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AAV ITR: Not at the End Yet

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The AAV ITR is an overall palindrome with two internal palindromes and an additional 20 nucleotide sequence at the internal boundary. The ITR is an important cis acting sequence that plays an integral role in AAV replication, transcription, recombination, integration and rescue from an integrated site. The sequence and the multiple orientations of the sequence have been known for 35 years, binding sites for multiple regulatory proteins have been identified, and the consequences of various small hairpins which can form have been determined. Yet there remain various properties of the ITR that are still poorly, if at all understood. This talk will review some of the unusual properties of the ITR, some of the various aspects of regulation associated with the ITR, and some still existing conundrums. At least some of the latter impinge on the utility of AAV as a vector for gene therapy.