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Mini Review

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Mini review on Protein – Protein and DNA/RNA – protein interactions in biology

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RNase H1 generally processes the RNA- DNA hybrids through non specific interaction between HBD and the ds RNA/DNA hybrid. There are no direct protein- protein interactions between the hybrid and HBD of RNase H1. The DNA binding region is highly conserved compared to RNA binding region and the K_d for RNA/DNA hybrid is less compared to ds RNA than to that of ds DNA [1]. HBD increases the processivity of RNase H1 and mutations in RNA binding region is tolerated compared to DBR. The RNA interacts between α2 and β3 region with in the loop and with the protein in shallower minor groove.

The HBD is similar to that of RNA binding domains of RNases like dicer, RNase III. RNase H1 and H2 and are involved in removal of R-loops. But RNase H2 is involved in post replicational removal of R loops and whereas RNase H1 R loop repair is not restricted to particular phase of cell cycle. RNase H2 also protects from toxic sensitivity of Methyl Methane sulfonate and from mismatched errors of Mono ribonucleotide excision repair and is not dependent on activity of TOPO1. Double mutants in RNase H2 are not tolerant but it promotes growth similar to single mutants.

Recent studies have identified so many proteins that bind to RNA/DNA hybrids rather than binding to ds DNA. The hybrid binding proteins many consists of RNA helicase domain and K domain. Some of the proteins like nucleolin binds to GC quadruplexes rather than to hybrid structures but we cannot ruled out the proteins that binds to GC Quadruplexes but doesn't acts as hybrid binding proteins. Usually the RNA/DNA hybrid binding proteins binds to R loops directly or by binding to the already bound proteins through protein protein interactions. For example UHRF1 binds to DNMT1 so, until the DNMT1 come in to contact with UHRF1 this protein is repelled from the nucleic acid [2]. There are some proteins which bind to ds DNA rather than to ds RNA or RNA/DNA hybrid. For example PARP1 binds to RNA/DNA hybrid to for poly (A) synthesis [3]. Other domains found in hybrid proteins include alpha-beta pleat which is dependent on protein interaction whereas OB helicase domain for nucleic acid interaction.

RNase H2 is known to inhibit loss of genome integrity by preventing R loop formation. Recent work has revealed that RNaseH2 through interacting with MOV 10 helicase prevent the L1 retroposition there by

having positive effect on genome integrity. RNase H2 and MOV10 interacts each other through the RNA strand synthesised during retroposition and depletion of either RNase H2 or MOV10 leads to overall process to be delineated and increase in heteroduplex formation in L1. In case of rheumatoid arthritis the effects are mediated by increased release of IL-6 and TNF-α in the synovial cells responsible for the pain associated with the disease.

Similar to Protein – protein interactions protein-DNA interactions also play a major role in biology. For example polΔ helicase plays a major role in unwinding of the helix through interaction with pol Δ polymerase and also ss DNA [4]. It specifically binds with ssDNA and requires ATP for its activity. Whereas this activity was not seen with ss RNA, absence of 2'OH is required for the activity, as the unwinding occurs even in the presence of dATP. It requires 3' overhang and polarity of unwinding is 3'-5'of ssDNA. Pol Δ helicase is also responsible for the strand displacement activity of polymerase in case of lagging strand synthesis.

R loops are mainly responsible for genome instability and cancer. DNA/ RNA hybrids or R loops are prevented by so many helicases but recent research adds DHX9 and PARP1 in the list and the effect is dependent on interaction with RNA/DNA hybrid and found to be transcription dependent [5]. DHX9 found to reduce R loop formation at the termination ends and necessary for transcriptional termination. PARP1 is also necessary for prevention of R loop formation and DHX9 was found to be localised in the nucleus. Both proteins are distributed to regions of promoter and In1of β actin and ɤ actin. The protein purely interacts with RNA/DNA hybrids but not with other proteins of nuclear origin.

NONO and SRF 1 are the proteins binding to TERRA a non coding RNA and inhibit alternative lengthening of telomere that promotes genomic instability. The proteins NONO and SRF1 forms homo as well as hetero dimers and involved in preventing telomere fragility in leading strand. So these proteins may protect the carcinogenesis by preventing the function of TERRA in cancerous cells. The non coding RNA forms R loops with telomeres and promotes genomic instability in HeLa cells [6].

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