Neuropathic pain is a chronic pain condition, which develop when the nerves involved in the mechanical stimulation (e.g., touch) and those that conduct information about pain and temperature, become injured in consequence of shingles, diabetes, trauma, injury, amputation, autoimmune inflammation or cancer. This pathology is a global health problem that afflicts a significant number of patients, resulting in personal suffering, reduced productivity, and substantially increased healthcare costs. European governments spend an estimated €300 billion /year for the treatment of chronic neuropathic pain. Unfortunately, only a minority of patients have an adequate analgesic response to pharmacological treatment and most drugs have dose-limiting harmful side effects. Chronicity of symptoms and the modest efficacy of available treatments make neuropathic pain a burning problem for the worldwide healthcare and represent a significant medical need. Chronic pain has bio-psycho-social implications, affecting relationships, capacity for work, mood and quality of life. Patients suffering from chronic pain conditions are at high risk of emotional and cognitive disturbances, manifested by mood swings and anxiety, impaired memory and attention. Similar physiological mechanisms may be responsible for the negative effects of chronic pain on memory function. Although most doctors deal with patients suffering from chronic pain and concomitantly complaining of problems with memory and concentration, there is very little research into the relationship between pain and memory.

The plant *Cannabis sativa* (cannabis) contains more than 100 chemical compounds, known as cannabinoids. Given the fact that the cannabinoid system modulates neuronal and immune cell function, both of which play key roles in pain, therapeutics targeting this system holds promise as novel analgesics. Among the many cannabinoids, CBD (cannabidiol) is a compound that lack psychostimulant and addictive properties, thus representing an interesting pharmacological compound to be further investigated as potential medicinal agent for pain and psychiatric disorders. Due to its complex pharmacological profile, the precise CBD's mode of action on different targets in the body remains vague. Based on our recently created analysis of CBD pharmacology, we hypothesize that CBD's mechanisms of action are far more complex than previously thought and involve a network of proteins concomitantly involved in the neuropathic pain and cognitive functions, providing original insights into its therapeutic role.

The presented project will elucidate the insights on chronic CBD's antiallodynic, 1recognitive and anxiolytic mechanisms of action in a rat model of neuropathic pain in order to support the initiation of clinical trials testing the efficacy of CBD-based compounds for treating neuropathic pain and comorbid memory and mood disorders. While no causal proof yet exists for CBD's effects at specific molecular targets in pain and cognition, once discovered (thanks to proposed advanced bioinformatic analysis) they may represent the most probable aim for chronic pain and the comorbid cognitive impairment. Therefore, with the use of comprehensive approach, using *in vivo* research, bioinformatics tools, spatial transcriptomics, a novel in situ hybridization: RNAscore and finally molecular targets validation (both *in vivo* and using gene-editing tool, CRISPR / Cas9), we will be able to perform an innovative study on CBD's therapeutic mechanism of action. We believe that our cutting-edge research will allow us to obtain substantial results and this knowledge will be translated into clinically useful applications.