

# **The regulatory impact of RNA-binding proteins on microRNA targeting**

Sukjun Kim\*, Soyoung Kim\*, Hee Ryung Chang\*, Doyeon Kim\*,

Junehee Park, Narae Son, Joori Park, Minhyuk Yoon, Gwangung Chae, Young-Kook Kim,

V. Narry Kim, Yoon Ki Kim, Jin-Wu Nam, Chanseok Shin<sup>#</sup> & Daehyun Baek<sup>#</sup>

Argonaute is the primary mediator of metazoan miRNA targeting (MT). Among the currently identified >1,500 human RNA-binding proteins (RBPs), there are only a handful of RBPs known to enhance MT and several others reported to suppress MT, leaving the global impact of RBPs on MT elusive. In this study, we have systematically analyzed transcriptome-wide binding sites for 150 human RBPs and evaluated the quantitative effect of individual RBPs on MT efficacy. In contrast to previous studies, we show that most RBPs significantly affect MT and that all of those MT-regulating RBPs function as MT enhancers rather than suppressors, by making the local secondary structure of the target site accessible to Argonaute. Our findings illuminate the unappreciated regulatory impact of human RBPs on MT, and as these RBPs may play key roles in the gene regulatory network governed by metazoan miRNAs, MT should be understood in the context of co-regulating RBPs.

\* These authors contributed equally.

<sup>#</sup> Corresponding authors.