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| I. Project Title |
| **Fine mapping of MHC region in lung cancer prognosis**pCode: 202002111102-Christiani | **Date:****Feb 4, 2019** |
| **II. Project Group Investigators** |
| **Project leaders:** Mulong Du, David C. Christiani, Paul Brennan, James Mckay **Investigators:** ILCCO contributing study/ data PI’s; Aida Ferreiro-Iglesias |
| III. Background |
| Previously, Aida and colleagues investigated the genetic effects of major histocompatibility complex (MHC) on lung cancer risk (*Nat Commun. 2018 Sep 25;9(1):3927.*). Currently, some studies demonstrated that certain MHC alleles and polymorphisms could target particular tumor antigens, inform tumor-specific immune responses and develop immunotherapies, which potentially contributed to their effects on lung cancer survival (*Onco Targets Ther. 2019 Sep 5;12:7281-7288.; Clin Pharmacol Ther. 2014 Sep;96(3):360-369.*). However, due to the limited sample sizes, the effect sizes of MHC genetic variants on lung cancer survival were not robust. |
| IV. Specific Aims |
| To delicately and comprehensively evaluate the association of genetic variants in MHC region with lung cancer survival. |
| **V. Methods** |
| 1. Imputation of HLA system: use both Beagle (SNP2HLA package) and HIBAG to impute HLA alleles into the genotype data of lung cancer. Details in Aida’s paper (*Nat Commun. 2018 Sep 25;9(1):3927.*).
2. Association evaluation: use Cox regression analysis to assess the effect of HLA alleles on lung cancer survival.
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| **VI. Materials or variables needed from the study PIs** |
| 1. Demographic and clinical descriptions of study samples
2. Number of lung cancer cases (need the largest sample size in European).
3. Age, gender, race, smoking status (never/ever/current), package-year of smoking, histology (LUAD/LUSC/others), tumor stage (1/2/3/4), vital status (death/live) and follow-up time.
4. The genotyping data of lung cancer from 25 to 35 Kb at chr6 (NCBI build 37) (if possible, all imputed genotyping data using 1KG phase 3).
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| **VII. Time line** |
| Once we receive the datasets from PIs, we need 3 months to deal with association analysis, and extra 3 months to write the manuscript.  |
| **VIII. Other remarks** (e.g. publication plan, etc) |
| We will plan a rapid publication in the Spring of 2020. |