MicroRNAs are non-coding RNAs approximately 22 nt long formed from stem-loop structures. The nuclear RNaseIII Drosha processes primary microRNA transcript yielding approximately 100 nt pre-miRNA. In cytoplasm Dicer cleaves pre-miRNA giving mature microRNA delivered to a silencing protein complex RISC responsible for repression of target mRNA at the post-transcriptional level or its degradation.

There are two most important steps in the informatics identification of potential microRNA binding sites: 1) complementarity analysis with microRNA seed, a region of 7 nt on the 5’end of the microRNA, and 2) cross-species conservation of a seed.

A genetic sequence variant with an allele in the 3’UTR creating a target site regulated by a particular microRNA are expected to have lower expression than the same gene with an allele eliminating this microRNA target. The difference in expression might be accountable for genetic association with disease. If the transcript’s 3’UTR is long and not conserved, existing programs might not detect a target site. It is also possible that the allele on the reference sequence does not create a target site but the alternative allele does.

Characterization of the full 3’UTR may reveal SNPs considered based only on informatics as non-3’UTR SNPs. Additionally, 3’UTR might be sequenced de novo in order to discover new SNPs. Then, a set of 3’UTRs with all combinations of alleles is run against the library of human microRNAs/seeds with FASTA. The variations in arrangement or appearance of microRNAs/seeds are caused only by alternative alleles. Genes having targets for selected microRNAs and novel transcripts are classified according to Gene Ontology categories. After initial computational predictions further experimental procedures such as real-time PCR of variants is necessary. Further experimental evidence includes transfection with microRNAs of cells having targets cloned under a luciferase gene as well as transfecting cell lines having these alleles. We will present a case study based on candidate schizophrenia genes.