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Viral epitranscriptomics

While it has been known for almost 40 years that a wide range of virally encoded RNAs, including mRNAs, are extensively modified by addition of a methyl group to the N6 position of adenosine (m^6A), the functional consequences of this epitranscriptomic modification had remained unclear. However, the prevalence of m^6A across multiple different viral species, and the recently demonstrated conservation of m^6A residues in several distinct isolates of HIV-1, clearly implies that m^6A favors some aspect of the viral replication cycle. More recently, the identification of the factors that add m^6A to mRNAs, especially the m^6A "writer" METTL3, and the definition of factors that bind m^6A on mRNAs, including the key m^6A "reader" YTHDF2, have recently allowed the phenotypic consequences of m^6A addition to be more fully characterized. Using overexpression and/or genetic ablation strategies, as well as by mapping and mutationally inactivating specific viral mRNA m^6A addition sites, we have now examined the effect of m^6A in the context of three distinct viral families: the lentivirus HIV-1, the paramyxovirus *influenza A virus* (IAV) and the polyomavirus SV40. In all three cases, we observe that addition of m^6A strongly enhances viral mRNA and protein expression, and hence replication, and, in the case of IAV, increases pathogenicity *in vivo*. In this presentation, I will discuss our current understanding of the mechanistic basis for this phenomenon.

Biography

Bryan R. Cullen obtained a B.Sc. in Biochemistry from Warwick University in the UK and a M.Sc. in Virology from the University of Birmingham before moving to the USA, where he obtained a Ph.D. in Microbiology from Rutgers University. In 1987, he was recruited to Duke University Medical Center as a Howard Hughes Medical Institute Investigator. He currently holds a James B. Duke Professorship in the Department of Molecular Genetics and Microbiology at Duke. His research interests have historically revolved around the use of viruses as genetic tools to understand aspects of the biology of the eukaryotic cell, focusing particularly on RNA-sequence mediated gene regulation. Currently, his laboratory is studying the regulation of viral mRNA expression by viral microRNAs and by epitranscriptomic modifications. He has published over 315 research papers and is on the editorial board of 11 prominent journals.

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