Highlights

Pathway focused or disease specific
With our pre-designed pathway-specific LncRNAs panels, researchers are able to focus on LncRNAs and their target genes which are the most relevant to specific biological pathways or disease states. Analysis can be achieved quickly and precisely due to a highly specific yet smaller data set. These pre-designed pathway or disease specific LncRNA microarrays will simplify, facilitate, and accelerate LncRNA functional studies and the understanding of their underlying regulatory mechanisms.

Reliable LncRNA collection for specific pathways
Our expert bioinformaticians use a very rigorous process to select the most meaningful set of pathway focused LncRNAs from authoritative databases and landmark publications. All the relevant LncRNAs are comprehensively and reliably collected, including LncRNAs whose genes are located at or near protein coding genes critical in pathways or disease states, competing endogenous RNAs (ceRNAs), LncRNAs transcriptionally overlapping with disease-related SNPs, and known LncRNAs proven to be associated with specific pathways or disease states.

Efficient and robust labeling system
Our smart RNA sample labeling system enhances the detection of both intact and degraded RNA inputs in limited quantities.

Spike in RNA controls
Many manipulations to RNA samples during a microarray experiment may skew the results. Arraystar now adds a set of exogenous RNA controls developed by the External RNA Controls Consortium (ERCC) to RNA samples. With these spike-in controls, procedural affects occurring during RNA amplification, labeling, and hybridization can be corrected. The limit of detection is more accurately determined, and the results across samples are compared more reliably.

Innovative probe design
Specific probes guarantee the accurate detection of transcript variants of LncRNAs , canonical mRNAs, and mRNA isoforms of the protein-coding genes , which adds important clues for unraveling the regulatory mechanisms of LncRNAs relevant to the focused pathway or the specific disease state.

Guaranteed performance

- Better sensitivity: Accurate detection of low abundance RNA with a wide dynamic range of over 5 orders of magnitude
- High reproducibility: Tight correlation between technical replicates of Arraystar's LncPath™ pathway-specific LncRNA microarray experiments (R^2=0.99).

LncPath™ Array List

Pathway Focused LncRNA Microarrays

- LncPath™ Wnt Pathway Array
- LncPath™ Hedgehog Pathway Array
- LncPath™ Cell Metabolism Array
- LncPath™ Epigenetic Pathway Array
- LncPath™ Epithelial to Mesenchymal Transition (EMT) Array

Disease Specific LncRNA Microarrays

- LncPath™ Cancer Array
- LncPath™ Cardiovascular Disease Array
- LncPath™ Neurodegenerative Disease Array

References

1. Gutschner, T. and S. Diederichs (2012) RNA Biol **9** (6): 703-19.
2. Cesana, M., *et al.* (2011) Cell **147** (2): 358-69.
3. Tay, Y., *et al.* (2011) Cell **147** (2): 344-57.
4. Chen, G., *et al.* (2013) Nucleic Acids Res **41** (Database issue): D983-6.

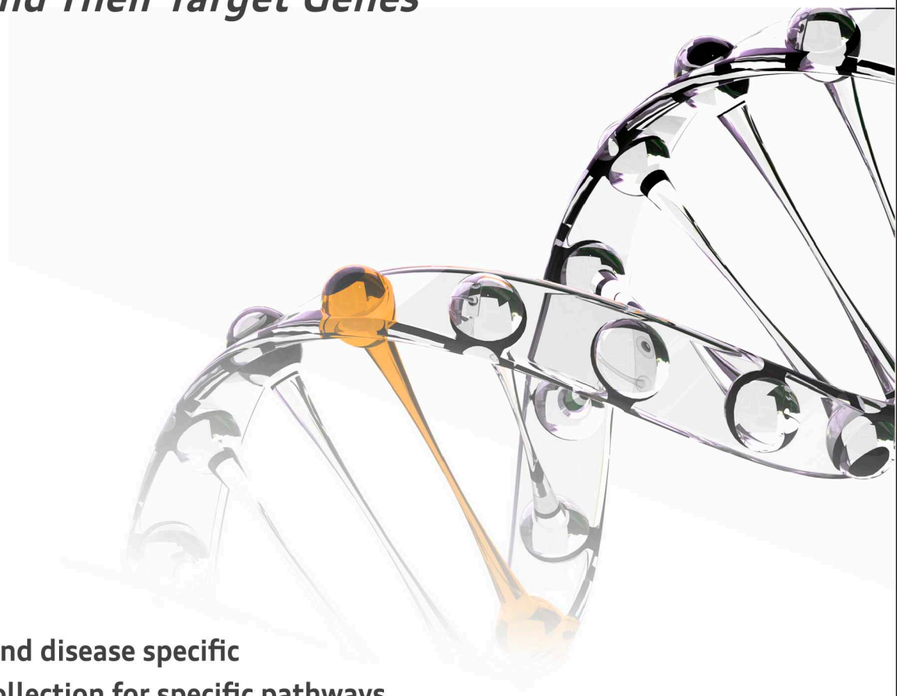
Contact Us
Call: 888-416-6343
Email: info@arraystar.com

www.arraystar.com

GO BEYOND RNA
ARRAYSTAR INC

LncPath™ Pathway Focused LncRNA Microarrays

Discover New Players in Pathways and Diseases – LncRNAs and Their Target Genes



Highlights

Pathway focused and disease specific
Reliable LncRNA collection for specific pathways
Efficient and robust labeling system
Spike in RNA controls
Innovative probe design
Guaranteed Performance

Introduction

Long non-coding RNAs (LncRNAs) are non-coding RNA transcripts longer than 200 nt. LncRNAs play important roles in a wide range of biological processes. Dysregulated LncRNAs are associated with many complex human diseases such as cancers, Alzheimer's disease, and heart diseases.

To facilitate the functional study of LncRNAs and the understanding of their underlying regulatory mechanisms, Arraystar has developed a product line of Pathway Focused LncRNA Microarrays. By limiting the number of LncRNAs and their potential protein-coding gene targets to a specific pathway or disease state, analysis can be achieved quickly and precisely due to a highly specific yet smaller data set. The expressional relationship between LncRNAs and their potential target genes can be established in less time to gain comprehensive insights into the underlying regulatory mechanisms of LncRNAs.

Our LncPath™ LncRNA arrays are available for important pathways including apoptosis, signal transduction, cancer and other diseases. Each microarray slide includes six identical arrays containing oligonucleotide probes for detecting pathway focused LncRNAs and their potential coding gene targets. Each probe is printed in triplicate on each array, offering increased sensitivity and statistical power. In addition, RNA Spike-In controls are used to monitor the labeling and hybridization efficiencies.

Pathway or disease focused LncRNA collection

LncRNAs whose genes are located at or near the protein-coding genes critical in a pathway or disease state

Although LncRNAs could work either in cis or in trans, cis-acting mechanisms are of particular importance. LncRNAs can regulate neighboring genes in cis at transcriptional level in several ways [1]: recruiting chromatin modifiers or remodelers to establish a local transcriptionally active or inactive chromatin conformation; opening up chromatin structure for gene activation or interfering with neigh-boring coding gene expression by the act of LncRNA transcription itself; acting as enhancers to promote neighboring gene expression; and decoying transcription factors to the promoters of the neighbor-ing genes or forming RNA:DNA:DNA triplex at the promoter sites to promote or repress gene expression. As an example, LncRNA-ANRIL, a natural antisense transcript (NAT) of the INK4b-ARF-INK4a gene cluster, induces silencing of the entire locus by recruiting both PRC1 and PRC2 complexes and promoting the formation of the repressive mark H3K27me3 in this locus. Additionally, LncRNAs can regulate their host gene activities at posttranscriptional levels by modulating RNA splicing and RNA stability.

LncRNAs play functional roles within a focused pathway or disease state by regulating their neighboring protein coding genes. Therefore, we have collected pathway focused LncRNAs whose genes are located at or near the protein-coding genes critical in a pathway or disease state (WNT 1 example in Figure 1 and Table 1).

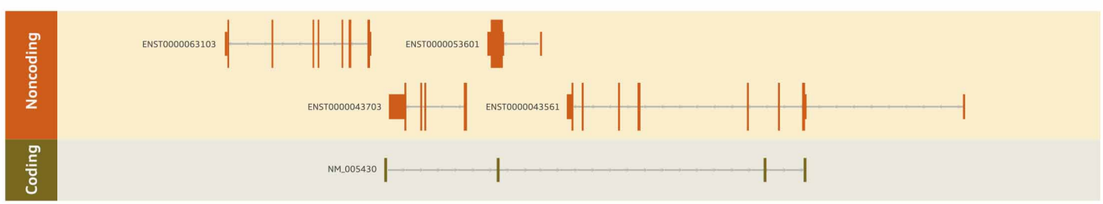


Figure 1. Genomic map showing the LncRNAs whose genes are located at or near the protein-coding gene WNT1 critical in the Wnt pathway.

Table 1. The LncRNAs whose genes are located at or near the protein coding gene WNT1 are critical in the Wnt pathway.

LncRNA	Relationship between LNCRNA and its Protein Coding Gene Target	Coding Gene Transcript	Coding Gene Symbol
ENST0000043561	natural antisense	NM_00530	WNT1
ENST0000043703	intronic antisense	NM_00530	WNT1
ENST0000053601	natural antisense	NM_00530	WNT1
ENST0000063103	bidirectional	NM_00530	WNT1

Competing endogenous RNAs (ceRNA) of the protein-coding genes critical in a pathway or disease state

In addition to the cis-regulation mechanisms, LncRNAs may also modulate target gene expression in trans. Several recent reports have provided a model that suggests that LncRNAs may function as competing endogenous RNAs (ceRNA) in modulating the concentra-tion and biological functions of miRNAs [2]. These ceRNAs generally share miRNA response elements with the transcripts of several important genes and prevent these mRNAs from being degraded, thereby constituting a new dimension of posttranscriptional gene regulation. For example, PTENP1 has been reported to be a ceRNA that protects PTEN mRNA from miRNA-mediated degradation [3]. Linc-MD1 has also been identified as a ceRNA that protects MyoD transcripts. Furthermore, Linc-RoR can function as a ceRNA to regulate the expression of core TFs OCT4, SOX2, and NANOG and differentiation-related miRNAs in hESCs. Arraystar has developed a powerful computational algorithm to identify LncRNAs with high probabilities as ceRNA for the protein-coding genes critical to focused pathways or specific disease states (WNT1 example in Table 2).

Table 2. The LncRNAs predicted to be ceRNAs of WNT1 mRNA in the

LncRNA	Relationship between LNCRNA and its Protein Coding Gene Target	MuTaMe Score	Coding Gene Transcript	Coding Gene Symbol
ENST00000476752	ceRNA	0.312374307	NM_00530	WNT1
ENST00000483961	ceRNA	0.182784303	NM_00530	WNT1
ENSG00000146477	ceRNA	0.068902341	NM_00530	WNT1

LncRNAs with their transcription units overlapping with disease-related single nucleotide polymorphism (SNP) loci

Many disease-related SNPs are mapped to non-coding intervals. However, the relationships between disease-related SNP loci and LncRNAs are largely unknown. LncRNAs are strongly associated with the same diseases as the neighboring mRNA or miRNA genes located within 2 kb. The observation has been utilized to predict novel LncRNA functions in diseases based on the LncRNA gene locations close to a known disease-carrying coding gene [4]. We expect the same correlation applies to both coding and non-coding regions in the genome. By integrating the authoritative phenotype-related SNP annotation projects such as MutaGeneSys, COSMIC and 1000 Genomes with the Arraystar LncRNA database, Arraystar expert bioinformaticians have annotated the disease-related SNPs at LncRNA intervals. Those LncRNAs whose transcription units overlap with disease-related SNPs were carefully collected in these disease state specific arrays.

LncRNAs proven to be associated with a specific pathway or disease state

Some cis-acting or trans-acting LncRNAs have already been proven to be associated with a focused pathway or a specific disease state. These LncRNAs were also carefully collected, and included in the corresponding LncPath™ Pathway Focused LncRNA Microarrays.

What do LncPath™ Arrays offer?

LncRNAs exert their functional roles as RNA molecules and regulate the expression of target genes at both transcriptional and posttran-scriptional levels. By quantifying the expression levels of LncRNAs and their potential target genes in parallel, our arrays provide comprehensive insights into the expressional relationship between LncRNAs and their potential target genes, which help to understand the underlying regulatory mechanisms of LncRNAs.

- Quantify pathway focused LncRNA expression levels using specific exon or splice junction probes. Our transcript specific probes are used to reliably and accurately detect individual LncRNA transcripts. Our probes can even specifically detect transcripts that overlap with other transcripts on the sense strand, which are generally difficult to analyze.
- Quantify the gene expression levels of the protein-coding genes which may act as the targets of the pathway focused LncRNAs.