

**Report 65:** Early life exposures in childhood and adult disease: role of susceptibility factors

**Convener:** Bill Suk and Steve Kleeberger

**Brief History:** From a mechanistic standpoint, evidence suggests that exposures to environmental agents during early life have adverse impacts on childhood and adult disease, as well as susceptibility to additional exposures. In addition, disease prevalence data indicate a dramatic increase in complex/chronic diseases, which may be the result of exposures to environmental agents in early life. These observations have led to questions regarding mechanisms of susceptibility and/or predisposition to this important disease etiology.

**Discussion Highlights:**

Parallels were drawn between challenges and opportunities in the role of epigenetics and genetics in this environmental disease process.

Exposure assessment is critical

- Need for incorporating exposure in GWA studies

- Need to build upon NIEHS GEI/Exposure biology investment

  - Which environmental exposures are important to measure (e.g. particulates, metals, infectious agents, endotoxin, etc.)

Biomarkers of exposure, development, and link of these exposure development markers to adverse outcome(s).

Primary outcomes that were discussed included complex diseases such as cancer, diabetes, asthma, autism, and neurodevelopmental/neurocognitive deficits. A secondary outcome that was discussed was growth stunting.

Interaction of early life exposures and childhood and adult disease is a global health concern.

Consideration of microbiota and microbiome signatures as important factors in disease susceptibility and progression.

There is a necessity to put in place as soon as possible mechanisms to intervene and/or prevent early life exposures to environmental agents. This could include putting in place interdisciplinary centers for research and prevention/intervention in maternal and child health.

Importance was stressed on the development of animal models to identify genetic and other mechanisms of susceptibility to tease out windows of opportunity to link exposures to adverse outcome.

Discussion regarding early life exposures and latency of disease onset (i.e. short- and long-term) and the ability to study and model/understand the link between exposure and disease: in addition to being an exposure and disease interaction, there is also an important temporal component.

**Recommendations:**

Need to identify and develop state-of-the-art methods and capabilities in analytic chemistry for measurement of 1) biomarkers of response and exposures, and 2) various environmental agents in the individual.

Develop interdisciplinary models for research, i.e. development of research programs to address this complex and important susceptibility by environment interaction in the development of disease.

Need to develop tools to understand the interaction between susceptibility factors, exposure modalities, disease outcomes, and time to disease onset.

Exposures should be inclusive to incorporate environmental chemicals, infectious/parasitic agents, and other biologics during early exposures. These are global health concerns and must be addressed within that context.

Develop a large prospective study to investigate early environmental exposures and multiple primary and secondary outcomes. This study should leverage resources from partner ICs. There was also identified a need for biobanking, miniaturization of samples, and bioinformatics expertise.

**Need to**

**Discussion Participants:**

Dawson

Edwards

Fargo

Finnell

Gilliland

Groopman

Hennig

Kiley

Kleeberger

Suk

Taylor, J

Taylor, P

Umbach

Waalkes

Wright