Taking a shot at neuropathic pain

For all the millions of analgesic pills taken worldwide to relieve everything from toothache to sore joints, there are still few options to tackle the pain from damaged nerves. Two decades ago, neuropathic pain was regarded as a mystery, but progress has been swift and today’s journals are awash with data on cellular changes triggered by an injured or diseased nervous system. The challenge, however, is to pick which of these myriad changes are essential to neuropathic pain and worth pursuing as drug targets. With this in mind, researchers and clinicians gathered at a Novartis Foundation symposium (Sept 30–Oct 2, Tsukuba, Japan) where the latest ideas were held up to scrutiny.

“Neural plasticity is becoming the most important key word in understanding pain even bigger.”

Injure a sensory axon, and the neuron starts firing spontaneously—a phenomenon known as ectopic discharge. These DRG neurons also become more responsive, and are more likely to fire in response to weak stimuli. The abnormal physiological nerve conduction. We cannot help our patients if the drugs also disrupt normal neurological functions.”

Neuropathic pain suggests that new pharmacological approaches are needed to treat this condition. McMahon has approached the problem knowing that, in neuropathic states, the cocktail of trophic factors and cytokines produced by the damaged nerves is substantially different to normal—hundreds of genes are upregulated or downregulated.

In a striking set of experiments, McMahon has recently managed to alleviate pain in some animals by reversing these changes in gene expression using glial-cell-derived neurotrophic factors (GDNFs) and artemin. The implications of these findings for future therapies are huge. “We now know that GDNFs can reverse ectopic activity, and change sodium channel expression in neuropathic pain models,” says an upbeat McMahon.

Mechanism-based medicine takes time to develop, and the delays in the translation from basic research to clinical practice can seem enormous.

“The good news is that the intense focus of academia and the pharmaceutical industry on the problem of neuropathic pain suggests that new drugs directed at novel targets should be available in the future”, says John Wood (University College London, UK), “The wait will unquestionably be worthwhile.”

Lisa Melton