

Meeting Report

Attended by some 80 participants coming from England, France, Ireland, Italy, Japan and Sweden, the first international meeting on “Molecular Targets for Novel Pain Therapeutics” has been held in Parghelia (Vibo Valentia, Italy), from the 22nd to the 24th of September, 2010. In the beautiful venue offered by the Tyrrhenian coast of Calabria, top scientists in the pain field have gathered to share the most recent findings in pain mechanisms unraveling new targets for potential development of more effective drugs in pain treatment.

The meeting was opened by the invited lecture delivered by Prof. Shinobu Sakurada (University of Sendai, Japan) that using a pharmacological approach showed that nociceptin, a 17-aminoacid peptide identified as the endogenous ligand of opioid-receptor like-1 (ORL-1) receptor, induces the disinhibition of histaminergic neurons enhancing the release of histamine which subsequently acts on the H1 receptor located on the substance-P containing neurons to produce the nociceptive spinal response.

The following two days the meeting then continued in four intense sessions that covered different aspects coupling with pain: the mechanisms of pain transmission, the pain control and sensitization process, the inflammatory components and the novel therapeutic approaches.

During the sessions, scientists coming from Universities of Japan (Tokyo, Sendai, Wakayama, Fukuoka and others), researchers from the Department of Pharmacobiology (UNICAL, Rende, Italy), the Department of Pharmacobiological Sciences (University of Catanzaro, Italy) and from international Scientific Institution (The London Pain Consortium, UK; The Center for Neurotherapeutics of Dublin City University, Ireland; The University College and King's College of London, UK; The University Consortium for Adaptive Disorders and Headache, UCADH, Pavia, Italy; The IRCCS Santa Lucia Foundation, Rome, Italy) took turns showing the results of their research.

Prof. Wood (London, UK) discussed the aspects of peripheral wiring and the rational basis for chronic pain treatment through manipulating sodium channel expression and function. Voltage-gated sodium channels are crucial for neuronal excitability and signaling, in particular, there is a close association between the expression of Nav1.8 and the response to noxious mechanical pressure, cold pain and the establishment of inflammatory pain. By using a Nav1.8 CRE mouse to specifically target nociceptors important for inflammatory pain, Prof. Wood and his group, gained relevant information on the role of Nav1.7 in acute pain.

On his side, Prof. Hunt (London, UK) showed how multiple descending pathways act together in neuropathic pain generating a sequence of events that includes activation of signaling pathway, induction of long-term potentiation and transcriptional and translational events. Among those events Prof. Hunt showed recent findings on the epigenetic changes in neurons occurring after injury and, more in details, the phosphorylation of DNA binding proteins that modify the acetylation of histone proteins.

Many speakers pointed out the need for animal models of neuropathic pain that mirror the sensory *sequela* of events seen in humans. To this end, the work presented by Dr. Iannetti (London, UK) showed, by functional neuroimaging studies, the complexity of the so-called “pain matrix” in humans and underlined the presence of confounding factors that have to be taken in account when using neuroimaging studies to investigate the action of centrally-acting pharmacological agents.

The recent findings on the influence of immune system in pain processing and the complex network between inflammatory cells and neurons in the pathogenesis of neuropathic pain, were discussed by Dr M. Malcangio (London, UK), Dr T. Kohno (Niigata, Japan), Dr C. Tassorelli (Pavia, Italy) and Dr N. Kiguchi (Wakayama, Japan)

In particular, Dr. Malcangio (London, UK) showed that in the dorsal horn, microglial release of the lysosomal cysteine protease Cathepsin S (CatS) contributes to the maintenance of chronic pain via liberation of neuronal fractalkine (FNK), a novel candidate target for intervention, whereas Dr. Kohno (Niigata, Japan) reported the potential of bradykinin, a peripherally acting inflammatory mediator, that contributes to pain hypersensitivity potentiating glutamatergic transmission, as a target for promising potent analgesics.

The research work presented by Dr. Sacerdote (Milan, Italy) and Dr. Tanabe (Kitasato, Japan) provided more information on the analgesic effects of opiates and gabapentin, respectively, while Dr. Mizoguchi (Sendai, Japan) described the analgesic profile of a new N-terminal tetrapeptide derivative of dermorphin and Dr. Nagase (Kitasato, Japan) shared the fascinating process that led to the design and synthesis of a new delta receptor agonist with potent analgesic effects. The session was closed by, Prof. Dolly (Dublin, Ireland), remarking the unmet need for long-term and effective pain therapeutics and showing his elegant as well as rigorous approach to bioengineer botulinum neurotoxins to yield chimeras with unprecedented biological characteristics and anti-nociceptive potential.

The meeting also offered to young scientists and PhD students the unique opportunity to discuss informally their results in an international as well as stimulating environment where they could meet the expertise and the knowledge of internationally recognized scientists also

opening interesting perspectives for their placement. Some thirty young scientists attended the meeting and eleven were the recipients of the generous financial support of The International Society of Neurochemistry. The latter young scientists have contributed to the meeting presenting their research work as oral or poster communications. Among the others, Dr. S. Watanabe (Sendai, Japan) showed the involvement of peripheral glutamate release in the nociceptive behaviors induced by gangliosides, whereas Dr. H. Watanabe (Uppsala, Sweden) reported the results of a study designed to identify the involvement of mu-opioid receptor subtype on the nociceptive effect induced by intrathecal injection of Tyr-W-MIT1. More information on the role of opioids in nociception were shared by Dr. C. Nazaki (Illkirch, France) that, using a model of chemogenic-heat nociception induced by capsaicin found that delta-opioid receptor is involved in pain transmission initiated by TRPV1 activation. Approaching the pain associated with migraine, Dr. Greco (Pavia, Italy) showed that elevation of endogenous fatty acid amides, such as anandamide and 2-arachidonoyl glycerol at the spinal and supraspinal level, through the inhibition of the enzymes FAAH and MAGL, may modulate pain perception. Finally Dr. Marinelli (Rome, Italy) reported an interesting study on the synergic analgesic action of the serotype A Botulinum neurotoxin and morphine suggesting the possibility to use their combined administration for lowering the effective dose of morphine and preventing the development of opioids tolerance.

The scenario offered by the shore of Parghelia (Vibo Valentia) facing the still erupting Stromboli Volcano, one of the seven Aeolian islands, together with the hospitality of Mrs Caterina's and Mr Mariano's team at the Hotel Porto Pirgos made all the rest needed for the conference to become a real success in every respect.

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