EDITORIAL

Morris-Coole Insignia

Interview with Cristina Roseti, 2013 Morris-Coole/*Epilepsia* Prize Winner

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The Morris-Coole Trust and the International League Against Epilepsy (ILAE) congratulate Cristina Roseti as the winner of the 2013 Morris-Coole/*Epilepsia* prize for the best study published in *Epilepsia* by a new investigator. Papers published in the 2013 calendar year are nominated by Associate Editors and Editorial Board members of *Epilepsia*, and then selected by the editors in conjunction with the ILAE president, Emilio Perucca. We wanted to know more about Cristina, her research, and the impact of this prize in this interview. We hope other prospective new investigators in epilepsy research can be recognized through this prize.

Who are You?

I got my degree in Pharmacy in 2005 at University of Padua; then I moved to Rome where I received my PhD in Neurophysiology from University of Rome "Sapienza" in 2010, working on the role of adenosine receptor antagonists in the modulation of $GABA_A$ receptors in human tissues from patients with temporal lobe epilepsy. Now, I am working as a post-doc in the group directed by Prof. Eleonora Palma, at Department of Physiology and Pharmacology of University of Rome "Sapienza," where I am using mainly electrophysiologic techniques.

What Got You Interested in Epilepsy Research?

My interest in epilepsy research arose for two simple reasons: (1) about 1% of population in the world is affected by this disease and even in the cases where symptoms are well controlled by drugs, the quality of the patient's life is extremely impaired; and (2) besides up to date, there are many papers studying animal models of epilepsy but very few on epileptic patients. Now my research interests focus on understanding the role of $GABA_A$ receptors in human epilepsies and on identifying possible approaches to ameliorate the dysfunction of the inhibitory transmission in drug-resistant temporal lobe epilepsy patients.

Explain for Our General Readership What Question Your Study Addressed and How Did You Go About Designing Your Study?

Temporal lobe epilepsy (TLE) is the most common form of focal epilepsy in adults, characterized by recurrent seizures, neuronal loss, and microglial activation. Recently, it has been shown that inflammatory mechanisms have a role in the pathogenesis of epilepsy and that seizure activity rapidly increases the synthesis of inflammatory mediators involved in the initiation and propagation of neuronal hyperexcitability. The chemokine fractalkine (CX3CL1) and its receptor CX3CR1 are widely expressed in the central nervous system. It is reported that fractalkine modulates glutamatergic currents, microglial neurotoxicity, and neuron survival. We have previously shown that in patients with drug-resistant epilepsy the inhibitory GABAergic transmission is strongly defective, increasing the bad effects of the disease and rendering not easy the pharmacologic approach. Our goal in this work was to investigate whether CX3CL1 can have a modulatory effect on GABAergic transmission. We investigated the role of CX3CL1 through electrophysiologic recordings performed in Xenopus oocytes microtransplanted with membranes isolated

from brain tissues of epileptic patients. In addition we performed electrophysiologic recordings (patch-clamp) on the pyramidal neurons in epileptic human slices. In collaboration with Dr. Eleonora Aronica, immunohistochemical staining and double-labeling studies were carried out on the same brain tissues to analyze if CX3CR1 expression was altered.

What Were the Results and How Do You Interpret Your Findings?

We found for the first time that CX3CL1 modulates GABA currents in human epileptic brain tissue. In particular, CX3CL1 reduces the loss of function of $GABA_A$ receptors affecting GABA current amplitude both in oocytes and native human neurons. Of interest, CX3CL1 does not influence GABA currents in oocytes injected with nonepileptic tissues. Consistent with a specific effect of CX3CL1 on tissues from patients with TLE, CX3CR1 immunoreactivity is higher in TLE sclerotic hippocampi than in control tissues, with a prominent expression in activated microglial cells. These findings suggest that CX3CR1 increase may be part of the inflammatory process present in epileptic hippocampus playing a role in epileptogenesis. Although we cannot demonstrate from our data that the increase of CX3CR1 precedes or follows the onset of epilepsy, our results on both epileptic hippocampus and cortex would suggest a potential neuroprotective role for the chemokine CX3CL1 in TLE.

What Next Steps in Epilepsy Research Are You Taking and What Are Your Career Goals?

I would like to continue in the study of the modulation of neurotransmission in epilepsy by chemokines and cytokines and generally on the role of inflammation in the disease. Most important, I would like to continue my studies on human tissues because my motivation is increased by the fact that this can imply the real application of scientific results to the patients, and this makes my work even more fascinating.

What Does The Morris-Coole *Epilepsy* Prize Mean for You, Your Laboratory, Research Institute, and Your Future?

I feel honored to receive this prestigious award so important for me and for my laboratory. That is a big satisfaction for the job and research done until now and it is a strong encouragement to go eagerly on with commitment. I would like to thank all members of the team; only their precious contribution allowed me to reach this important result. This is the first prize I received for my job and I'm particularly proud and thrilled, and I hope this will push further my passion and career!

Gary Mathern
Astrid Nehlig