

ORAL PRESENTATION

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Analysis of the miRNA targetome in EBV-infected B cells

Rebecca L Skalsky^{1*}, David L Corcoran², Eva Gottwein³, Christopher L Frank¹, Markus Hafner⁴, Jeffrey D Nusbaum⁴, Regina Feederle⁵, Henri-Jacques Delecluse⁵, Micah Luftig¹, Thomas Tuschl⁴, Uwe Ohler^{2,6}, Bryan R Cullen¹

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microRNAs (miRNAs) are ~22 nt, non-coding regulatory RNAs expressed by all metazoans and several viruses. During latent infection, Epstein-Barr virus (EBV) expresses 25 pre-miRNAs and influences the expression of cellular miRNAs, such as miR-155 and miR-21, all of which potentially have roles in viral oncogenesis. To date, only a limited number of EBV miRNA targets have been identified; thus, the role of viral miRNAs in viral pathogenesis and/or oncogenesis is not well defined. Using photoactivatable ribonucleoside-enhanced crosslinking and immunoprecipitation (PAR-CLIP) [1] combined with high-throughput sequencing and computational analysis [2], we interrogated the miRNA targetome in EBV-infected B cells. We identified miRNA binding sites in over 5,700 cellular 3' untranslated regions (UTRs), 25% of which contained sites for EBV miRNAs. miRNA binding sites were also identified at a lower frequency in coding regions. Our results reveal that EBV miRNAs predominantly target host cellular transcripts, thereby reshaping the host environment. Furthermore, viral miRNA targets are involved in multiple biological processes that are directly relevant to EBV infection, including modulation of immune responses, cell proliferation, and cell survival. Finally, we identified a number of viral transcripts that contained conserved binding sites for cellular miRNAs, including members of the myc-regulated miR-17/92 cluster. This comprehensive survey of the miRNA targetome in EBV-infected B cells is a positive step towards identifying novel therapeutic targets for EBV-associated malignancies.

* Correspondence: rebecca.skalsky@duke.edu

¹Department of Molecular Genetics and Microbiology, Duke University, Durham, NC, USA

Full list of author information is available at the end of the article

Author details

¹Department of Molecular Genetics and Microbiology, Duke University, Durham, NC, USA. ²Duke Institute for Genome Sciences and Policy, Duke University, Durham, NC, USA. ³Department of Microbiology-Immunology, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA. ⁴Laboratory of RNA Molecular Biology, The Rockefeller University, New York, NY, USA. ⁵German Cancer Research Center, Department of Virus-associated Tumours, Im Neuenheimer Feld 242, Heidelberg, Germany. ⁶Department of Biostatistics and Bioinformatics, Duke University, Durham, NC, USA.

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