

Report 73: Genome/Environment Interactions

Convener: Richard Mural

Brief History: The genome is shaped over evolutionary time by the environment and an organism's genome determines how it interacts with the environment. The interaction of the genome and the environment leads to the observed phenotype. Since the completion of the human genome 10 years ago the cost of whole genome sequencing (WGS) has dropped to the point that it is now, or soon will be, possible to use WGS as a method for discovery of genetic variants that are associated with phenotypes of interest to NIEHS. It is also possible to generate very complete data such as complete genetic variation within and between populations, the intergenerational mutation rate, estimation of the selective pressure on various alleles, etc. The use of WGS and the use of data generated by WGS that illuminates basic human biology should be a central focus of the NIEHS five year plan.

Discussion Highlights: A number of interesting point were discussed:

WGS shows promise in extending and expanding the results of Genome Wide Association Studies (GWAS) which have often been disappointing to those studying the genetics of responses to environmental factors.

GWAS often lack data on environmental exposures of the study populations.

Family studies using WGS to study effects of environmental exposures may be powerful and useful.

In addition to powerful new tools for WGS or resources such as the mouse diversity plan and the mouse strains generated by the Collaborative Cross will provide substrates for proof of principle studies for populations based studies of the effects of various environmental exposures.

Recommendations:

NIEHS should leverage data from WGS studies that give new insights into human variation, population structure and critical parameters of human biology such as intergenerational mutation rates in the design of future studies.

NIEHS should support the use of WGS methodologies to discovery human variation associated with response to environmental exposures.

NIEHS should support the use of WGS for family studies to understand the genetics of response to environmental exposures.

In addition to using various WGS technologies, NIEHS should leverage new mouse resources like the diversity panel and Collaborative Cross as models for studies of the role of variation in human population responses to environmental exposures.

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