Nanoplastics and Human Health Initiatives

University of New Mexico, Plastics and Environmental Analysis Research Laboratory

Significance, Innovation, and Impact: Nanoplastics are *an exponentially emerging concern* due to their ubiquitous presence in the environment and potentially detrimental effects on the human body, which have only recently come to light.[2,3-7] With global concentrations of nanoplastics rising with a doubling time of every ~10-15 years[4], and the reality that nanoplastics may take decades to form from the degradation of discarded plastic material, yet appear to be a dominant and understudied mode of accumulation[6,8], there is an urgent need to assess potential health effects before critical exposure thresholds are achieved.

Below we propose research projects that we deem of highest priority across 4 major areas of health: Neurological conditions, Cardiovascular disease, Reproductive health, and Cancer.

1. Neurological Disorders. Our recent publication highlights the ability of microplastics to accumulate in the human brain, an effect that was more alarming in dementia cases. The chemical and physical nature of nanometer-scale plastic particles may promote aggregation of proteins involved in diseases like Alzheimer's and Parkinson's. There is also reason to consider the role of plastics – which are increasing rapidly in our world – as a cause of other increasing conditions like autism spectrum disorder and multiple sclerosis. The unique characteristics of plastics in the brain may make both syndromes more frequent and severe.

1.1 Clinical Studies: Can a low plastics diet reduce plastics in the brain and slow neurocognitive decline?

We will work with our UNM Alzheimer's Disease Research Center (ADRC) to recruit patients with early-stage cognitive decline. They will be divided into two groups: a low plastics diet (limiting meats, processed foods, and plastic packaging) and a no intervention group. Cerebrospinal fluid will be obtained prior to and after 6 months of this intervention; serum and urine will be collected on a monthly basis for nanoplastics and disease progression measurements. We would also conduct plastics assessments in diets to compile a quantitative comparison of exposures between groups and link to serum and urine levels to better understand uptake and elimination of nanoplastics. Approximate cost - $2M, study duration - 3 years

1.2 Clinical Studies: Survey of the Nanoplastic Landscape in Normal, Dementia, and Parkinson's Disease Brains.

Conducting 3-D sampling using donor brains from the ADRC and Office of the Medical Investigator, we can conduct a thorough exploration fo the regional differences throughout major functional regions of the brain (e.g., frontal cortex, hippocampus, thalamus, cerebellum, etc) and construct 3D models to compare between different individuals and across these major diseases. Understanding the presence of plastics in the substantia nigra in Parkinson's disease, for example, might help us understand whether plastics can specifically impact dopaminergic centers. Approximate cost - $1M, Study duration - 2 years

1.3 Preclinical Mechanistic Studies: Does microplastics exposure drive neurodegeneration in mouse and cell culture models?

As human studies will provide mainly associative data, controlled exposure studies are needed to confirm whether plastics ingestion causes dementia or neurodegeneration. We will leverage our ocean-derived microplastics model, which is an environmentally relevant sample of aged plastics that are all <20 μm in diameter. Using mouse models that are prone to developing neurodegeneration we will conductplastics exposure studies to examine the changes in the brain biochemistry, histopathology, and behavior in response to the microplastics model.

We will conduct further studies in cell culture models to better understand how the ocean-derived microplastics models may affect the blood-brain barrier, trigger inflammation, and cause aggregation of key proteins (Tau, Abeta, etc). Approximate cost - $1M, study duration - 2 years

2. Cardiovascular disease.

2.1 Clinical Studies: How are nanoplastics trafficked to vascular lesions?

Rafaele Marfella's group in Italy published a landmark plastics paper last year in the New England Journal of Medicine, which showed a link between plastics in arterial lesions and the risk of having a later heart attack. Our work with UNM vascular surgeon, Dr. Ross Clark, confirms the major findings of that paper. We can dive deeper to understand the links between plastics distribution in carotid and coronary lesions that can be life-threatening and discern where the plastics are, in which cell types, and how the plastics impact the transcriptiomic and proteomic profile of those cells. Approximate cost - $2.5M, study duration – 3 years

2.2 Preclinical studies: Models of atherosclerosis and vascular inflammation

Again, causality will need to be shown with the controlled exposures to microplastics in rodent chow studies and in cell culture models. We have vast experience with both, and a network of investigators for this work at UNM, the University of Louisville, and UC-Riverside. Approximate cost - $1-3M, study duration 2-4 years (depending on the scope)

3. Reproduction.

3.1 Male Reproductive Health: Sperm Quality and Motility

Initial findings revealed that human testes contain three times the concentration of plastics as compared to dog testes. This was only the beginning of the concerning data in which our collaboration with Dr. John Yu in the College of Nursing was able to address. We are now resolving a clear relationship between higher nanoplastics concentrations and lower sperm counts, reduced motility, and impaired sperm quality. In terms of gestation, we have found that plastics concentrations are higher in placentas from preterm births compared to term pregnancies, even though they had a month less time to accumulate. Rising rates of preterm pregnancy and other disorders of pregnancy, along with a 50% decline in sperm counts in the past 50 years, merit research into how parallel increases in microplastics may be linked.

3.2 Female Reproductive health and Gestational Outcomes.

In Collaboration with Enrico Barrozo and Kjersti Aagaard at Baylor College of Medicine, we have demonstrated that elevated micro- and nanoplastics concentrations in human placentas are significantly associated with preterm births. These findings, suggest rapid maternal-fetal transfer, despite having less time to accumulate as compared to healthy term pregnancies and raise concerns for potential health outcomes for both mother and fetus. In this study we will focus on placental transport pathways, linking incidence of maternal gestational hypertension and gestational diabetes, placental dysfunction, and work to establish target interventions by understanding regional and demographic exposure variations through multi-site recruitment analysis.

Approximate Cost: - $2M, Study duration: 1-3 years.

3.3 Children's Follow-up Study

We will leverage a collaborative framework already established with our partners at Baylor College of Medicine and Texas Children's Hospital as well as in collaboration with Phoebe Stapleton at Rutgers University to design and implement longitudinal follow up studies of children (F1 generation) with documentation of in utero nanoplastic exposure and work to track growth and neurodevelopmental milestones, monitor metabolic health and early cardiovascular risk markers and examine nanoplastic exposure

over significant growth and development periods. The collaborations established will significantly strengthen our study design, cohort diversity, and ensure translational relevance and robust findings.

Approximate Cost: - $2.5M, Study duration: 5 years.

4. Cancer.

Numerous kinds of cancer are rising without explanation. For instance, while colorectal cancers in general are declining thanks to improved early detection, colorectal cancers in persons under the age of 50 have been rising consistently since 1994. Cancers of the appendix, though rare, are rising rapidly in the past 30 years. Similarly, ER-positive breast cancers are more frequent and aggressive. Our research with animal models and cell culture paints a concerning picture – tumor cells exposed to microplastics grow more rapidly and metastasize more aggressively. Brain tumors, namely glioblastomas, are improving in terms of detection and outcomes, but steadily increasing in incidence globally. Working with the UNM Comprehensive Cancer Center and similar programs worldwide, we have the opportunity to make a major impact on this issue.

4.1 Breast Cancer: Partnering with Mayo, Karolinska, and Moffitt Cancer Center, we can tap into repositories with hundreds of samples of tumor and tumor margin and measure the plastics by Py-GC/MS. Those data can then be linked back to clinical outcomes like age of onset, treatment success and survival, and metastasis. Further linkages to geography, diet, and other demographic information may also be possible. We can also collect information on plastics regional deposition using advanced microscopy techniques. Approximate cost - $1.5M, Study duration - 2 years

4.2 Colorectal and Appendiceal Cancer: Partnering with UC-San Francisco, New York University, and Wake Forest University, we can obtain previously collected samples as well as procure samples prospectively. We can also collect information on plastics regional deposition using advanced microscopy techniques. Approximate cost - $1.5 M, Study duration - 2 years.

4.3 Glioblastoma and Meningioma: Partnering with Cedars Sinai and University of Alabama Birmingham, we can obtain tumor and margin tissue surgical discards for Py-GC/MS and histological assessment of microplastics. Data can be linked to clinical outcome and demographic information. $1.5 M, Study duration - 2 years.