

Report 17: Regenerative Approaches to Correcting Complex Structural Birth Defects

Convener: Richard H. Finnell

Brief History: Despite advances in environmental health sciences that include the recognition that maternal folate supplementation reduces the risks for some structural birth defects (neural tube, craniofacial and conotruncal heart defects and others), the prevalence of complex congenital abnormalities as a whole has not been substantially reduced over the last 100 years. As prevention remains imperfect, it is of potential interest to expand our focus and consider newly initiated efforts to correct-either *in utero* or post-parturition-infants born with structural abnormalities.

Discussion Highlights:

- Concept of environmentally-induced birth defects (structural) has been largely replaced with an emphasis on the developmental origin of adult diseases. For the sake of ‘teratologists’/‘reproductive toxicologists’, it is important to expand the definition of ‘birth defects’ to encompass environmentally induced changes during development that potentially impact the life of the conceptus.
- As our knowledge base of the genomes of humans as well as model organisms has increased dramatically, the identification of developmental pathways have enlightened our understanding of many structural birth defects, most notably those of the neurocristopathies. It should be possible to use this emerging information to develop pre-conceptual, *in utero*, post-parturition approaches to correct developmental defects.
- Understanding developmental pathways that are critical to embryogenesis (e.g., notch, Shh, Wnt, etc.) can inform us about adult diseases.
- Are there environmental factors/stimulants that could promote *in utero* healing?
- Does *in utero* surgery to correct structural malformations such as spina bifida actually alter epigenetic markings that might have serious, adverse consequences in later life?

Recommendations:

- Need something like the Northern European model of large mother-child cohorts to study the effects of environmental exposures on birth outcomes, as well as the diseases of childhood and beyond. The newly initiated Children’s Health Study goes towards meeting this need, but it needs to be larger.
- Regeneration recapitulates development. Need to learn the underlying basis/mechanisms that promote regeneration to ‘heal’ developmental defects, both structural and neurobehavioral. Thus it is critical to learn more about the environmental factors that impact developmental processes.

- Promote the use of model organisms with which to identify stemness factors or appropriate developmental pathways to target in efforts to promote regeneration and correcting of both structural and neurodevelopmental abnormalities.

Discussion Participants:

- Antonio Planchart
- Karin Russ
- Clarice Weinberg
- William Slikker