New method described for quantifying antisense oligonucleotides in nuclei

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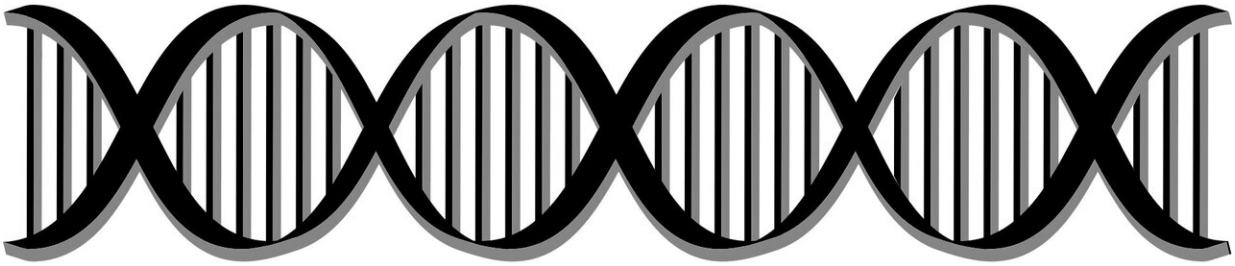

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A novel method uses subcellular fractionation to quantify label-free antisense oligonucleotides (AONs)- designed to silence targeted genes—that have crossed into the nucleus of a cell, where they can exert their effects. Researchers used this method to correlate nuclear entry of several AON molecules with target gene knockdown and they report their results in *Nucleic Acid Therapeutics*.

Troels Koch and colleagues from Roche Innovation Center Copenhagen, Hørsholm, Denmark coauthored the article entitled "Nuclear and Cytoplasmatic Quantification of Unconjugated, Label-Free Locked Nucleic Acid Oligonucleotides." Their method combines three main techniques: subcellular fractionation; nucleus counting; and Locked Nucleic Acid (LNA) sandwich Enzyme-Linked Immunosorbent Assay (ELISA) to determine the absolute numbers of AONs in nuclei. These unconjugated LNA oligonucleotides lack any labels that could alter their distribution in the cell. The researchers showed that increased nuclear entry was proportional to increased target gene knockdown, but depending on the compound and the target, other factors could impact the target transcript level reduction.

"As we anticipate the increase in oligonucleotide-based therapeutics, we must acknowledge it is one thing to know how many oligonucleotides are administered to the patient, it is quite another to know how many accumulate in the target cell nuclear fraction," says Executive Editor Graham C. Parker, Ph.D., The Carman and Ann Adams Department of Pediatrics, Wayne State University School of Medicine, Children's Hospital of Michigan, Detroit, MI.

More information: Hannah Pendergraff et al, Nuclear and Cytoplasmatic Quantification of Unconjugated, Label-Free Locked Nucleic Acid Oligonucleotides, *Nucleic Acid Therapeutics* (2019). DOI: 10.1089/nat.2019.0810

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