Introduction:
Cushing’s disease is a devastating condition associated with a five-fold excess mortality. It is usually due to a small (few mm) benign corticotroph tumour in the pituitary expressing excess pro-opiomelanocortin (POMC), the peptide product of which, adrenocorticotrophin (ACTH), drives excess secretion of cortisol from the adrenal. There is a clear clinical need for better treatment options.

Background: We have designed, optimized and validated unique siRNAs to POMC and shown highly effective and durable knockdown in vitro and in vivo. Here, we have extended these data to assess the effectiveness of polymersomes, which are biomimetic and polymer-based vesicles, for enhanced delivery of anti-pomc siRNA.

Methods: Polymersomes were formed using the amphiphilic, pH sensitive, PMPC (poly (2-(methacryloyloxy) ethyl phosphoryl-choline) - PDPA poly (2-(diisopropylamino)ethyl methacrylate) copolymers. Effectiveness of polymersomes –mediated siRNA delivery was studied in the AtT20 cell line.

Results: Polymersomes are effective for the delivery of siRNA, supporting their application to deliver anti-pomc siRNA as therapy.

Conclusion: These data further support the potential of a novel epigenetic therapeutic approach for Cushing’s disease.