Of Good and Evil: Biological Impact of Endogenous Retroviruses and Other Invasive Genetic Elements

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The genomes of various eukaryotes are replete with viral sequences that are integrated or 'endogenized' in chromosomes. Recent studies have revealed that virtually all types of viruses can be endogenized, but retroviruses are by far the best-characterized and most common source of endogenous viral elements in mammalian genomes. Endogenous retroviruses (ERVs) comprise 6-14% of mammalian genome sequences and their pervasive infiltration represents a substantial source of genetic variation across and within species. However, we understand surprisingly little about the impact of this class of mobile elements on the biology and evolution of their hosts. ERVs are known to cause specific pathologies in animals, including cancer, but their association with human disease remains controversial, despite half a century of investigation. Even less understood are the potential beneficial functions ERVs may confer on their host cells. In this talk, I will present an overview of the many ways through which ERVs have influenced, for better or worse, the biology of their hosts. I will argue that the conflict between hosts and viruses has led to the invention and diversification of molecular arsenals, which, in turn, promote the cellular co-option of endogenous viruses. I will summarize a body of evidence supporting this model and showing that prefabricated regulatory and coding activities carried by ERVs have been repeatedly coopted throughout the mammalian radiation to promote the advent of novel developmental and physiological functions. Specifically I will present recent evidence obtained in our laboratory that ERVs have been coopted during mammalian evolution to rewire a transcriptional network orchestrating the interferon response, a crucial arm of innate immunity. These data shed new light on the mechanisms by which misregulation of ERVs may promote disease states, such as autoimmunity and tumorigenesis.