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| I. Project Title | |
| GWAS-based meta-analysis on variants in autophagy and ubiquitin proteasome pathways | **Date: April 21, 2023** |
| **II. Project Leaders (List Names and Institutes)** | **Primary Contact**  **Information** |
| Qingyi Wei, Hongliang Liu, David Christiani, Jennifer Anne Doherty, Chris Amos, | **Name: Qingyi Wei**  **Email:** [**Qingyi.wei@duke.edu**](mailto:Qingyi.wei@duke.edu)  **Tel: 919-660-0562** |
| III. Progress to date. *What has been done so far to move the project forward (data pooling, grant submission, etc), and when it was done* | |
| The study of of genetic variants in one sub-pathway (Cullin-RING ubiquitin ligases) of these proposed pathways had been done and published on Carcinogenesis (2017 May 1;38(5):541-551. 28383684).  We have collected the summary data of genetic variants in autophagy pathway from TRICL and got some preliminary results (2019 March). | |
| **IV. Project Status and Preliminary Results**. *S****ummarize the current status of the project. Report preliminary results if there is any*** | |
| We have analyzed the association of SNPs in genes involving authopahgy pathway with lung cancer risk using the TRICL summary data and found SNPs in *ATG12* passed multiple comparisons correction with FDR < 0.2. Further functional annotation revealed that one SNP rs26534 was correlated with the mRNA expression of *ATG12* significantly in normal lung tissues.  We are performing in-silico functional replication for these identified SNPs and related genes using other data source (e.g, GTEx and TCGA).  We will investigate the associations of genetic variants in these two pathways with lung cancer risk by using the OncoArray data of lung cancer, and explore the racial disparisity of the identified associaitons. | |
| **V. Justification of Extension** | |
| In this project, we have proposed to investigate the association of SNPs in mulitiple pathways and lung cancer risk. One of our study (about Cullin-RING ubiquitin ligases gene-set) using the TRICL summary data has been done and published. Another study of the genetic variants of autophagy genes is ongoing. Now we are also interested in exploring the racial disparisity of the identified associaitons. We have gotten some prelimitary results and would like to get a extension of this project. | |
| **VI. Future Plans & Timeline** | |
| 1. Summarize the TRICL and Oncoarray results of autophagy genes: 3 months 2. In-silico functional annotation: 2 months 3. Draft manuscript and circulate to participation ILCCO-INTEGRAL groups:  3 months 4. Submission for publication. | |