**eMERGE Network Proposal for Analysis**

Project/Manuscript Concept Sheet

|  |  |
| --- | --- |
| **Reference Number** | **NT263** |
| **Submission Date** | **11/27/2017** |
| **Project Title** | **Genetic risk for gout in patients with hyperuricemia** |
| **Tentative Lead Investigator (first author)** | R. Knevel |
| **Tentative Senior Author (last author)** | Beth Karlson, Daniel Solomon  |
| **All other authors**  | TBD |
| **Sites Involved** | We encourage sites to sign up. Sites joining this collaboration are expected to be able to deliver uric acid levels (+ date of lab result). |
| **Background / Significance** | Approximately 4% of adults in the US will develop an attack of gouty arthritis on some point in their lifetime. While hyperuricemia (HU) is present in virtually all patients with gouty arthritis, over 80% of patients with HU never develop gout.(1-3) The genetics of HU and the genetics of gout have each been thoroughly examined, but almost all of this work has used general population controls.(4) In contrast, the lack of studies of risk factors for gout among HU persons presents a major gap in knowledge that impacts clinical care but also is a fundamental deficit in understanding innate immunity; why does HU (and monosodium urate, MSU, crystals) trigger the inflammatory cascade in some individuals, in some situations, but not others?**Our aim is to identify genetic risk factors for gout among persons with hyperuricemia (HU)**This project will be part of a larger project that will aim to create a gout risk prediction score.. The eMERGE data will be used for the GWAS to identify genetic risk factors for gout among patients with HU. This work will likely provide a new understanding of the pathways between MSU crystals and innate immunity. |
| **Outline of Project** | 1. Data collection from participating site of eMERGE
2. Case and control assignment (HU/no HU, gout/no gout)
3. eMERGE imputed genetic data
4. GWAS analysis
5. Meta-analysis combining eMERGE data with results of previous GWASs
6. Development of clinical risk prediction score for gout
7. Manuscript
 |
| **Desired****Variables (essential for analysis****indicated by \*)** | eRC data: ICD9/ICD10, age, race, sex, BMI with datesdata from sites – uric acid with dates, meds with datesICD 9 / 10 code \*Age\*Race\*Sex\*BMI with dates at any date availableChange in BMIDiuretics with datesAspirin with datesSmoking status (ever/never) |
| **Planned Statistical Analyses** | GWAS, Logistic regression |
| **Ethical considerations** | The data will be a limited dataset. The extent of this study lies within the scope of eMERGE of studying genetic association of clinical phenotypes |
| **Target Journal** | TBD |
| **Milestones\*\*** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Months** | **1-6** | **6-12** | **12-18** | **18-24** | **18-24** |
| A. Data collection |   |  |  |  |  |
| B. Case control assignment |   |  |  |  |  |
| C. GWAS analysis |  |  |  |  |  |
| E. Meta-analysis  |  |  |  |  |  |
| F. Development of clinical risk score |  |  |   |  |  |
| H. Refine analysis and write manuscript  |  |  |  |  |  |

 |

**References**

1. Lin KC, Lin HY, Chou P. The interaction between uric acid level and other risk factors on the development of gout among asymptomatic hyperuricemic men in a prospective study. J Rheumatol 2000;27(6):1501-5.

2. Lin KC, Lin HY, Chou P. Community based epidemiological study on hyperuricemia and gout in Kin-Hu, Kinmen. J Rheumatol 2000;27(4):1045-50.

3. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum 2011;63(10):3136-41.

4. Köttgen A, Albrecht E, Teumer A. Genome-wide association analyses identify 18 new loci associated with serum urate concentrations. Nat Genet. 2013 Feb; 45(2): 145–154.