Newsletter November 2019
Volume 1 Issue 1

INSIDE THIS NEWSLETTER

"Targeting neuroinflammation to combat pathological pain in neurodegenerative diseases and chronic pain syndromes."

Getting Started

By TOBeATPAIN

TOBeATPAIN is funded by the Horizon 2020 programme of the European Union (Marie Skłodowska-Curie Grant Agreement No 764860).

TOBeATPAIN does propose an innovative approach that will examine the neuroinflammation associated with pain in peripheral and central diseases and will identify the critical non-neuronal cellular players and mediators involved in pathological pain signalling. The following two hypothesis will be tested. The first is that neuroinflammation represents an underlying mechanism of pathological pain that occurs as a result of diseases within the brain as well as in the peripheral nervous system. The second is that the precise mechanisms of neuroinflammation in peripheral and brain diseases share some features but also vary and possess individual characteristics.

TOBeATPAIN is structured around two scientific themes:

- Pathophysiology of pain in neurodegenerative diseases characterised by neuroinflammation.
- Pathophysiology of neuroinflammation in chronic pain syndromes.

Welcome words…

By Prof. Marzia Malcangio (King's College London)

TOBeATPAIN is a research training programme, which is funded by the Horizon 2020 programme of the European Union. The project is coordinated by the Institute of Psychiatry, Psychology and Neuroscience, at King's College London (KCL) and is funded for 4 years.

TOBeATPAIN Network is offering eleven researchers a unique training platform across different research/training environments and cultures working with 3 biotech SMEs, 2 large companies and 1 non-profit research charity. Our partners are: Karolinska Institutet, Medizinischen Universität Innsbruck, Universitätsklinikum Jena, Universitätsklinikum Würzburg, Kancera AB, Bionorica GmbH, Eli Lilly and Company Ltd, Mabtech AB, European Research and Project Office GmbH (EURICE) and the Alzheimer's Society .

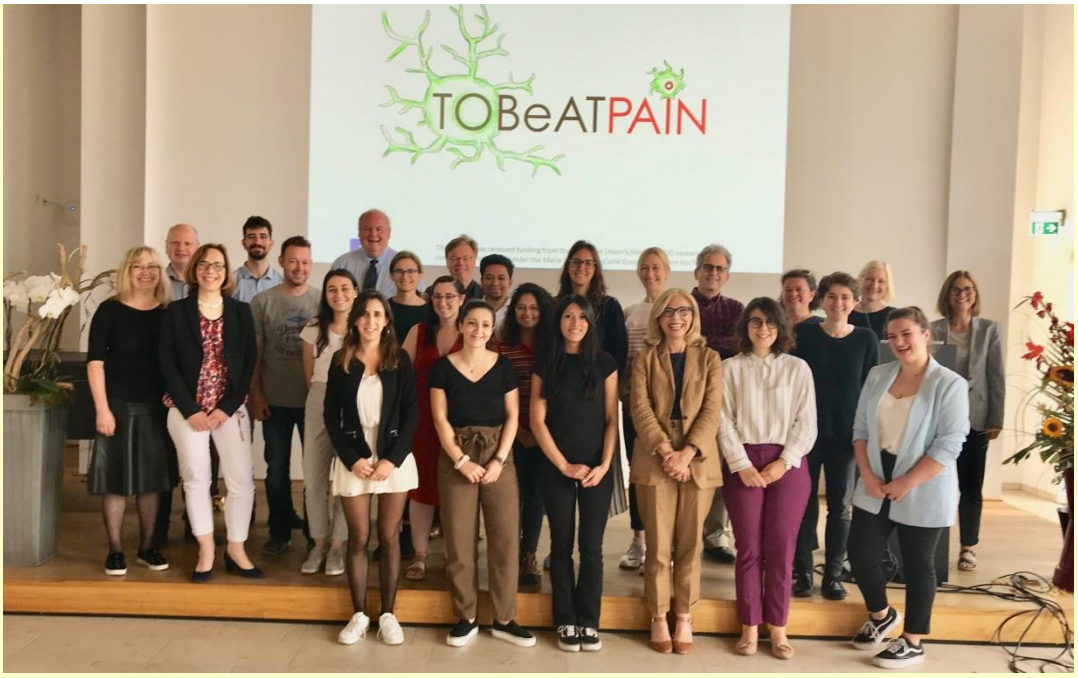
TOBeATPAIN training programme aims to target neuroinflammation to combat pathological pain in neurodegenerative diseases and chronic pain syndromes.

It is based on state-of-the-art lab-based Network-wide and local training activities, including secondments and scientific visits and specialised complementary skills focused on entrepreneurship and societal engagement.

The central role of the private sector highlights the ethos of this ITN whereby both translation of scientific training into practice and strengthening of private-public sector links are essential for the success of the EU2020 strategy, as well as for significant economic and societal outcome.

More information on the plans and progress of the project can be found on our website https://tobeatpain-itn.net

If you have any specific questions please email tobeatpain@kcl.ac.uk.



Neuroinflammation and pain in Alzheimer's disease

By George Sideris Lampretsas

I have graduated from the School of Pharmacy at the Aristotle University of Thessaloniki in Greece. During my 5-year bachelor, my main research project focused on RNA editing in Alzheimer's disease in post-mortem tissues, while I have also spent six months working on ER-stress and protein synthesis machinery in APP/PS1 mice in Idibell in Barcelona. I have applied for a PhD position within TOBeATPAIN European Training Network since it is a unique opportunity for a research project with translational implications that incorporates both clinical and experimental approaches to study chronic pain and neurodegeneration. Moreover, TOBeATPAIN constitutes an amazing platform that provides us with high quality doctoral education at the King's College of London, with meetings and courses held by word-leading scientists from notable academic institutes as well as with the opportunity to build collaborations with other PhD students all over Europe.

PROJECT SUMMARY

Alzheimer's disease (AD) is a human age-related biological process which causes dementia and degeneration of the neurons in the brain. Although many drugs are being tested in clinical trials, there is still no adequate palliative treatment to slow or stop the degeneration. The clinical challenge of treating individuals with AD is often exacerbated by the inability of most patients to communicate thoughts thus leading to substantial unmet needs in individuals with dementia. One such unmet need is the treatment of pain, which is thought to be a contributory cause to psychological symptoms of dementia, such as aggression, agitation and depression. Although the complications of pain in individuals with dementia are well-documented, a better understanding of the effect of the AD pathophysiology on pain is required.

Reactive gliosis and neuroinflammation are hallmarks of Alzheimer's disease, while recent genetic studies have shown that microglia, the CNS resident immune cells play a key role in the pathogenesis and the progression of the disease. Moreover, more and more studies in rodents and are implicating microglia in pain transmission and perception as stimulation of microglia themselves under normal conditions can induce pain hypersensitivity. Thus, the working hypothesis of my project is that neuroinflammation or "activated" microglia in pain-related areas of the CNS may contribute to pathological profile of pain present in Alzheimer's disease.

During my PhD I will be using a transgenic mouse model with AD pathology, where I will isolate microglia using flow cytometry to investigate whether there is a specific genetic signature or "activated" state of microglia in pain related areas. Furthermore, along with techniques such as immunohistochemistry and behavioral assays I will be also using micro-PET to study microglia in vivo.

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Neuroinflammation and pain in Parkinson's disease

By Xhoana Lama

During my studies at the Department of Biological Applications and Technology of the University of Ioannina I got acquainted with several undergraduate courses related with neurobiology and immunology. So early on, I realized that I was extremely fascinated by the rapidly evolving field of neuroimmunology. For this reason, I decided to conduct my master's thesis at the Biomedical Research Foundation of the Academy of Athens in a project aimed to delineate the anti-inflammatory role of the cytokine activin-A in a mouse model of Parkinson's disease. After finishing my Master's I received an Erasmus+ scholarship in order to conduct a placement in University Hospital Frankfurt. I joined the Cellular Immunology lab, where I optimized T helper differentiation protocols and studied the role of IRF4 in Th1 polarization.

The reason why I applied at the ToBeATPAIN Innovation Training Network program was that it was a unique opportunity for me to utilize the theoretical background and experience that I had already acquired and to deepen my knowledge in the role of neuroinflammation and pain in PD. Moreover, ToBeATPAIN program provides a great chance for high quality training held from world leading institutes in an international environment.

PROJECT SUMMARY

Parkinson's disease is the second most common neurodegenerative disorder characterized by both motor and non-motor symptoms. Pain is one of the most debilitating non-motor signs of Parkinson's disease (PD) but is poorly understood and inadequately treated by current analgesics in patients; 45% of people report no pain relief or improvement by PD medications. Whilst neuroinflammation has been implicated in the neurodegenerative side of PD, its involvement in pain is still unexplored. We propose that micro(glia) activity in multiple descending pathways from the brain is involved in modulation of pain signalling and contributes to pain in PD.

This hypothesis will be tested by

1. Application of rodent models of PD (e.g. toxin and alpha-synuclein pre-formed fibrils to assess pain sensitivity and(micro)glial and neuronal activation in pain pathways by microPET imaging, autoradiography and immunohistochemistry (IHC), and quantify cyto(chemo)kines tissue levels by ELISA
2. Examination of the extent of (micro)glia activation in post-mortem brain and tissue (IHC) from PD patients with confirmed pain.
3. Analysis of PD skin biopsies for inflammatory mediators detected in rodent models.
4. Examination of the efficacy of established anti-inflammatory agents and (micro)glia inhibitors on relieving pain in PD rodents

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Neuroinflammation and cerebral pain processing in fibromyalgia, osteoarthritis, and disc degenerative disease

By Silvia Fanton

I am from Italy and currently pursuing my PhD in the Department of Clinical Neuroscience at Karolinska Institutet (KI, Stockholm) while being appointed the post of Early Stage Researcher 3 in the TOBeATPAIN network.

I graduated from a Bachelor's Degree in Cognitive Psychology and Psychobiology and a Master's Degree in Cognitive Neuroscience and Clinical Neuropsychology (entirely held in English) at the University of Padua (Italy). During my studies, I felt the need to constantly confront myself with diverse academic realities in order to enrich my understanding about the relationship between cognitive processes and their biological foundation in the human brain. This is why I took part in a Summer School at the Experimental and Applied Psychology Lab at Vrije University in Amsterdam and I spent two semesters abroad, the first one in Linköping (Sweden) and the second one as a research trainee in the Department of Neuroscience at KI.

I am now very excited to be part of a top-notch multidisciplinary research environment, such as the one offered by the TOBeATPAIN network, as I strongly believe it will enable me to achieve my goal/dream of becoming a well-rounded neuroscientist.

PROJECT SUMMARY

The overall purpose of my PhD project is to increase the understanding about the still largely unknown mechanisms responsible for the chronification of musculoskeletal pain by focusing, specifically, on the transition from nociceptive to nociplastic pain. With this scope, osteoarthritis (OA) and disc degenerative disease (DDD) will be explored as models of the former, while fibromyalgia (FM) will be examined as a prototype of the latter.

The FM cohort will be compared to heathy controls with the aim of investigating whether the Ala147Thr functional polymorphism of the translocator protein (TSPO) gene (rs6971), which is considered a biomarker of glia activation, influences expectancy-modulated pain processing and descending pain inhibitory mechanisms. In addition, functional magnetic resonance imaging (fMRI) and magnetic resonance spectroscopy will be employed to look at the effects of the herein studied polymorphism on, respectively, cerebral pain processing and cerebral metabolism in pain related areas, such as the rostral anterior cingulate cortex and the thalamus. These two brain regions have been previously found to present functional and structural abnormalities associated with the patients' inability to activate the descending pain inhibitory mechanisms (e.g., Jensen et al., 2009, 2012).

In the OA and DDD cohorts, the role of the different genetically inferred variants of TSPO will be also investigated in relation to measures of pain sensitivity. Furthermore, fMRI and diffusion tensor imaging will be used to measure whether aberrant functional and structural coherence between the nucleus accumbens and the medial prefrontal cortex, previously shown to predict persistence of chronic low back pain (Baliki et al., 2012), are also present in patients suffering from nociceptive pain. If so, the idea is to see whether these measures predict negative treatment outcome and if such pre-treatment abnormalities can normalize following successful surgical treatment.

The attempt of unrevealing the mechanisms underlying FM, OA, and DDD pathologies might be of relevance for preventing the development of centralized nociplastic pain.

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Role of brain and spinal cord micro(glia), TSPO and IL-8 in arthritis associated pain

By Joana Menezes

I am from Lisbon, the Portuguese Capitol, known as the city of light. I studied Human Biology at the historical Evora University at a bachelor level followed by a Master degree in Molecular Genetics and Biomedicine at Nova University in Lisbon. I spent the second year of my Master's in the BRAINlab at the University of Copenhagen. The subject of my thesis was on crossmodal neuroplasticity and I got a unique opportunity to work with congenitally blind subjects in Denmark and to study the somatosensory and visual cortex of mice with a Crx knockout in Montreal, Canada. After defending my thesis, I worked as a research assistant at the Neurobiology Research Unit (NRU), Rigshospitalet, under supervision of Professor Jens Mikkelsen. Atthe NRU I investigated original and truncated subunits of the alpha7 receptor, respective genes and polymorphisms using fresh human cortical tissue. Through my work experience I gained a diverse range of lab techniques and skills that I will enjoy the benefits of as a Ph.D. student. The TOBeATPAIN project focusing on fibromyalgia in Professor Camilla Svensson's lab at Karolinska Institutet, Stockholm, Svensson seemed like a great opportunity to advance my knowledge and career in Neuroscience, a field which I have great passion for. The project is important and timely as chronic pain is becoming increasingly common. Unfortunately, effective treatments for chronic pain are limited and individuals often lack a clear explanation fortheir pain. While many of the questions concerning chronic pain are still unknown, I am optimistic that we can find answers. The prospect of working to better understand pain is super exciting and will surely make me grow as a researcher. I also look forward to contributing to my research field as well as engaging in scientific outreach activities to share my ideas and findings with the public. Through my PhD work in the Svensson lab, and through collaborations within the TOBeATPAIN network, I am confident that we will identify new strategies to reduce the burden of chronic pain and improve the quality of life for the millions suffering from pain.

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PROJECT SUMMARY

My project is focused on chronic pain in Fibromyalgia (FM). FM has a prevalence of approximately 2% and predominantly affects women. The cause of FM is unknown and the disease processes are poorly understood. Despite the high prevalence, the current treatments often lack efficacy and FM is diagnosed based on criteria as no diagnostic tests exist. As a result, people suffering from FM have a drastically reduced quality of life. The Svensson lab is part of a collaboration that recently found evidence of an autoimmune component in FM and developed a disease-relevant mouse model. My Ph.D. project will extend these findings and my aims are: i) comprehensively characterize of the pain-like behavioral changes in the FM mouse model, ii) examine the activation of glia cells or elevation of glia-associated factors in the CNS of the FM mice, and iii) investigate peripheral neuroinflammation in the mouse model. My Ph.D. project will entail these 3 parts to contribute to a vastly unknown causality in FM and thereby contribute to a highly relevant and clinically significant issue involving approximately 1 in 50 people.

Exploring novel macrophage-associated mechanisms in autoantibody-induced pain

By Zerina Kurtovic

My name is Zerina Kurtovic and I have just started my PhD as a part of Kancera AB and the Molecular pain group at Karolinska Institute. During the various stages of my education, I have had the privilege to live and study in several countries which has enabled me to experience science in different academic environments. I was raised in Denmark and Bosnia & Herzegovina. Later, I went on to do my bachelor's degree in Molecular Biology and Genetics at the Istanbul Technical University and my master's degree at Ludwig Maximilian University in Munich. During this period, I gained insights into different research areas like aging studies, the cell biology around cytokinesis, immunology and neuroimmunology. I did my master thesis as a visiting student at the University of Cambridge, as a part of the Multiple sclerosis genetics group. My working environment consists of both academic and industrial researchers and is very varied, with a wide range of skills and backgrounds, which means I have the opportunity to learn something from everyone and hence grow as a scientist.

PROJECT SUMMARY

My specific project is focusing on studying pain mechanisms in animal models of rheumatoid arthritis and whether we can target these mechanisms with Kancera's KAND567 molecule. Our preliminary data suggests that, when injected into mice, collagen specific patient-derived autoantibodies (CAIA model) as well as recombinant monoclonal antibodies against citrullinated proteins (ACPA) alter macrophage related parameters. I will, therefore, within the scope of project 5 do an in-depth characterization on how mACPA and CAIA alter macrophage phenotype, number and activity. Furthermore, I will explore the roles of circulating versus dorsal root ganglion resident macrophages in ACPA and CAIA-induced pain-like behavior. Finally, it will be my aim to investigate if targeting macrophages with Kancera's CX3R1 antagonist, KAND567, has analgesic effects on mice injected with the autoantibodies. The outcomes of this project are of relevance to many individuals who suffer from pain prior to the development of RA and often also after the inflammation is controlled. It is becoming increasingly clear that there is a link between autoantibodies and pain that is independent of clinical joint inflammation. The proposed studies will reveal how a subset of RA autoantibodies and immune cells contribute to pain in the absence of overt joint inflammation.

The project is supervised by Professor Camilla Svensson and co-supervised by Dr. Sally Abdelmoaty and Dr. Harald Lund as a part of the TOBeATPAIN grant. Secondments are planned at the University of Jena with Professor Hans-Georg Schaible and the University of Innsbruck with Professor Michaela

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Neuroinflammation and pain in a mouse model for Fabry disease

By Jeiny Luna-Choconta

I come from Sogamoso "city of the sun" in Colombian Andes. I studied a bachelor's degree in Biology in the Universidad Nacional de Colombia; however, my bachelor thesis took place in Clinical Parasitology Lab at the Universidad Nacional del Sur, Bahia Blanca, Argentina. Afterward, I completed a master's degree in Neuroscience at Universidad Miguel Hernandez and I had the opportunity to begin research on the interaction of brain-resident macrophages under neuroinflammatory conditions in Cellular plasticity and Neuropathology Lab at Instituto de Neurociencias, Alicante, Spain.

In my opinion, get involved in the TOBeATPAIN research training program, strengthen both scientific and communication skills. This offers a great network within universities, institutes, companies, organizations, and early-stage researchers. All together working around neuroinflammation research and pathological pain therapy.

PROJECT SUMMARY

Fabry disease (FD) is an X-linked lysosomal storage disorder due to deficiency of the enzyme α-galactosidase A (αGal), which leads to accumulation of neutral glycosphingolipids, mainly globotriaosylceramide (Gb3) and an early life neuropathic pain phenotype. The main objective is to investigate the effect of macrophage infiltration dorsal root ganglion and spinal cord, and microglia activity in spinal cord and brain on nociception in a mouse model of Fabry disease to elucidate novel mechanisms of neuro-immune communication with special emphasis on cytokines and microRNAs. Previously, has been observed significant deficits in neuronal function in a mouse model of Fabry disease, we predict alterations in nociceptive processing in the CNS are related to neuro-immune deficits. Detailed aims:

1. Assess macrophage infiltration and microglia activity in dorsal root ganglia (DRG), spinal cord and brain (IHC) in a mouse model of FD.
2. Explore cytokine mRNA and microRNA expression profiles and perform associated target gene analysis (qPCR) in DRG, peripheral nerve, spinal cord and brain.
3. Identify mechanistic pathways through a bioinformatics approach.
4. Validate specific FD related new targets as well as cytokines and microRNAs in vivo (behaviour using pharmacological blockers/activators followed by expression analysis).

The host institution for this project is in the Institut. für Physiologie und Medizinische Physik at the Medizinische Universität Innsbruck and the planned secondment is Eli Lilly. Under the supervision of Prof. Michaela Kress and co-supervision of Dr. Michiel Langeslag and Prof. Ray Chaudhuri.

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Mechanisms of spinal neuroinflammation and hyperexcitability in models of joint inflammation

By Anutosh Roy

I am originally from Kolkata, India. I was graduated in Zoology with Honours from the University of Calcutta, later I obtained my MSc degree in Molecular & Human Genetics from Jiwaji University, Gwalior. My masters' thesis was about the expression of suicidal biomarkers in major depressive disorder. Later I attended Summer School of Molecular Medicine in Jena, Germany and also received prestigious travel award from DAAD, Germany for the same. TOBeATPAIN innovative training network provides me a good oppurtunity to learn from specialists in the field, and the possibility to work in both basic research and advanced clinical research combined together with University Hospital Jena, Germany and Eli Lilly Pharmaceuticals, United Kingdom and other collaborators in this network.

PROJECT SUMMARY

Spinal hyperexcitability is a hallmark of many chronic pain states including joint inflammation. Communication between glial cells, immune mediators and neurons plays an important role in generation and maintenance of spinal hyperexcitability. Despite of significant interactions between different cell types in the spinal cord, the underlying mechanisms are poorly understood. Our primary query is to understand the role of IL-6 trans signaling in spinal pain mechanism. We have evidence from research articles that some EGF blockers play an important role to reduce the inflammatory response in cancer by blocking the effect of IL-6 trans signalling, but there is no evidence whether EGF blockers will also reduce the effects of IL-6 trans signaling in the spinal cord. To achieve the primary target I am using our labs' state of the art In Vivo Electrophysiology technique combined with Molecular Techniques. Later on, during my proposed secondment at Eli Lilly, UK, it is planned to explore our further findings with the help of Multiple Electrode Assay. To be specific, to achieve the goal, we will assess spinal hyperexcitibility in normal rats and rats with inflamed knee joint. After having explored the role of IL-6 signalling and EGF, we will investigate the role of other cytokines which might be involved in spinal hyperexcitability.

Supervisor: Prof. Hans Georg Schaible (UKJ)

Co-supervisor: Dr. Andrea Ebersberger (UKJ)

Planned Secondments: Eli Lilly, United Kingdom under supervision of Dr. Emanuele Sher

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Impact of neuroinflammation and neurodegeneration on brain and spinal cord homeostasis: relevance to nociception

By Fátima Gimeno-Ferrer

My name is Fátima Gimeno-Ferrer and I am originally from Valencia (Spain). I was graduated in Biochemistry and Biomedical Sciences from the University of Valencia (UVEG) and then I obtained my MSc in Research in Molecular, Cellular and Genetics Biology in the UVEG as well. Also, I did a postgraduate in Medical Genetics in the same university. During my studies in Valencia I took part in different internships in some research fields such as biomaterials, spinal cord injury (curricular internship to get the BSc), molecular biology and biochemistry of plants (Master´s thesis project), animal models for skin diseases and genetics of obesity. Part of this work has been published from 2017 and on.

This extensive and multidisciplinary formation allowed me to have a wide perspective of science to face scientific questions as well as to take part in TOBeATPAIN at Universitätsklinikum Jena (UKJ) in a project involving different techniques: in vivo and in vitro electrophysiology, histology and the use of different animal models of neuroinflammation and neurodegeneration.

PROJECT SUMMARY

Homeostasis is a key element in the physiology of brain and spinal cord for a normal neuronal function. This refers to the control of changes in extracellular fluid volume, ion concentrations and pH, perfusion and vascular permeability, turnover of transmitters/mediators and energy supply. Some possible changes regarding homeostatic parameters can be measured by using ion selective microelectrodes, such as K+ sensitive electrodes or electrodes to measure the extracellular volume. It has been proposed the normal functioning of the brain depends on different players: microglia, neurons, astrocytes and extracellular volume. The associated changes in homeostasis they make in the brain can be measured using different techniques. In our project, we will use an electrophysiological phenomenon of a stable homeostasis in the brain, the so-called Cortical Spreading Depolarization (CSD). CSD is defined as "*A wave of depression in spontaneous activity of the electrocorticogram that propagates through continuous cerebral gray matter at a typical velocity of 2-5 mm/min*". So, the main aim of the Project 8 entitled "Impact of neuroinflammation and neurodegeneration on brain and spinal cord homeostasis: relevance to nociception" is to characterize the homeostatic changes using CSD and regional Cerebral Blood Flow (rCBF) recordings in a model of neuroinflammation (CGRP treatment as neuroinflammatory driver) and in a model of neurodegeneration (Alzheimer's disease model). As more elaborated aims, we will characterize in both models (1) Extracellular volume, ion concentrations and diffusion of mediators in brain and spinal cord in electrophysiological studies in vivo; (2) Assess the effect of CGRP in neuronal activity in brain slices; (3) Histological comparison of controls and models in neuroinflammatory parameters.

This project takes place in the Institut für Physiologie I/Neurophysiologie of the Universitätsklinikum Jena (Germany) and is supervised by Prof. Frank Richter as part of the TOBeATPAIN network. Part of this project will be performed in Medizinischer Universität Innsbruck (Division of Physiology, DP), KI, Karolinska Institutet (Department of Physiology & Pharmacology) and the Company Mabtech.

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Neuroinflammation in pain and nerve degeneration and regeneration in peripheral neuropathies

By Patricia García Fernández

In February, 2019, I came from Spain to become one of the early stage researchers of the TOBeATPAIN Project, hosted by the Universitäts Klinikum Würzburg (Germany). Previously I studied a Bachelor degree in Biotechnology, with clinical specialization, in the Technical University of Madrid. After this period I studied a two years master program in Molecular and Cellular Integrative Biology taken place in the Biological Research Centre (Spanish Research Council) with the collaboration of the Menéndez-Pelayo University.

For four years, during my Bachelor internship and Thesis, and my master Thesis, I worked in the 3D LAB research group: Development, Differentiation and Degeneration of Dr. Flora de Pablo and Dr. Enrique de la Rosa. In this period I studied the implication of the immune system in the retinal degeneration and developed new therapies to preserve the retinal structure and function and delay the degeneration. This was a very rewarding experience, in which I not only learned to carry out a research Project but I also found my passion. I discovered that the immune system was incredibly involved in neuropathologies and it is one of the main promotors of the neural degeneration. It is still a very unkown topic with high future perspectives as the perfect common therapy to treat neurological diseases and I am very grateful to contribute into its development.

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PROJECT SUMMARY

The balance of pro- and anti-inflammatory mediators after nerve injury and in polyneuropathies not only determines painfulness of the disease, but also modulates nerve degeneration and regeneration. This project will evaluate the profiles of pro- and anti-inflammatory cytokine and chemokine expression and secretion in peripheral blood leukocytes, cerebrospinal fluid (CSF) and CSF lymphocytes, macrophages and Schwann cells isolated from patients' nerve biopsies.

Objectives:

1. Prospectively characterize patients with neuropathies for their pain phenotypes;
2. Isolate white blood cells and measure cyto(chemo)kine expression and secretion upon stimulation (ELISA), analyse CSF cyto(chemo)kine expression and production (ELISA), perform laser capture microdissection on nerve biopsies for single cell PCR, and establish Schwann cell culture from nerve biopsies for stimulation studies;
3. Repeat these analyses after standard anti-inflammatory and analgesic therapy, and follow-up patient pain and functional outcome; and 4) examine the effect of selected CSF cytokines on spinal cord neurons excitability (in vivo electrophysiology in mouse).

Assessment of medical marijuana bioactive substances in a mouse model of neuropathic pain

By Cristiana Dumbrăveanu

Originally from Romania, I am one of the early stage researchers of the TOBeATPAIN project, hosted by Bionorica research GmbH (Innsbruck). I graduated from Alexandru Ioan Cuza University of Iaşi with a bachelor's degree in Biology and a master's degree in Microbial and cellular biotechnologies. During my studies I took advantage of the opportunities that the university offers, and I completed a practical traineeship at Konstanz University, Germany and a semester of study and research at Clarkson University, New York. The time spent at Clarkson University, in Proteomics and Biochemistry lab was truly valuable for me due to the chance to get involved in one of the projects which aimed to identify a protein biomarker from rat brain after inducing Obstructive sleep apnea.

TOBeATPAIN project gather academic and industry professionals and not at least, early stage researchers that share a common goal: novelty and development in the field of pain research. Being part of the consortium, I consider myself a fortunate and I am looking forward to bring together our results and communicate them with the large public.

PROJECT SUMMARY

Although pharmacological targeting of peripherally expressed cannabinoid CB1 receptors has pronounced analgesic effects and CB2 receptor activation suppresses neuroinflammation in the CNS, the use of medical marijuana is still limited mainly because, apart from tetrahydrocannabinol (THC) and cannabidiol (CBD), its active components have not been studied in sufficient detail. In this projects I am focused to:

1. Characterise the analgesic action of medical marijuana preparations with and without THC and CBD in the spared nerve injured (SNI) mouse model for neuropathic pain.
2. Isolate blood, DRG, peripheral nerve, spinal cord and brain of medical marijuana treated versus non-treated neuropathic mice, measure cytokine profiles in these tissues (ELISA) and perform microglia and macrophage analysis in DRG, spinal cord and brain sections (IHC and FACS).
3. Assess the bioavailability of medical marijuana bioactive substances (LS-MS) in the aforementioned tissues and correlate it with analgesic and anti-inflammatory effects.

Supervisor: Dipl.-Ing. A. Neumann, (Bionorica research GmbH), co-supervisor: Prof. M. Kress (Medical University of Innsbruck). The secondment will take place at Karolinska Institute, Stockholm, in the lab of Prof. C. Svensson.

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Neuroinflammation and CNS hyper-excitability in chronic pain and neurodegeneration mice models

By Rita Silva

Originally from Vizela, the youngest city in the north of Portugal, I spent my academic years studying Biochemistry and Neurobiology where the Douro river meets the ocean, the beautiful city of Porto. I wanted to be a doctor when I was a kid but definitely ended up forgetting that idea when I joined the fire station and decided to be a paramedic. Being a paramedic made me grow. But also made me ask why a thousand times and made me look for an answer. I remember all the years in which more than 50% of the cases I worked with were related to pain, stroke and neuropsychiatric disorders. We do have a lot of cardiac and respiratory calls but, at the end, are the ones involving the nervous system, the ones we can't deal with, the ones you end up asking more questions. That's when my little romance with Neuroscience started. Sooner I saw myself doing internships and, inclusive, my thesis in the pain field. I decided to apply for a PhD position within the TOBeATPAIN European Network as it is an unique opportunity to continue the mission I started a few years ago. It's not only a great programme, engaging well-known professors and institutions, but also great for us, young researchers, to develop our skills and be a better version of ourselves every day. It is also about sharing science together and getting the best out of it.

PROJECT SUMMARY

Alzheimer's disease (AD) and chronic pain are amongst the biggest co-morbidities needed to be addressed in the growing ageing population. Neuroinflammation plays a significant, and possibly differential role in the sensory versus cognitive components of chronic pain under neurodegenerative conditions. To understand how neuronal function is altered under inflammatory conditions and to determine if pain is present in tau pathology animal models, we aim to answer:

1. Which are the acute and long-term effects of neuroinflammatory mediators on neuronal excitability and synaptic plasticity in the hippocampus and spinal cord?
2. If tau is present and glia is activated in areas involved in pain processing, is pain perception altered?

Expected results: Identification of CNS cytokines and neurotrophins associated with AD and pain in mice and their potential effect on neuronal excitability and synaptic plasticity in the spinal cord.

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Events

Upcoming

Febuary 2020: Hosts Medizinische Universitat Innsbruck, Austria. Scientific Workshop - Mass spectrometry analysis - and Transferable Skills – Leadership and Research Governance

September 2020: Hosts Kancera AB and Karolinska Institutet. Scientific Workshop - Pharmacokinetics and multi-cytokine quantification - and Transferable Skills – Society Innovation and patenting

January 2021: Hosts Medizinische Universitat Innsbruck, Austria. Winter School and Transferable Skills – Business Entrepreneurship and Innovation

July 2021: Hosts King's College London, England. Scientific Workshop - Genomics and bioinformatics - and Transferable Skills – Science, Media and Communication

January 2022: Hosts Universitat Klinikum Jena, Germany Project Conference and Transferable Skills – Grant Proposal Writing

July 2022: Hosts King's College London and Eli Lilly, Ascot, England. Project AGM

Previous events

May 2019: Hosts King´s College London, England. Scientific Workshop - Experimental Design and Practical Data Analysis in Positron Emission Tomography (PET) - and Transferable Skills - Knowledge communication: Public engagement, fundraising and CSR

July 2019: Hosts Universitätsklinikum Würzburg, Germany. Annual Meeting and Transferable Skills –IP and commercial exploitation

Other events

98th German Physiological Society, Ulm (Germany) (30th September to 2nd October 2019)

European Researchers Night (27th September 2019)

Pain in Europe XI – The 11th Congress of the European Pain Federation (EFIC) Valencia (Spain) (4th-7th September 2019)

World Parkinson's Day, King's College London Parkinson's Centre of Excellence (12th April 2019)

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie Grant Agreement No 764860.