

## **The Erythromelalgia Association Footsteps, December 2014**

### **Pfizer reports EM research findings at pain conference**

While heat and exercise are frequent triggers for pain attacks in those with inherited erythromelalgia, the majority of attacks occur spontaneously with no identified trigger. Patients vary considerably in the frequency and severity of pain attacks—even those with the same genetic mutation—and some suffer significant pain between attacks while others are relatively pain-free. These are among the findings presented by Pfizer Neusentis, a UK-based research division of the global pharmaceutical company, at the International Association for the Study of Pain in Buenos Aires in October.

This 2013 study followed the natural history of pain in 13 patients with inherited EM during a three-month period and represents one of the most detailed investigations in EM patients and their symptoms over time. Performed at the Pfizer clinical research unit in New Haven, CT, U.S., the study was made possible by the collaboration between Pfizer and the Yale research group led by Stephen Waxman, M.D., Ph.D., according to Ruth McKernan, M.D., Chief Scientific Officer at Neusentis.

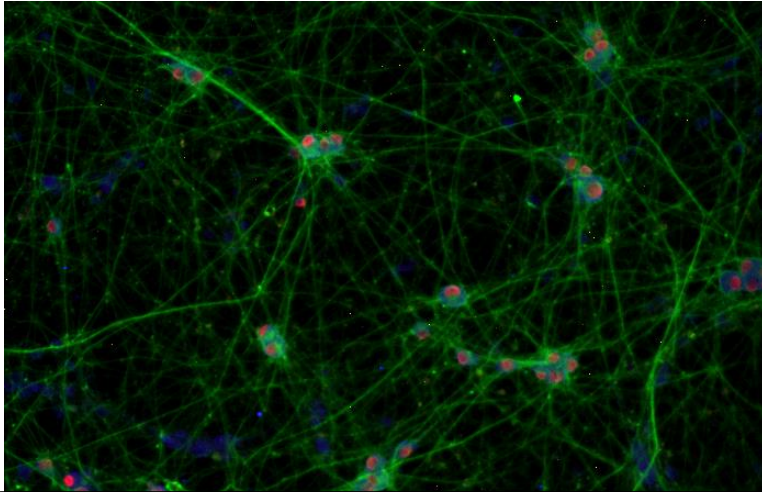
A second study of five people with inherited EM found most responded well to an experimental drug and experienced less heat-induced pain on days when they received the drug compared to when they received a placebo. Still at an early stage in its development, the experimental drug is designed to block the Nav1.7 sodium channel proven by Dr. Waxman's group to be involved in the transmission of EM pain. While these results are encouraging, Dr. McKernan stresses additional investigations need to be conducted to better understand whether this drug has the potential to provide long-term relief. Interestingly, the same drug is also being tested in patients suffering from diabetic neuropathy, she says. Known as a double-blind cross-over study, patients were given the drug on one occasion and a placebo on the other, and neither patients nor doctors knew which time the patients received the drug. Each day pain attacks were triggered three times by warming the skin using heated blankets.

An optional part of this study asked participants to donate blood. Using state-of-the-art technology, the Pfizer research team generated stem cells from the blood cells and then made them into sensory neurons. (The stem cells have the same genetic forms of Nav1.7 channel as do the donor blood cells.) Scientists at Neusentis found sensory neurons made from EM patients' blood were more active than those obtained from healthy donors. They also became even more active when warmed up, reproducing just what happens in patients. When the drug was added to the sensory neurons, it blocked the activity and returned them to a more normal state. Additionally, the effect of the drug was greater in neurons from patients than from unaffected donors. These findings have given the researchers clues to the potential

effectiveness of the drug, not just in people with inherited EM, but with other pain conditions, too.

Dr. McKernan adds, “As always, we are indebted to the patients and their relatives who participated in these clinical trials. Without their dedication we would not be able to conduct our research. Having cell systems in which we can test new drugs, and even drug combinations, in the lab before giving them to patients, is a big step forward.”

In response to a request from TEA for comment, Dr. Waxman writes, “We are pleased to be collaborating with Pfizer on this study. In my view this work moves the field in the right direction. While we still have a lot of work to do, I am optimistic and I believe that, in the end, we will win the battle against EM.”



Made from the blood of a patient with EM, these pain-sensing sensory nerve cells—colored green to make them more visible—behave just like the nerves that stretch from the spine all the way to the hands or feet. These fibers show abnormal sensitivity to heat just as some patients with EM do. (Photo courtesy of Pfizer)