Recognition of 5’ triphosphate by RIG-I helicase requires short blunt double-stranded RNA as contained in panhandle of negative-strand virus.

Abstract:
Antiviral immunity is triggered by immunorecognition of viral nucleic acids. The cytosolic helicase RIG-I is a key sensor of viral infections and is activated by RNA containing a triphosphate at the 5’ end. The exact structure of RNA activating RIG-I remains controversial. Here, we established a chemical approach for 5’ triphosphate oligoribonucleotide synthesis and found that synthetic single-stranded 5’ triphosphate oligoribonucleotides were unable to bind and activate RIG-I. Conversely, the addition of the synthetic complementary strand resulted in optimal binding and activation of RIG-I. Short double-strand conformation with base pairing of the nucleoside carrying the 5’ triphosphate was required. RIG-I activation was impaired by a 3’ overhang at the 5’ triphosphate end. These results define the structure of RNA for full RIG-I activation and explain how RIG-I detects negative-strand RNA viruses that lack long double-stranded RNA but do contain blunt short double-stranded 5’ triphosphate RNA in the panhandle region of their single-stranded genome.