MULTIDISCIPLINARY APPROACH TO THE STUDY OF UROLOGIC CHRONIC PELVIC PAIN (MAPP) RESEARCH NETWORK

Discovery Site-Specific Study Protocol

IC/PBS Phenotypes in a Community Sample of Female Twins

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Collaborating Sites (if any): None

Abstract: In this comprehensive phenotyping study, we bring together our expertise in chronic pain syndromes , urological chronic pelvic pain syndromes (UCCPS), and twin studies to fully explore UCPPS phenotypes and possible risk factors in a unique sample of community-based twins. A co-twin control study, with pairs who are discordant for interstitial cystitis/painful bladder syndrome (IC/PBS), is a powerful research design to identify and characterize pathological and physiological associations with IC/PBS and the relationship between UCPPS and related chronic pain syndromes (RCPS). Additionally, a co-twin control study with monozygotic (MZ) and dizygotic (DZ) IC/PBS-discordant pairs as well as pairs free from IC/PBS, will allow us to assess the relative contributions of genetics and environment to these conditions, RCPS, and other illness characteristics. In this project, we will compare MZ and DZ female twin pairs in which one member has IC/PBS and the other is pain-free (IC/PBS-discordant). This co-twin control design will allow us to assess many key characteristics of IC/PBS while controlling for genetic variability and common familial

exposures and experiences. We will augment this co-twin control design to include pain-free control twin pairs, allowing us to better understand the influence of genetics and environment on the relationship between IC/PBS and its illness characteristics.

Rationale for Site-Specific Study: Access to the twin population is unique to the University of Washington Twin Registry.

Study Hypotheses:

1.) In comparison with their pain-free control twins, twins with current symptoms of IC are more likely to report symptoms of related chronic pain syndroms (RCPS), to have increased symptoms of depression, anxiety, and PTSD, and poorer psychosocial and functional status;

2.) Consistent with previous findings in RCPS, familial influences (i.e. genetic and common environmental factors) play a role in the associations of IC;

3.) In comparison with their pain-free co-twins, twins with current IC symptoms will exhibit greater pain sensitivity and markers of central sensitization on multiple evoked pain tests, perturbations in salivary cortisol values, and differential brain activation changes in functional MRI;

4.) Familial influences (i.e. genetic and common environmental factors) play a role in the association between IC symptoms and neurobiological illness characteristics.

Specific Aims:

1.) Assess within-pair differences in demographic characteristics, symptoms, clinical features, psychiatric symptoms, and psychosocial and functional status in female MZ and DZ IC-discordant twins;

2.) Assess between-pair effects to examine the genetic and common environmental contributions to the association between IC-discordant MZ twin pairs with IC-discordant DZ and female control pairs;

3.) Examine within-pair differences in physical and uroneurological findings, pain sensitivity and indicators of central sensitization, neuroendocrine function, and neuroimaging findings in a selected sample of female MZ and DZ twins with IC symptoms and their pain-free control twins;

4.) Ascertain between-pair effects to examine the genetic and common environmental contributions to the association between IC and neurobiological characteristics, by comparing female IC-discordant MZ twin pairs with IC-discordant DZ and female control pairs.

Proposed Patient Cohort to be Studied (and any Control or Comparator Groups): 30 pairs of IC/PBS-discordant female twins and 10 healthy-healthy pairs.

Proposed Tissues/Specimens to be Studied and their Source: As per Trans-MAPP biomarker protocols.

Statistical Analysis Plan and Sample Size Estimates: Univariate and bivariate genetic modeling and mixed-effects random regression modeling of 40 twin pairs (15 each MZ and DZ IC/PBS-discordant and 10 healthy-healthy pairs).

Anticipated Burden to Sites: None.

Anticipated Risks to Participants: We will use phenotyping, sample collection, and neuroimaging protocols taken from or similar to the Trans-MAPP protocols in those areas. The risks will therefore be largely the same as for the Trans-MAPP efforts.