INTRODUCTION

Spherical nucleic acids (SNAs) are a novel class of therapeutic molecules consisting of densely packed oligonucleotides arranged radially around a spherical nanoparticle core. As a consequence of their 3-dimensional structure, SNAs have increased cellular uptake compared with the same oligonucleotide sequence in the conventional linear format.

SNA delivery and activity have been previously demonstrated in various tissues including topical administration to the skin, aerosol delivery to the lung, and intracerebroventricular injection to the central nervous system. Here we assessed the delivery, biological activity, and disease-modifying activity of an antisense SNA targeted to murine TNFα mRNA (anti-mTNFα SNA) in gastrointestinal (GI) tissues.

RESULTS

Anti-mTNFα SNA is Distributed Throughout the GI Tract With Increasing Accumulation in Distal Segments Over Time

Anti-mTNFα SNA Treatment Improves Survival

Anti-mTNFα SNA Treatment Significantly Improves IBD Clinical Scores

CONCLUSIONS

Orally delivered SNAs:
- Accumulate throughout the GI tract in mice
- Show target mRNA knockdown
- Produce clinical improvement in the TNBS-induced IBD mouse model, including increased survival, increased body weight, reduced IBD clinical score, and reduced gross pathology

These data support the therapeutic potential of orally delivered SNAs for treating GI diseases.