A new general principle of virology

Shin et al describe for the first time a novel strategy used by persistent viruses to temporally regulate expression of the structural proteins that make up their virus particles.

The viruses that infect humans and other mammals can be classified into 22 discrete families. Each family is distinguished by a number of unifying characteristics: whether the genetic information is DNA or RNA; whether the genetic information is one strand or two strands; whether the virus particle is encased in an envelope; whether the genetic information is complex or simple. Examples include: the influenza virus in the paramyxovirus family; HIV (the AIDS virus) in the retrovirus family; Ebola virus in the filovirus family.

These 22 families of viruses include 6 families that are classically “persistent” and the remainder that are for the most part “acute”. For the acute viruses, viral infection is either cleared by the immune response to the virus or the virus kills you. For the persistent viruses, infection persists for life despite the immune responses to them persisting for life. The persistent viruses include: the varicella zoster virus in the herpesvirus family which is responsible for chickenpox in children and its recurrence in adults as herpes zoster; HIV in the retrovirus family which persistently replicates for life and, in the absence of antiviral therapy, uniformly induces a chronic disease course and death; and HPV16 in the papillomavirus family which is responsible for the subsequent development of cervical carcinoma in some women.

One feature common to all persistent viruses is what is called “temporal regulation of viral gene expression”. When acute viruses infect a cell -bang- they make all of their protein products at once to make as much progeny virus as quickly as they can to infect more cells or to spread to another individual. Persistent viruses, when they are not in a latent period, have a time-ordered synthesis of their protein products, first making early proteins and then making the major components of the virus particle late in the cycle. The reasons for this temporal regulation have not been clearly elucidated but it likely relates to the need for these persistent viruses to be able to make at least some virus particles in the face of existing, persisting immune responses.

The publication by Shin et al demonstrates for the first time a means by which these persistent viruses temporally regulate late expression of their structural gene products. It has to do with a skewed usage of the codons that encode these structural gene products. There are 20 amino acids that are used to compose the unique features of every individual protein. A, G, C, and T are the four individual units of genetic information and the genetic code is read in units of three. Thus ATG encodes one particular amino acid: methionine. Other amino acids such as glycine have four different combinations of the genetic code that may encode this amino acid: GGU, GGC, GGA, or GGG. It turns out that some codons are used rarely and other codons are used more commonly. The six families of persistent viruses have somehow evolved a way to utilize a skewed codon usage as a means to temporally regulate late expression of their viral gene products. The exact biochemical mechanisms by which this is achieved are yet to be defined.

These findings are very basic, very fundamental, in their nature. Nonetheless, there are ways that can be envisioned by which these fundamental observations can be harnessed, can be translated, into new or better viral vaccines for use in humans.

Publication

Importance of codon usage for the temporal regulation of viral gene expression.
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