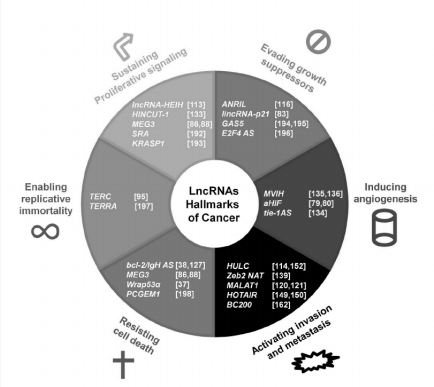
lncRNA in Cancer



Key Facts on long non-coding RNA

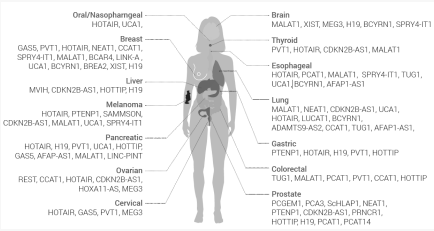
Non-protein coding RNA molecules >200nt in length

Can be oncogenic or tumor-suppressive by either inhibiting growth suppressors or targeting growth promoters

Can be upregulated or downregulated in cancer - Majority are upregulated due to their low expression under normal conditions

Exhibit a high degree of tissue- and disease-specificity, making them an ideal candidate for cancer diagnosis and prognosis. Often expressed in a spatial, temporal, and tissue-specific pattern

lncRNA Biomarkers



Important lncRNA Biomarkers in Cancer

Prostate Cancer:

PCA3, SChLAP1, PCGEM1, PCAT1, DLEU1, PCAT14

Breast Cancer:

HOTAIR, MALAT1, H19, XIST, NEAT1, ZFAS1, LINK-A

Lung Cancer:

MALAT1, NEAT1, UCA1, HOTAIR,

circRNA in Cancer

CircRNAs are a novel type of RNAs. Over 30,000 circRNAs have already been found. Owing to their unique structure, they are more stable than linear RNAs. CircRNAs play important roles in the carcinogenesis of cancer. Similar as splice variants they can be detected with BaseScope.

Somatic Mutations

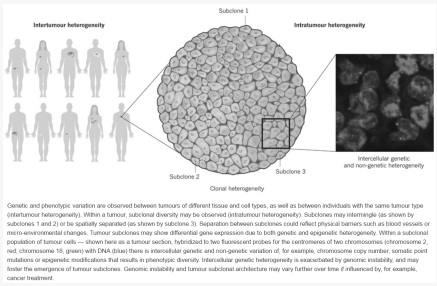
Identification of **somatic mutations** in tumors is becoming increasingly important for patient selection for targeted therapies. High-throughput sequencing (RNAseq) technologies allow for comprehensive mutation-profiling, however:

- Do not permit assessment of **intratumoral heterogeneity** or the association of genetic alterations with cellular morphology
- DNA mutational status **does not predict expression of the mutant allele**, which may provide information connecting genotype to phenotype

Solution: Detection of point mutations by Basescope is currently available **only** through ACD's pharma assay services.

Example: BRAF V600E data

Intertumour and Intratumour heterogeneity



Genetic and phenotypic variation are observed between tumours of different tissue and cell types, as well as between individuals with the same tumour type (intertumour heterogeneity). Within a tumour, subclonal diversity may be observed (intratumour heterogeneity). Subclones may intermingle (as shown by subclones 1 and 2) or be spatially separated (as shown by subclone 3). Separation between subclones could reflect physical barriers such as blood vessels or micro-environmental changes. Tumour subclones may show differential gene expression due to both genetic and epigenetic heterogeneity. Within a subclonal population of tumour cells — shown here as a tumour section, hybridized to two fluorescent probes for the centromeres of two chromosomes (chromosome 2, red; chromosome 18, green) with DNA (blue) there is intercellular genetic and non-genetic variation of, for example, chromosome copy number, somatic point mutations or epigenetic modifications that results in phenotypic diversity. Intercellular genetic heterogeneity is exacerbated by genomic instability, and may foster the emergence of tumour subclones. Genomic instability and tumour subclonal architecture may vary further over time if influenced by, for example, cancer treatment.

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Gene Fusions

Traditionally, gene fusion events are detected by **DNA fluorescent** *in situ* hybridization (DNA FISH) methods. However, these can be laborious with **complex workflows (2 days assay)** and do not provide information on the transcriptional activity of the fused genes. BaseScope provides an alternative chromogenic method for the detection of specific **junctional sequences** created by gene fusions because it can provide single cell level detection of **fusion transcripts with specific cell localization.** Furthermore, this assay can easily be performed in histology labs on routinely available FFPE samples, and results can be obtained rapidly since the assay can be performed in **one day** and reviewed under the light microscope.
Example: The **CRTC1-MAML2 fusion oncogene** is typically associated with low-grade tumors and may signify a favorable prognosis in cases of mucoepidermoid carcinomas (MEC) - data available

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