Microplastics Induce Osteoarthritis by Modulating Chondrocyte Inflammation and Disrupting TGF-β Signaling in Mesenchymal Stem Cells

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ABSTRACT BODY:

ABSTRACT INTRODUCTION:
Microplastics (MPs), defined as tiny plastic particles less than 5 mm in size. With the increasing consumption of plastics in daily life, microplastics pollution have been widely detected in water, ice, soil, air, and even in the indoor environment. Osteoarthritis (OA) is the most common degenerative joint disease with an increasing prevalence due to global aging and obesity, both of which are closely influenced by dietary habits. However, the impact of microplastics on osteoarthritis pathogenesis remains unclear.

METHODS: Font is Times New Roman 8 point Font.
Differences in the types, size, and chemical features of the MPs were analyzed in the synovial fluids of OA patients to verify the harmful effects of MPs within human body. In addition, microplastics were administered in animal models to mimic the long-term MPs exposure to influence OA pathogenesis. The resulting OA phenotype and underlying mechanical pathways were subsequently examined. All human experiments were approved by the Medical Ethics Committee of Peking University Third Hospital (No. 2013003) All animal experiments were approved by the Animal Ethics Committee of the China Agriculture University (AW91505202-5-01).

RESULTS SECTION:
Here, we identify different types and sizes of MPs in the synovial fluid of patients with osteoarthritis of varying degrees. Moreover, chronic oral MPs exposure in mice reproduces OA features, including cartilage degeneration and subchondral bone destruction. Further experiments validate that MPs induce apoptosis and oxidative stress in both chondrocyte and bone marrow mesenchymal stem cells (BMSCs), while inhibiting chondrogenic differentiation. Mechanistic studies revealed that IL-1β/SPP1 signaling in chondrocyte and TGF-β signaling in BMSCs both contribute to the MPs-induced OA. In particular, pharmacological inhibition of the TGF-β signaling pathway significantly attenuates MPs-induced OA progression in mice.

DISCUSSION:
Our study not only demonstrates MPs as a novel environmental risk factor for OA, but also highlights TGF-β pathway inhibition as a potential therapeutic strategy for MPs-induced osteoarthritis. The primary limitation is a limited sample size, a future study with a larger cohort size will be better to find the connection of MPs with osteoarthritis.

SIGNIFICANCE/CLINICAL RELEVANCE:
Microplastics (MPs) are widely distributed pollutants that can accumulate in the human body, however, their impact on knee joint health remains largely unexplored. To gain insight into the influence of MPs on osteoarthritis, this study identifies various types and sizes of MPs in the synovial fluid of patients with osteoarthritis. Further experiments validate that oral treatment with MPs induces cartilage damage in mice, with many osteoarthritis-related factors demonstrated. This study provides evidence that MPs are a novel environmental risk factor for OA, and indicates that targeting TGF-β signaling in bone marrow mesenchymal stem cells helps prevent MPs-induced OA. Our results highlight the need to study preventive strategies against environmental exposures that contribute to chronic diseases such as OA.

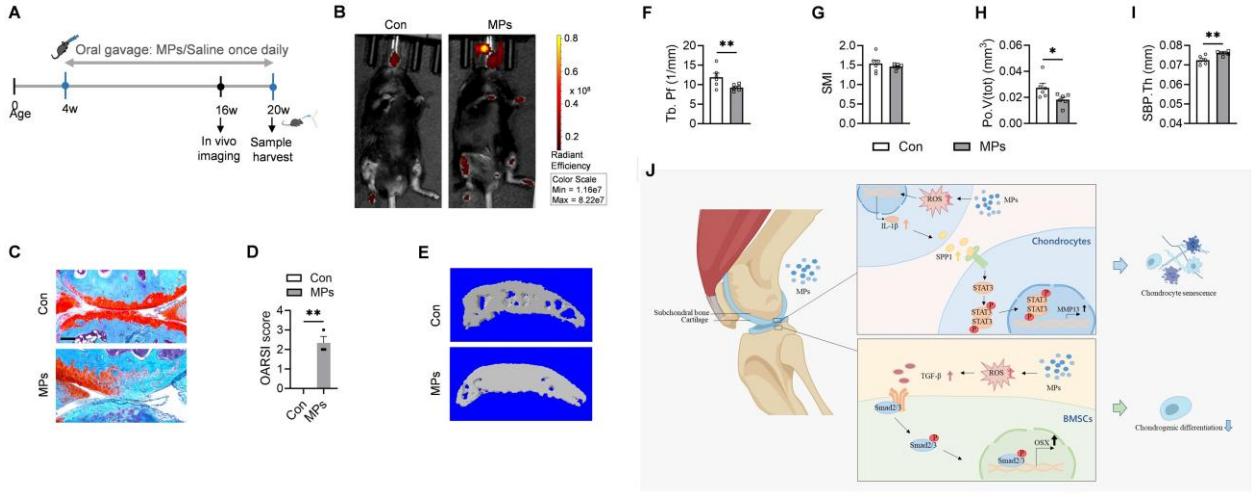

Figure 1: Microplastic induced joint degeneration in mice. (A) Schematic outline of oral MPs treatment on WT mice. (B) In vivo fluorescence imaging shows the distribution of MPs accumulated in the limbs and knee joints of MPs-treated mice. (C) Representative SafraninO/fastgreen (SOFG) staining of the knee joints from mice treated with of MPs or control for 16 weeks. Proteoglycan (red) and bone (blue). Scale bar, 50 μm. (D) Quantitation of OARSI scores for mice in Figure 1C. (E) Three-dimensional (3D) reconstructed μCT images of the tibial subchondral bone from mice receiving control or MPs for 16 weeks. (F-I). Quantitative analysis of subchondral bone trabecular pattern factor (Tb.Pf), structure model index (SMI), total volume of pore space (Po.V(tot)), and subchondral bone plate thickness (SBP.Th) by μCT. (J) Graphic abstract