.nl/2011/08/charcot-tapestry.html*. Inspired by the Bayeux Tapestry I decided on the name the Charcot Tapestry, after Jean-Martin Charcot (1825-1893), an eminent 19th Century neurologist who worked at the Salpêtrière hospital, Paris. Charcot was one of the most important figures in the history of MS, his findings representing a huge breakthrough for the understanding of the disease. The Tapestry is actually a series of tapestries showing

**The Charcot Tapestry**

How multiple sclerosis lesions develop

how the damage builds up in the brain in MS. The first in the series is a slice of a brain as we see it at post-mortem showing the scars, panel 2 is control and 3–5 represent what MS looks like under a microscope.

***The ImmunoTools products are key to discovering the molecular make-up of this process.***
My research in pathology at VUmc, Amsterdam is aimed at understanding the early events in the formation of MS pathology. We have unique access to tissues from people that allow the development of unique in vitro culture systems alongside the study of human brain tissues. My honorary position in QMUL, London, UK allows translational studies to and from experimental systems to humans to design and test new therapeutics.

Although the damage in MS is generally considered to be due to activated macrophages that phagocytose damaged myelin thereby leaving the neurons and axons vulnerable to further damage, we believe that changes in the brain occur before this otherwise irreversible step. In the normal-appearing white matter of the brains of MS patients, small clusters of activated microglia are frequently observed. Previously, we have shown that these microglial clusters, which we call “pre-active MS lesions”, are closely associated with stressed oligodendrocytes and myelin sheaths that contain markedly elevated levels of the small stress protein alpha B-crystallin. At this stage we believe the brain is able to restore tissue homeostasis. Using a combination of molecular biology, in vitro studies and immunohistochemistry we are investigating the pathways involved in oligodendrocyte stress and why in some cases the brain fails to control this stage thus activating the pathway leading to myelin damage and neurodegeneration.

As well as rodent models of the disease, we use human CNS cultures of microglia, macrophages, oligodendrocytes and brain slice cultures. Using these models we focus on the signals produced by stressed oligodendrocytes that activate the innate immune cells of the brain the microglia. Like macrophages, microglia can be classified as pro-inflammatory (M1) and anti-inflammatory (M2) and attempts to switch them to the reparative type is a key aim to control lesion development. We have performed genome-wide microarray analysis of macrophages and microglia that have yielded a number of candidate molecules also expressed in MS lesions. We are in the process of comparing the expression profiles in the early (reparative) lesions compared to the active (destructive) lesions in MS, a step that may identify lead components to control lesion progression.

In this context, the use of monoclonal antibodies, ELISA Assays and recombinant cytokines produced by ImmunoTools are key for the development of the project. These reagents will enable us to dissect the molecular make-up of multiple sclerosis lesions at all stages of development, and to further optimize rodent models for their ability to mimic the human disease.

# GESINAS ImmunoTools AWARD for

## **Sandra Amor** includes 50 reagents

FITC - conjugated anti-human CD11a, CD11b, CD14, CD40, CD80, CD86, Control-IgG1, Control-IgG2a, Control-IgG2b, HLA-ABC,

PE - conjugated anti-human CD11c, CD14, TNFα, IFN-gamma, Control-IgG1, Control-IgG2a, Control-IgG2b,

human IL-4 ELISA-set for 96 wells, human IL-6 ELISA-set for 96 wells, human TNFa ELISA-set for 96 wells (each 3 reagents),

recombinant human cytokines: rh BDNF, rh beta NGF, rh IFNgamma, rh GM-CSF, rh M-CSF, rh IL-1beta, rh IL-4, rh IL-10, rh IL-12, rh IP-10/CXCL10, rh TNFα, rh GDNF, rh MCP1/CCL2, rh MIP-3/CCL19, rh PDGF-AA, rh RANTES/CCL5, rh VEGF-A/VEGF-165,

recombinant rat cytokines: rr TNFα, rr IL-1beta, rr IFNgamma, rr CNTF, rr GM-CSF, rr MCP1/CCL2, rr RANTES, rr FGF-b/ FGF-2, rr IL-4, rr IL-6, rr IL-10

DETAILS more AWARDS