

INSPECT - Intron encoded reporter transcripts for minimally invasive monitoring of coding and non-coding RNAs

Keywords: transcriptional reporter, non-coding genes, cell engineering, T cell, cell therapy, lncRNA, saRNA, miRNA, siRNA

INVENTION NOVELTY

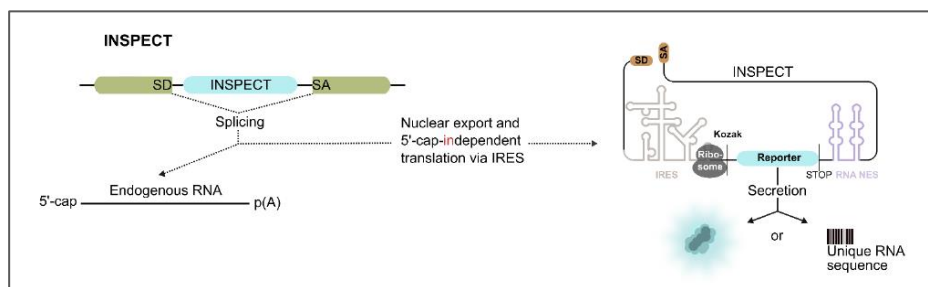
INSPECT reporter systems (Intron-encoded Scarless Programmable Extranuclear Cistronic Transcripts) offer transcriptional monitoring and analysis of coding and non-coding RNAs [lncRNAs, miRNAs, small activating RNAs (saRNAs) or siRNAs] without altering the mature mRNA of the target of interest or the ncRNA sequence.

VALUE PROPOSITION

INSPECT is based on a reporter gene embedded in a native or artificial intron, combined with RNA elements ensuring nuclear export and efficient cap-independent translation and/or secretion. Utilizing the endogenous splicing machinery, the intron-resident construct is excised in an entirely traceless manner and can be analyzed as a surrogate for the unmodified target RNA sequence. INSPECT can be applied in minimally invasive studies of coding and non-coding gene expression and mammalian cell engineering, e.g., for validation studies of therapeutic RNA candidates or for temporospatial mapping of engineered T-cell activation (e.g., via IL2 expression).

TECHNOLOGY DESCRIPTION

The minimally invasive INSPECT reporter are embedded within an intron of a gene of interest. Post-transcriptional excision results in unmodified mRNA and an additional synthetic transcript that leaves the nucleus by hijacking the nuclear export machinery for subsequent translation into a reporter or effector protein. The INSPECT system also offers the possibility to monitor the transcription of non-coding genes (such as lncRNAs, miRNAs, saRNAs or siRNAs) e.g., by direct analysis of the surrogate transcript. INSPECT was used to monitor the levels of the lncRNAs NEAT1 and GUARDIN in response to CRISPR interference.



Scheme of the design of an INSPECT reporter system [Truong et al., Nature Cell Biology]

COMMERCIAL OPPORTUNITY

The technology is available for licensing or further co-development and optionally includes access to material.

DEVELOPMENT STATUS

Established reporter systems are available for research applications and for validation of RNA therapeutics that are modulating gene expression. Additional tailored reporter systems could be developed in collaboration or by licensee.

PATENT SITUATION

WO2022008510A2 "Intron-encoded extranuclear transcripts for protein translation, RNA encoding, and multi-timepoint interrogation of non-coding or protein-coding RNA regulation" was filed in 2021 and national phases were entered in US and EP.

FURTHER READING

Truong et al. (2022) Nature Cell Biology, Vol. 24, p. 1666–76; <https://doi.org/10.1038/s41556-022-00998-6>