Virol Mycol 2018, Volume 7
DOI: 10.4172/2161-0517-C2-027

Regulation of host microRNAs by herpesviral transcripts

Paulina Pawlica and **Joan A Steitz**
Yale University, USA

MicroRNAs (miRNAs) are small non-coding RNAs that post-transcriptionally regulate gene expression of more than half of human messenger RNAs (mRNAs); aberrant miRNA levels are linked to disease. While the biogenesis of miRNAs has been well studied, their turnover is not fully understood. Three herpesviral RNAs contain so-called miRNA degradation elements (miR DEs) that selectively bind to host miRNAs and, instead of being subjected to decay, induce degradation of these miRNAs. This process, called target-induced miRNA degradation (TIMD), requires high yet incomplete complementarity between a miR DE and the corresponding miRNA. Here, we used HSUR1 – a small non-coding RNA from the oncogenic Herpesvirus saimiri that induces degradation of host miR-27a as a model to study TIMD. We performed systematic mutagenesis of HSUR1 to define the sequence complementarity requirements for TIMD, which are serving as a model to computationally search for novel miR DEs in other herpesviruses. Interestingly, while some mutants efficiently decrease the levels of mature miR-27a, they result in appearance of additional miRNA isoforms, which likely represent extended, yet undegraded, miRNAs. As RNAs are often tagged for degradation by 3′ end nucleotide additions, these extended isoforms are likely stalled TIMD intermediates. We found that extended miR-27a isoforms are associated with Argonaute (Ago) proteins – the main components of RNA-induced silencing complex (RISC) suggesting that TIMD commences on Ago. To identify nucleotide additions driving TIMD we used small RNA sequencing and found that in the presence of a miR-DE, a mixture of adenylates and uridylates is added to 3' ends of miRNAs. This study hints at the existence of host miRNA regulation mechanism hijacked by some herpesviruses and will lead to discovery of novel miRNA-targeting transcripts in other herpesviruses.