

Report 70: The role(s) of ncRNAs in environmental health

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Brief History: A number of functional roles in cell biology are emerging for classes of RNA transcripts that are not translated. These non-coding RNAs (ncRNAs) appear to contain a hidden level of internal signals that: control gene expression in development and help determine cell/tissue specificity; are involved in maintenance and establishing chromatin architecture; involved in development of epigenetic memory; and regulate alternate splicing and RNA editing. ncRNA regulatory networks may be involved in the determination of complex characteristics and play a significant role in disease pathogenesis. There are programs such as the NHGRI funded ENCODE that are cell specific ncRNAs but these are being examined in static situations, or the absence of environmental toxicants. Questions have been raised about how exposures might induce SNPs that alter ncRNA function or non-genotoxic agents may alter binding of ncRNAs. There is emerging data indicating that ncRNAs can be modified by environmental stressors but much of this is preliminary. Exploration of how exposures interact with ncRNA function represents an opportunity for the NIEHS to practice **proactive toxicology**, taking advantage of novel biology and exploiting exposures to inform both normal biological processes associated with ncRNAs and elucidate the role of exposures and ncRNAs in disease pathogenesis.

Discussion Highlights:

- Environmental agents trigger cascades of signal transduction networks via ncRNAs.
- ncRNAs (tRNAs) can serve as sensors of exposures, tRNAs have modifications associated with stress responses.
- Determine the extent of exposure responses to ncRNA regulated editing and generation of splice variants.
- How does the subcellular localization of miRNAs contribute to polarity.
- What is the role of miRNAs in cell migration.
- How do exposures contribute to RNA turnover/decay factors/termination factors.
- Do exposures impact ncRNA chaperones or ncRNA repair.
- How might exposures influence genome instability through ncRNA mediated stress responses.

Recommendations:

- NIEHS support development of novel technologies to discover unknown miRNAs; improve on currently used mass spectrometry technologies for the detection of modified RNAs;
- Invest in the elucidation of the roles of ncRNAs and responses to environmental stressors in disease etiology and pathogenesis;
- Incorporate the study of ncRNAs in defined model systems with coordinate epigenomic and underlying genetics analysis;
- Include the study of ncRNA exposure responses in the broader exposome program.

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