

# **Arraystar GlycoRNA Array**

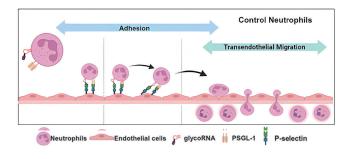
Discover the Pivotal Roles of Glycosylated RNAs in Cancer and Disease

# **Highlights**

- Unprecedented scientific and medical opportunities.

  The newly discovered glycoRNAs now join the ranks of biologically, clinically, and pharmaceutically important glycoproteins and glycolipids.
- Comprehensive glycoRNA profiling. One array simultaneously covers all classes of glycosylated Y-RNA, pre-miRNA, tRNA, rRNA, snoRNA, snRNA and their fragments.
- Discovery of novel glycoRNAs. Previously unknown glycoRNAs can be detected for glycosylation comprehensively on the Array.
- Suitable for all sample types. Chosen glycoRNA capture method detects glycoRNAs for any sample types: living or non-living cells, tissues, biofluids.
- High sensitivity and reliability. Direct glycoRNA end labeling bypasses challenges of RNA modification/folding, and distorted PCR in small RNA sequencing.

Aberrant protein and lipid glycosylation has long been established hallmarks of various human diseases. Similarly, glycoRNAs have the potential for disrupted glycan networks in diseases. GlycoRNAs have been found involved in breast [5] and pancreatic cancers [2, 6], autoimmune, atherosclerosis and cardiovascular diseases [7, 8], stoke [9], inflammatory lung diseases [10], and immunomodulation [11] (Fig. 1).



**Fig 1.** GlycoRNAs on the neutrophil surface control neutrophil recruitment in immune modulation [11].

# What Are GlycoRNAs?

While only lipids and proteins have long been believed to be modified with sugars, RNAs were not thought to be glycosylated. In 2021 in Nobel laureate Bertozzi lab, mammalian small noncoding RNAs were discovered to link with sialylated glycans, challenging the old beliefs and making significant advancement in the RNA and glycobiology fields [1].

GlycoRNAs are primarily glycosylated small non-coding RNAs, including small nuclear RNAs (snRNAs), ribosomal RNAs (rRNAs), small nucleolar RNAs (snoRNAs), transfer RNAs (tRNAs), Y-RNAs, and miRNAs [1, 2]. They may have molecular functions fundamentally different from their un-glycosylated counterparts.

# Why Study GlycoRNAs?

GlycoRNAs are predominantly located on the cell surface [1], which suggests their role in mediating extracellular interactions. Particularly, GlycoRNAs bind to the sialic acid-binding immunoglobulin-like lectin (Siglec) receptor family, participating in cell adhesion, signaling, and immune response modulation [1]. Moreover, as the ligands for Siglec receptor family are largely unknown, newfound glycoRNAs could be the long sought-after ligands [3, 4].

As a new avenue for therapeutic research, modifications to glycoRNA glycans could influence responsiveness to immunotherapies. Antisense targeting the RNA moieties is amenable to rational drug design and can be highly selective. Notably, large molecule drug can react with glycoRNA targets without the difficulties to enter the cells. For biomarker applications, the glycan and RNA moieties have the biochemical properties for both immunochemical and sequence based detection methods, allowing highly sensitive and specific diagnosis and prognosis of diseases [12, 13].

GlycoRNAs hold transformative potential in transcriptomics, epitranscriptomics, RNA biology, glycobiology, cell biology, biochemistry, signal transduction, immunology, fundamental biology, and biomedical/clinical sciences.

### How to Study GlycoRNAs

Arraystar GlycoRNA Array uses glycoRNA capture by lectin (WGA) affinity binding that works on regularly purified RNA samples from any sources (e.g. cells, tissues, biofluids), without the limitation of cultured living cell metabolic labeling. The captured glycoRNAs are detected by microarray to quantify and profile the glycoRNA expression. The integration of these two advanced techniques leverages the strengths of both methods for high specificity, sensitivity, and accuracy.

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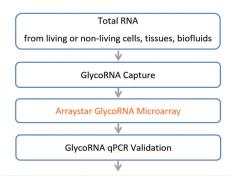
The array covers a wide range of glycosylated small RNA classes, including Y-RNAs/Y-RNA fragments, tRNAs, tsRNAs (tiRNAs & tRFs), pre-miRNAs, miRNAs, snRNAs/snRNA fragments, snoRNAs/snoRNA fragments, and rRNAs/rRNA fragments.

Using this cutting edge approach, researchers can gain comprehensive glycoRNA expression details to discover and understand this new class of RNA molecules in gene regulation, cellular functions and human diseases.

#### Overcoming the Limitations of Sequencing

For glycoRNA microarray, glycoRNAs are directly end-labeled by simple Cy3C ligation, without the problems of RNA modifications and RNA folding that hinder and block reverse transcription as required in RNA sequencing library construction. PCR amplification, which can introduce bias and distortion greatly, is no longer needed. Now all classes of glycoRNAs, particularly the heavily modified tRNAs and tsRNAs, can be profiled simultaneously on one array with unbiased, accurate, and sensitive quantification, effectively overcoming the limitations of sequencing.

### **GlycoRNA Research Roadmap**



### **Clinical Studies**

- Large-scale clinical validation
- · Biomarker analysis

#### **Functional Studies**

- Glycosylation related gene knockout or overexpression
- Inhibition of glycosylation using chemical inhibitors

#### Molecular Mechanisms

- ARPLA to validate GlycoRNA localization on the cell surface
- GlyinsRNA for glycosylation site prediction
- FACS to detect GlycoRNAprotein interaction
- LC-MS analysis of glycan composition changes

### **Arraystar GlycoRNA Array Specifications**

Probe design	Small RNA specific sequence with 5'-hairpin cap and 3'-spacer			
Probe-binding sites	miRNA/5'tsRNA: 3'-sequence 3'tsRNA/Y-RNA/snRNA/snoRNA/rRNA-derived fragment: Any segment in the full-length sequence pre-miRNA: Loop region of the pre-miRNA tRNA: Anti-codon loop sequence of the mature tRNA Y-RNA/snoRNA/snRNA/rRNA: Specific sequence within the entire length of the RNA			
Probe specificity	Specific for the small RNAs			
Array Format	8x15K			
Coverage of small RNA classes				
	Human	Mouse	Rat	
Total number of distinct probes	7,646	7,420	5,312	Sources
YsRNA (Y-RNA- derived small RNA)	10	5	7	
snsRNA (snRNA- derived small RNA)	4	35	35	Human: Literatures  Mouse and Rat:  Predicted
sdRNA (snoRNA- derived small RNA)	289	1,334	1,464	
rRF (rRNA-derived small RNA)	210	479	280	Human: MINTbase(V1) Mouse and Rat: Predicted
miRNA	2,627	1,949	749	miRBase(v22)
tsRNA (tRNA- derived small RNAs)	1,432	910	653	tRFdb, MINTbase, GtRNADb (v18.1, 2019.08)
pre-miRNA	1,745	1,122	448	Literatures up to 2019 miRBase(v22)
mature-tRNA	338	267	195	GtRNAdb (v18.1, 2019.08) ENSEMBL (v99)
snoRNA	955	1,297	1,464	ENSEMBL (v99)
Y-RNA	4	2	3	RNAcentral (V24)
snRNA	27	15	9	RefSeq (2024.08)
rRNA	5	5	5	Nelocy (2027.00)

### References

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