One minute pitch

RNAscope® and BaseScope™ are ideal solutions to detect therapeutic or target gene expression and vector sequences in individual cells within the tissue morphological context, addressing critical questions on the efficacy and safety behind nucleic acid based therapeutics.

Therapy and RNAscope application

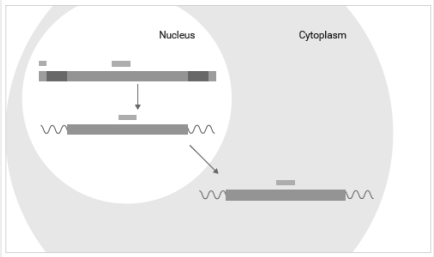
Nucleic Acid Therapeutics includes 3 main categories of therapy:
Gene Therapy: insertion of genetically altered genes into cells to replace defective genes. Use viral or non-viral vector.
RNAscope Technology is used to detect vector distribution and viability, and transgene expression in tissue. See publication P0187, P0643, P0693
RNA Therapy: Direct delivery of mRNA (altered or not) into cells to replace defective gene expression.
RNAscope technology is used to detect mRNA expression in tissue. See publications P0504, P0783
RNAi Therapy: use of siRNA or miRNA to silence or turn off gene expression. Note that a viral vector can be used to transduct the siRNA/miRNA.
RNAscope is used to measure impact of the RNAi on targeted gene expression. See publications P0420, P0357, P0575, P0481

CRISPR/Cas9

When applied to gene therapy, CRISPR/Cas9 can be used in 2 ways:
ex vivo gene correction: modification of target ex vivo before reintroduction in the body (example: CAR-T cell). RNAscope technology is used to localize and monitor expression of the modified target in tissue.
in vivo gene correction: introduction of CRISPR/Cas9 system in tissue/body for modification in vivo. RNAscope technology could be used to localize and monitor guide RNA and expression of the modified target in tissue.

Gene Therapy: AAV transgene and detection

AAV transgene structure and the RNAscope® or BaseScope™ probe design



Schematic of AAV transgene detection in a cell with the RNAscope® or BaseScope™ assay

RNAscope provides the unique capacity to localize and measure AAV vector expression at the single cell level in tissue. Not feasible with IHC.

Question to ask and solution

How do you verify that the vector TARGETs the right cells and right gene?

> **RNAscope**: Visualize in vivo delivery of therapeutic gene expression and vector sequences (viral or non-viral) with tissue specificity, cell type specificity and subcellular localization. **Multiplex ISH or dual ISH-IHC** localize target (ISH) and identify cell type (ISH or IHC) if needed.

How do you verify the transgene gets ACTIVATED?

> **RNAscope**: visualize and measure transgene expression over time with high sensitivity and specificity.

How do you measure the EFFICIENCY of the therapy?

> **RNAscope**: Allows quantification of vector copy #, transgene expression level, and AAV+ cell number in both target and non-target tissues

Which animal models do you use or plan to use for safety testing?

> **RNAscope**: an assay for any target and any species and any tissue - allows to easily measure expression of vector and target in different animal models and tissues.

Key tools/References

Gene Therapy Flyer
Pubcrush and presentation
Leads and Web sites
Publication List
email template

Recommanded products

Both the RNAscope & BaseScope Assays are relevant for this application. Nevertheless, RNAscope will cover the majority of the needs.

Targeted Species, Tissues & Diseases

Species	Tissues	Why?	Diseases
Mouse	Eye/Retina	Easily accessible, small space, somewhat protected from immune system	Blood disorders (Hemophilia)
Humanized mouse			Immune deficiencies
Rat	Liver	Fenestration of vasculature allows for movement of large macromolecules from blood vessel into liver	Hereditary blindness
Dog	Brain/CNS	No other therapeutic options	Muscular dystrophy (Duchenne)
Non-human primates	Muscle	Non-dividing cells	Fat metabolism (LPL deficiency)
Rabbits	Bone marrow/Blood cells	Need only a small amount of gene transfer into true progenitor stem cells for therapy to work	Cancer (multiple types)
Pig			Neurodegenerative diseases (Parkinson's, Huntington's)
Human			

List of target

Gene Therapy: AAV vector and targeted gene (specific to the disease)
RNA Therapy: Targeted gene (specific to disease)
miRNA Therapy: Targeted gene (specific to disease)

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