microRNA (miRNA) - are highly conserved, small non-coding RNAs that negatively regulate gene expression at the post-transcriptional level. These molecules play essential roles in many cellular pathways & biological processes, regulating over half of all mammalian genes.

What are miRNA’s functions in endocrinology? There is an intricate reciprocal relationship between these two important regulatory systems:

- Many miRNAs regulate hormones and many miRNAs are in turn regulated by hormones.
- miRNAs have been shown to target many genes important for proper endocrine function and metabolism.
- Dysregulation of miRNAs can contribute to endocrine related diseases: Hormone-dependent Cancers, Obesity, Diabetes, Hyperglycemia, Lipodystrophy.

miRNA mediates lipid deposition in mouse adipose tissue

Prostate (PG) is a key vascular progenitor, metabolized from endogenous endocrine miRNAs.

miRNA microarray analysis of a mouse adipose tissue-derived primary culture cell line revealed that PGs is involved in regulating cellular miRNA expression.

The array data suggest that PGs regulates miRNA expression that inhibits insulin-mediated lipid deposition in cells. This is the probable reason because peripheral lipid deposition (adiposity) is the hallmark of obesity. miRNAs are directly related to impaired PGs production.

miR-126 as a potential biomarker and therapeutic target for diabetes mellitus-associated vascular complications

Diabetic mellitus (DM) adversely affects the number and function of circulating endothelial progenitor cells (EPCs).

Using mirRNA microarray, the first evidence that miR-126 is downregulated in EPCs from diabetic patients, and impaired EPSC mediated function via its target, Spry-3, and x is partially mediated through K/Ras/ERK1/2 and Forkhead/Wnt signaling pathway.

miR-126 is uniquely modified by diabetic vascular injury and may be capable of adding to the prediction of conventional risk factors and miR-126 in EPCs should be further explored for miRNA-based therapeutic interventions of DM-associated vascular complications.

miR-93 is a novel regulator of vascular endothelial growth factor in hyperglycemic conditions

Vascular endothelial growth factor (VEGF) is a direct glucosetase that plays a crucial role in microvascular complications of diabetes, including diabetic nephropathy.

Comparative miRNA expression profile arrays identified miR-93 as a signature miRNA in hyperglycemic conditions. Findings also indicate that high glucose decreases miR-93 expression by down-regulating the LDH of the host MCM7 gene.

Disrupting molecular mechanisms by which miR-93 regulates VEGF both in normal and pathological conditions could lead to new insights into preventing microvascular complications of diabetes. miRNA mimic and miRNA antisense constructs could potentially pave the way for the design of a new generation of drugs for the treatment of patients with diabetic kidney disease.

Loss of miR-146a function in hormone-refractory prostate cancer

Normal prostate cell growth is controlled by androgen, whereas prostate cancer often occurs when this control is disturbed in one or more stages.

Compared miRNA expression in endogenous endocrine human prostate cancer cells and endogenous prostate cells using microarray analysis, and detected eight down-regulated and three up-regulated known miRNAs.

One of the eight down-regulated miR-146a, was found to suppress prostate cancer transformation from androgen-dependent to androgen-independent cells through the regulation of expression of the targeted protein-coding gene, ROCK2.

Endocrine disruptor regulation of miRNA expression in breast carcinoma cells

Several environmental agents termed “endocrine disrupting compounds” (EDCs) have been reported to bind and activate the estrogen receptor (ER).

miRNA microarray results suggest that in addition to E2, the EDG-18, and DDT affect endogenous levels of estrogen regulated miR-126.

miR-126 in breast cancer cells, supporting the possibility that environmental compounds with estrogenic activity have the potential to play an important role in breast carcinogenesis.

Defining the molecular mechanisms underlying EDC-induced miRNA changes and the subsequent cellular consequences may provide insights into the role of EDGs in human disease, including breast cancer.

Let-7 family miRNAs regulate estrogen receptor alpha signaling in estrogen receptor positive breast cancer

Identification of miRNAs associated with normal or disrupted estrogen signaling is critical to enhancing our understanding of the diagnosis and prognosis of breast cancer.

A miRNA expression microarray screening was performed using RNA from formalin-fixed paraffin-embedded (FFPE) breast tissue, which included benign (n=13), ductal carcinoma in situ (DCIS) (n=10), and invasive ductal carcinoma (IDC) (n=13).

Results show that let-7 family miRNAs were down-regulated in human breast cancer tissues at stages of DCIS and IDC compared to benign stage. Additionally found out that significantly between let-7a/b expression and several members of let-7 family in the FFPE tissue and that let-7b is a target of let-7.

Findings indicate a new regulatory mechanism of let-7 family miRNAs in ERα mediated cellular malignant growth at breast cancer.