

Decoding the Major Challenge of RNA Delivery

A Therapeutic (Re)purpose

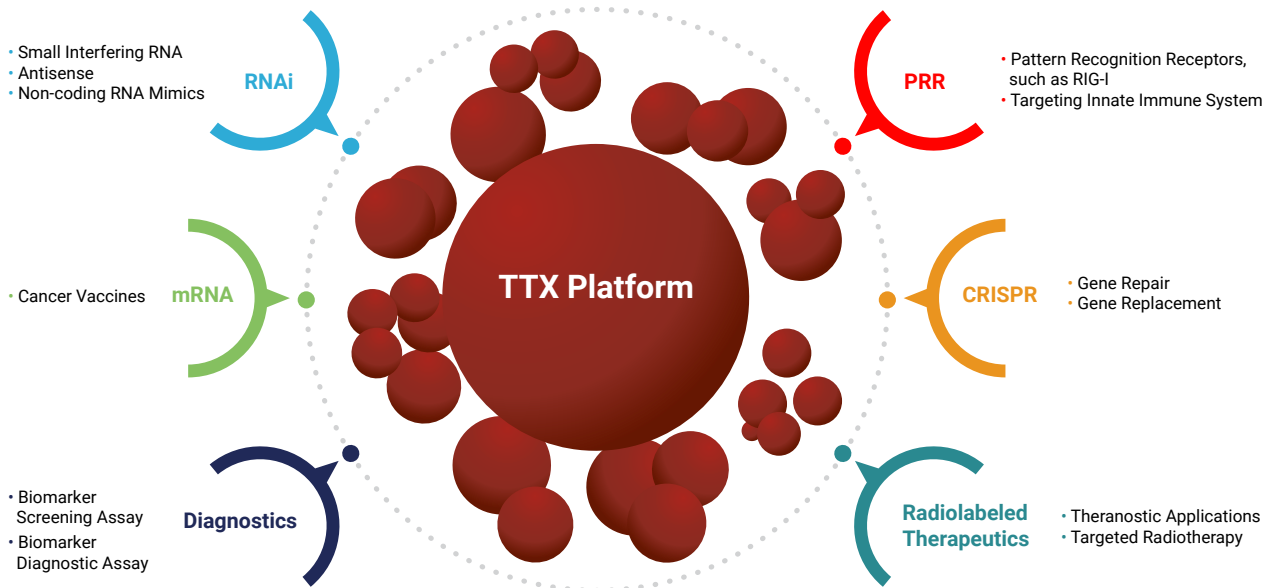
The therapeutic potential of RNA in oncology remains an unrealized promise due to the difficulty in safely and effectively delivering RNA oligonucleotides to tumors. TransCode is now closer to solving this challenge by means of an ingenious exercise in repurposing. We have developed an RNA delivery platform, the TTX platform, which leverages an iron oxide nanoparticle already approved as a clinical cancer imaging agent and a treatment for iron deficiency anemia as the physical carrier.

TTX Delivery System

The TTX delivery system is built around a core iron oxide nanoparticle that minimizes kidney and liver clearance, which translates into a long circulation half-life that allows for efficient accumulation in tumor cells and metastatic sites. These particles have an excellent clinical safety record of low toxicity and low immunogenicity, and their built-in imaging capabilities have the bonus of enabling quantification of the

particles' delivery to target organs. The iron oxide cores are coated with dextran which is cross-linked to provide stability. The particles are subsequently functionalized with amino groups creating stable links useful in attaching therapeutic oligonucleotides of interest. The design of the complex actually protects oligonucleotides from degradation and provides overall stability to the particle. The small hydrodynamic size and positive charge of the resulting nanoparticles allows them to infiltrate the tumor microvasculature, extravasate into the interstitium of tumors and metastases, and be readily taken up by the cells. The coating with dextran further facilitates the rapid uptake of the particles by exploiting the high avidity of cancer cells for glucose, a process analogous to the mechanism behind the systemic loading of metastatic cancer cells with fluorodeoxyglucose (FDG) for diagnostic PET imaging. The combined result of a hydrodynamically favored distribution and a metabolically triggered uptake result in the enhanced ability of TransCode's nanoparticles to access genetic targets inside tumor cells.

One Platform, Multiple RNA Approaches In oncology and beyond



De-risked TTX Platform Advantages:

- Strong binding affinity and specificity to RNA target
- Properties allow for quantitative non-invasive imaging via MRI & measurement of drug bioavailability during treatment
- Allows for target engagement and avoids early clearance by the liver and kidneys
- Low toxicity potential; low immunogenicity potential and highly stable
- Similar constructs have proven to be clinically safe