

MicroRNAs (miRNAs) In Virology: A Promising Transnational Research Approach

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Translational Medicine (TM) has revolutionized traditional research and development processes. The main purpose of TM is to accelerate the translation of scientific findings into practical applications for preventive, diagnostic or therapeutic purposes [1,2]. Given that viral infections constitute a major part of worldwide morbidity and mortality caused by infectious diseases; this is a critical area of focus for TM. The clinical manifestations of viral infections span a wide spectrum from minor pathologies such as sore throat to devastating and life threatening infections such as AIDS. To add to the complexity, viruses can cause acute or chronic infections. Interestingly, some viruses like those belonging to the viral family, *Herpesviridae*, cause both a lytic replication (acute) and a latent infection. In cells harboring latent virus, the viral genome circularizes and only a small subset of viral genes are expressed [3]. Reactivation of latent virus often causes disease more severe than that produced during primary infection [4]. For example Varicella Zoster Virus (VZV) causes varicella (chickenpox) on primary infection, and the zoster (shingles) following reactivation [5]. Given the number of different viruses and various infectious states, the field of Virology faces many challenges.

Another area of study in which there is limited knowledge is viral immunology. Understanding how the virus interacts with the host immune system (innate and adaptive) is critical to effectively identify and target gene(s) or pathway in the design of effective therapeutics or vaccines. To date, there are many viral diseases for which there is no effective treatment option or cure; e.g. Japanese encephalitis virus, West Nile virus, JC virus, Ebola virus. In addition, there are many viral infections that do not have an effective vaccine; e.g. herpes simplex virus, Epstein Barr Virus, Cytomegalovirus, SARS, HIV. Given our limited knowledge about viruses, the diseases they cause, their various life cycles (acute, chronic or latent), and the challenges of virus discovery and propagation, there is a demand for a translational approach to address these needs. Due to its potential benefits, translational approaches are now being employed in many areas of virology. Translational medicine utilizes tools and expertise from various disciplines to strengthen efforts for finding potential solutions [1]. Among these include Omics sciences, Bioinformatics, biomarkers, and miRNAs.

Many miRNAs are evolutionary conserved and offer promising areas of focus in virology research. miRNAs play important roles in the regulation of gene expression involved in cell proliferation, differentiation and apoptosis [6, 7]. The transcription of miRNAs can be ubiquitously or in a cell-dependent manner [8,9]. miRNAs usually act to repress translation or target mRNA for degradation [10]. A single miRNA can act on many targets [11]. It is predicted that 10-30% of all human genes are regulated by miRNAs [11,12].

A large number of studies have been carried out to explore potential

applications of miRNAs in virology, where they are important in virus-host interactions [10]. Both host cell and virus encode miRNAs which can regulate each other's genetic machinery. Virus encoded miRNAs help to bypass the host innate antiviral defense by blocking interferon production and apoptosis [13-15]. Host encoded miRNAs typically limit viral infection, but exceptions can be found; e.g. hepatitis C virus (HCV). In the case of HCV infection, host miRNAs facilitate the virus infection process [16]. Additional studies have shown that miRNAs are intimately involved in the establishment and maintenance of latent viral infections [17-19].

As mentioned previously, viruses within the *Herpesviridae* family can establish latent infections, and miRNAs have been shown to be critical for this host-virus interaction. In this class of viruses, many viral encoded miRNAs have been identified, for example Epstein-Barr virus encode 44 miRNAs, HCMV encodes 17 miRNAs and Kaposi's sarcoma-associated herpes virus encodes 25 miRNAs [20]. However, in most cases, their function(s) and target(s) have yet to be identified and validated. Within the *Herpesviridae* miRNAs usually do not share homologies and their genetic location is not fixed [20]. In fact, some members of the family do not encode miRNAs; e.g. VZV [21].

In addition to providing a better understanding of virus-host interactions, knowledge of miRNAs is being applied to creating novel therapeutics. Anti-miRNAs Oligonucleotides (AMOs) are a promising approach to silence viral miRNAs and provide a new means of limiting virus infections or increase host defenses [22,23]. This approach is relatively inexpensive to synthesize, highly specific and offer a nontoxic therapeutic approach when compared to conventional antiviral drugs. Even though there are many hurdles to be overcome before this new class of antiviral can make its way to clinics, utilizing a translation medicine approach has significantly increased our knowledge of virus-host interactions and provided insight for designing a novel class of anti-viral therapeutics.

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