**NCCRAHS 2019 Application: Pre-Proposal**

Project Theme/preliminary title

Epigenetic deconvolution to immune system and environment exposures for Amish Asthma Child

Project “fit” within larger research program (if applicable)

Burden (evidence of the problem)

2016 Dr. Stein and colleagues provided the evidence that Amish child have 4-6 times lower prevalence of Asthma which was caused by the response to farming environment from the innate immune. Dr. Johnson provided evidence that DNA methylation in lung cells is associated with asthma endotypes and genetic risk and DNA methylation have been demonstrated to play significant role in cell plasticity, immune differentiation and response to environment exposure. We are intent to investigate the genome-wide methylation profiles for the Amish child individuals and to explore the roles of DNA methylation on the interaction between human immune systems and specific farming environment exposures. We will identify the methylation changes responding to different environment exposure, deconvolution of the methylation change to different immune system and cells (innate immune system/cells or adaptive immune system /cells). Meanwhile differential methylation genes/regions (DMR) will provide the drug target and Asthma subtype classification in precision medicine.

Need (gap the proposed project fills; relates to stakeholder needs)

1. Amish child enrollment for the peripheral blood mononuclear cell (PBMC) methylation profile.
2. PBMC methylation profile by Human Methylation 450K BeadChip
3. Environment exposure indicator/responser profile detection in the blood
4. Epigenome-wide association analysis based on Marshfield Clinic High Performance Computer.
5. Paper publishing fee for the EWAS (Asthma) and EWAS (environment exposures)

Potential Impact of this project (intermediate outcomes of new knowledge, guidance, technology, etc.)

1. Improve the understanding to the mechanism to the protective roles of human epigenetics derived by farming environment on child Asthma susceptibility.
2. Provide the epigenomic landscape of Amish child living in farming environment
3. Provide risk prediction models for normal individual based on DMR identified above.
4. Identify potential epigenetic drug target for Asthma patients.
5. Provide epigenomic map for different environment exposures.

Methodology/Approaches (over 5-years)

1. Genome-wide DNA methylation landscape based on [Infinium Human Methylation 450K BeadChip](https://support.illumina.com/array/array_kits/infinium_humanmethylation450_beadchip_kit.html)
2. Epigenome-wide association study (EWAS) to identify Asthma specific methylation signals.
3. Deconvolution analysis to Asthma specific abnormal methylation to human immune system, human immune cells to evaluate the corresponding contributions.
4. Epigenome-wide association study (EWAS ) to identify environment exposures related DNA methylation signals.

Relationship with other NCCRAHS projects/resources or other NIOSH Ag Center projects

Project Leader (P.I.)

Shicheng Guo

Collaborators, staff, consultants (preliminary)

Steven Schrod and other TBD member.