

Podium Presentation 4 Carotid Plaque Microplastics are Associated with Clinical Symptoms and Mesenchymal Stem Cell-Macrophage Immunomodulatory Effects

Presenter: Ross M. Clark MD, MBA, FSVS

Ross M. Clark MD, MBA, FSVS; Pierce Massie MD; Marcus Garcia PharmD; Aerlin Decker BSPS; Rui Liu PhD; Milad MazloumiBakhshayesh Mpharm; Deepali Kulkarni MD; M. Ali Rana MD; Carolyn Pace BS; Matthew Campen PharmD

Introduction: Micronanoplastics (MNPs) in human tissues are a recently recognized fact and the clinical effects have not yet been studied. Recent reports in asymptomatic carotid stenosis indicate an association between atherosclerotic plaque MNPs, immune cell deposition and poor long-term clinical outcomes. Mesenchymal stem cells (MSCs) modulate immune signaling and plaque stability. A mechanism for how MNPs affect atherosclerotic lesions has yet to be proposed and the association of MNPs with carotid symptom status as well as gene expression has not been investigated.

Hypothesis: We evaluated the hypothesis that carotid plaque MNP concentrations are positively related to clinical symptoms and perturbations in MSC-immune cell signaling.

Methods: Whole carotid plaques were collected during carotid endarterectomy for carotid stenosis and flash frozen. Symptomatic subjects had stroke, TIA or amaurosis fugax. Age-matched control non-atherosclerotic carotid arteries were obtained from fresh cadaveric donors. Quantitative MNP concentrations were determined by pyrolysis-GC/MS. Electron microscopy documented MNP size and morphology. Single cell RNA sequencing (scRNAseq) differentiated clustered cell types and permitted comparative gene expression by MNP concentration and symptom status. ELISA quantified plaque TNF- α and IL-6.

Results: A total of 48 carotid specimens were analyzed. Mean MNP concentrations in control arteries were 57 μ g/g. Plaques from subjects with asymptomatic carotid stenosis had significantly more MNPs with mean 895 μ g/g (+16 fold, P<0.001) and those from symptomatic carotid stenosis had the highest MNP concentrations at 2888 μ g/g (+51 fold, P<0.001). Polyethylene and polypropylene were the most common polymers. scRNAseq reveals two-fold downregulation of heat shock protein modulator FKBP5 in both MSCs and macrophages from high plastics lesions (P<0.001). In MSCs, genes for cytoskeletal stabilizing proteins TPM1andHIP1R were upregulated (P<0.001) while anti-inflammatory geneCD163 was downregulated in macrophages from high plastics plaques (P<0.001). Plaque TNF- α ranged from 129 to 784 pg/mL and did not correlate with MNP concentration.

Conclusions: These data provide the first evaluation of the effects of microplastics in carotid atherosclerotic plaques and demonstrate a clear association with symptom status. Lesion MSC and macrophage signaling differs based on MNP concentration, suggesting a possible mechanism for plaque instability.