Project title: The mechanisms of chronic post-surgical pain: how psychological and genetic vulnerabilities interact to hijack the system

P**roject leader**: Professor Dr. Madelon Peters

Function: Full professor

Collaborators: Professor Dr. Bert Joosten

Proposal (250 words):

Introduction: Chronic post-surgical pain (CPSP) is a highly unwanted outcome after surgery. Depending on type of surgery, 5-30% of patients experience pain that persist for months or years after the intervention. Several risk factors have been identified, among which psychological factors such as anxiety and pain catastrophizing. Also genetic vulnerability may play a role, and several polymorphisms are implicated. So far the research on genetic versus psychological vulnerability for CPSP has developed relatively independent. However, probably CPSP is multifactorially determined. Genetic vulnerability may not automatically lead to chronic pain, but only in combination with an added psychological vulnerability. The present project seeks to find evidence that the risk of developing CPSP is dependent on the interaction between psychological and genetic vulnerabilities. Epigenetics (i.e. gene-expression) could play a mediating role. **Hypothesis and Objectives**: - Patients having a pain-sensitive polymorphism AND a vulnerable psychological profile (high anxiety and pain catastrophizing) report higher levels of acute post-surgical pain and have an elevated risk of chronic post-surgical pain. - Chronic-post surgical pain is associated with epigenetic changes after surgery. - These epigenetic changes are related to pre-surgical psychological traits. **Setting and Methods**: In an existing cohort of >400 patients psychological traits have been assessed before surgery, and blood samples for (epi)genetic analyses have been collected pre- and post-surgery. Patients were followed up for one year to assess pain levels. In addition to this existing cohort a new surgical study is planned. **Impact**: Identifying risk factors for the development of CPSP may enable preventive strategies.

Requirements candidate: Highly motivated student with good English communication skills and proactive and resolute attitude. Preferably the student has a background in biological psychology. Interest in genetics is essential, and the candidate should be willing to gain expertise in epigenetics.

Keywords: Chronic post-surgical pain, genetic vulnerability, psychological vulnerability, epigenetics

Top 5 selected publications:

1. Stessel, B, Fiddelers, A.A, Marcus M.A., van Kuijk, S.M., **Joosten, E.A., Peters, M.L**., Buhre, W.F., Gramke, H.F. (2017). External Validation and Modification of a Predictive Model for Acute Postsurgical Pain at Home After Day Surgery. Clinical Journal of Pain;33:405–413
2. Theunissen, M., **Peters, M.L.,** Schepers, J., Maas, J.W.M., Tournois, F., van Suijlekom, H.A., Gramke, H.F., Marcus, M.A.E. (2016). Recovery 3 and 12 months after hysterectomy: epidemiology and predictors of chronic pain, physical functioning and global surgical recovery, Medicine, 95: 26 (e3980)
3. Hoofwijk DM, van Reij RR, Rutten BP, Kenis G, Buhre WF, **Joosten EA**. Genetic polymorphisms and their association with the prevalence and severity of chronic postsurgical pain: a systematic review. British journal of anaesthesia 2016;117(6):708-719.
4. Hoofwijk, D.M.N., Fiddelers, A.A.A., **Peters, M.L.,** Stessel, B. Kessels, A.G.H., **Joosten, E.A**., Gramke, H.F., Marcus, M.A.E. (2015). Prevalence and predictive factors of chronic postsurgical pain and poor global recovery one year after outpatient surgery. Clinical Journal of Pain, 31, 1017-1025,
5. Theunissen, H.M., **Peters, M.L.**, Bruce, J. Gramke, H.F., Marcus, M.A. (2012). Preoperative anxiety and catastrophizing: a systematic review and meta-analysis of the association with chronic postsurgical pain. *Clinical Journal of Pain,* 28, 819-841.