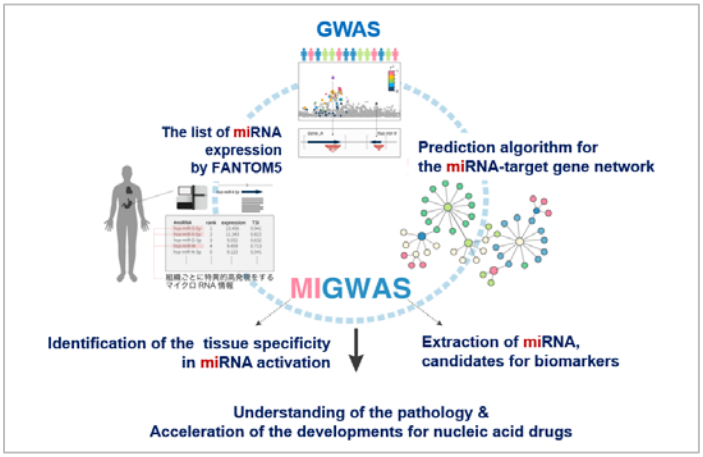
Integration of genetics and miRNA–target gene network identified disease biology implicated in tissue specificity

Keywords: miRNA, genome-wide association study, big data analysis, biomarker

MicroRNAs (miRNAs) modulate the posttranscriptional regulation of target genes and are related to biology of complex human traits, but genetic landscape of miRNAs remains largely unknown.

Given the strikingly tissue-specific miRNA expression profiles, Yukinori Okada (Graduate School of Medicine, Osaka University and IFReC) and his research group expand a previous method to quantitatively evaluate enrichment of genome-wide association study (GWAS) signals on miRNA–target gene networks (MIGWAS) to further estimate tissue-specific enrichment. Their approach integrates tissue-specific expression profiles of miRNAs (~1800 miRNAs in 179 cells) with GWAS to test whether polygenic signals enrich in miRNA–target gene networks and whether they fall within specific tissues. The group applied MIGWAS to 49 GWASs (n_{Total} = 3 520 246), and successfully identified biologically relevant tissues. Further, MIGWAS could point miRNAs as candidate biomarkers of the trait.

As an illustrative example, the group performed differentially expressed miRNA analysis between rheumatoid arthritis (RA) patients and healthy controls (n =63). They identified novel biomarker miRNAs (e.g. hsa-miR-762) by integrating differentially expressed miRNAs with MIGWAS results for RA, as well as novel associated loci with significant genetic risk (rs56656810 at MIR762 at 16q11; n = 91 482, P = 3.6 × 10−8). This result highlighted that miRNA–target gene network contributes to human disease genetics in a cell type-specific manner, which could yield an efficient screening of miRNAs as promising biomarkers.



Concept of a novel in silico screening method MIGWAS, which integrates genetics and miRNA-target gene network.

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