RNASeq of in vitro transcription: a new tool leading to new directions for RNA nanotechnology and RNA therapeutics

Yasaman Gholamalipour
Elvan Cavaç, Kithmie MalagodaPathirana

RNA therapeutics have huge potential for the treatment of a wide variety of diseases. However, the field is challenged by unwanted immunogenicity of prepared RNAs (thought to arise from the cytokine response to contaminant dsRNA). Similarly, synthetic RNA is key to advances in nanotechnology and systems biology, but impurities complicate the implementation of design.

The Martin lab has studied structure and function in T7 RNA polymerase, the key enzyme used in the in vitro synthesis of RNA (with in vivo applications as well!). The gel at far left shows an analysis of a not atypical reaction - messy. We have size and quanity estimates, but no other information.

Enter RNASeq: a tool that allows us to analyze products in full detail and now reach conclusions about the nature of the “wrong stuff,” leading to new mechanistic understandings.

These new understandings are also leading us to design approaches to avoid the unwanted products from the outset, leading to dramatically improved RNA synthesis, and overcoming the barriers currently challenging nanotechnology, systems biology, and RNA therapeutics - at least that’s the plan!