

**Tentative Outline**  
**Special Issue for CNS & NEUROLOGICAL DISORDERS-DRUG TARGETS**

*Guest Editors: Stephen D. Skaper and Cinzia Volonté*

## **MIRNACLES IN THE BRAIN: WHAT TO WISH AND WHAT TO FEAR**

### **Aims & Scope:**

MicroRNAs (miRNAs) are endogenous, small non-coding RNAs that regulate protein expression through sequence-specific post-transcriptional gene silencing. They are produced as long primary transcripts (pri-miRNAs) and processed inside the nucleus by the RNase III “Drosha” to liberate the ~70-nucleotide miRNA precursor hairpins (pre-miRNA). After being exported to the cytoplasm, the second RNase III “Dicer” further processes these transcripts to produce the mature 21-23 nucleotide-long miRNA (Kim et al. *Nat Rev Mol Cell Biol* 2009). MiRNAs have emerged over the past decade as key mediators of virtually all biological processes: they are highly expressed in the CNS with several being specifically found in brain, where they play important roles in normal development and function.

As one single miRNA simultaneously regulates hundreds of proteins, dysregulation in the expression of just a few miRNAs can become hugely amplified at the translational level – conceivably leading to the complex pathological phenotypes of nervous system diseases that are seemingly distinct yet have many features in common. Consider cortical damage, which is a mutual hallmark of multiple sclerosis, of merely inflammatory tuberculous meningitis and Rasmussen’s encephalitis, as well as of neurodegenerative B cell lymphomas and Alzheimer’s disease. Within the framework of these complex pathological phenotypes, might miRNA dysregulation constitute the common link in cortical lesion that will be amplified to the point of finally distinguishing these very heterogeneous diseases? Being sequence-specific fine-tuners of post-transcriptional gene silencing, miRNAs are surely well-appointed to do this “dirty” job. Moreover, they are implicated in a number of CNS disorders, such as brain-blood barrier dysfunction, brain cancer and ischemia, Parkinson’s, Alzheimer’s and Huntington diseases, multiple sclerosis, amyotrophic lateral sclerosis, spinocerebellar ataxia, Rett, fragile X and Tourette’s syndromes, and even neuropsychiatric disorders.

Until now we have mainly studied gene expression and its participation in putative pathological functions. We believe that the time has arrived to more closely look at the specific repertoire of miRNAs regulating gene expression, in order to explain and, hopefully, begin to ameliorate complex gene-protein pathological relationships. This special issue “miRNacles in the brain” will provide up-to-date knowledge on the involvement of microRNAs in nervous system biology and pathology. It is intended to cover miRNA general concepts and novel insights, miRNA specification at the cellular level in endothelial cells at the blood-brain barrier, in neurons and glia, and the link between miRNA deregulation and brain functioning in normal and neuropathological conditions. Furthermore, it will highlight the role of miRNA formulations as new drugs to treat nervous system diseases. What we wish most, is what we fear less.

### **Key words:**

MicroRNA, blood-brain barrier, inflammation, CAG repeat, amyotrophic lateral sclerosis, pain, neuropsychiatric disorders, glioblastoma, opioids.

### **Subtopics:**

- MicroRNAs regulate brain endothelial cell-barrier function in inflammation
- MicroRNAs landscape in Alzheimer’s disease
- MicroRNAs in CAG trinucleotide repeat disorders: an integrated review of the literature
- MicroRNAs: new comers into the ALS picture
- MicroRNAs and pain
- MicroRNAs and neuropsychiatric disorders
- Involvement and modulation of microRNAs in glioblastoma
- MicroRNAs and the opioid system

**Schedule:**

Manuscript submission deadline: June, 2014

Peer review due: August, 2014

Revision due: September, 2014

Notification of acceptance by the Guest Editor: September, 2014

Final manuscript due: October, 2014