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Modern Assessment of ncRNAs as Biomarkers of Prognosis in Clear Cell Renal Cell Carcinoma.

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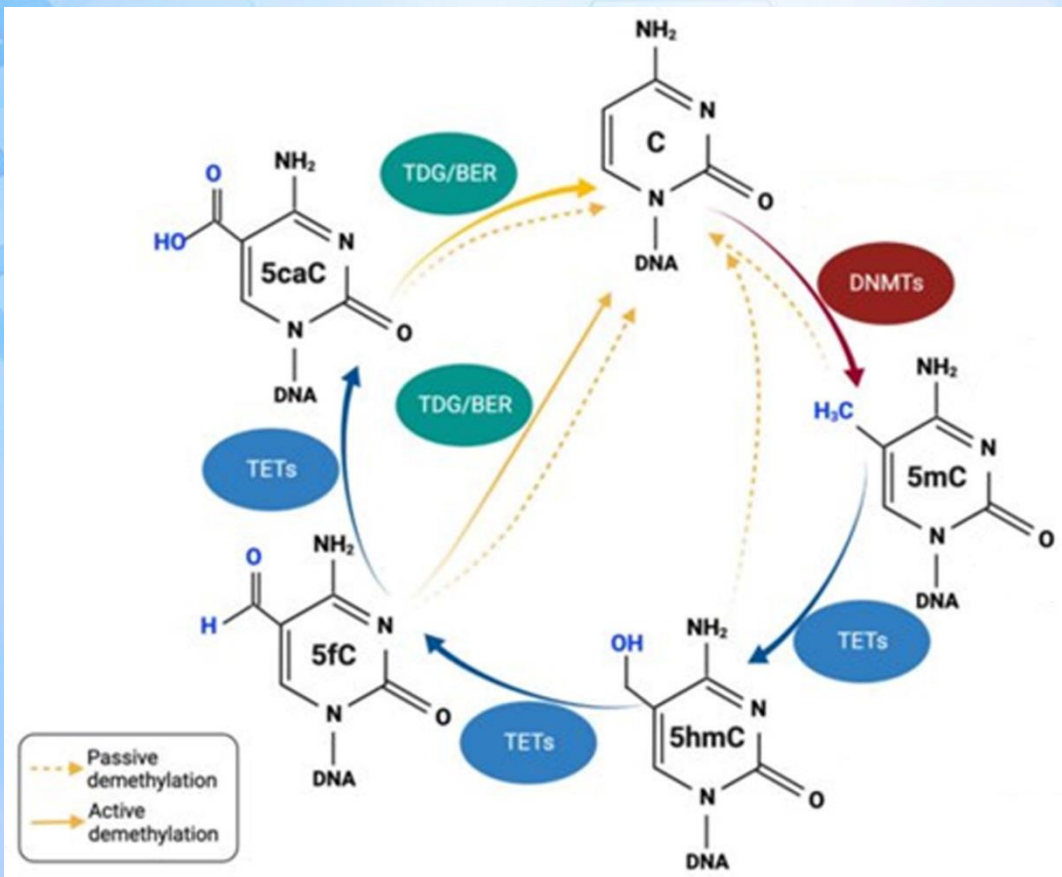
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DNA Methylation and Demethylation Mechanisms.



DNA methyltransferases (DNMTs) add a methyl group to the C5 position of cytosines (C) to form 5-methylcytosines (5mC). DNMT3A and DNMT3B are responsible for *de novo* methylation during development, while DNMT1 is involved in maintaining DNA methylation in the newly replicated DNA strand. DNA methylation can be reversed passively via replication-dependent dilution. Active DNA demethylation processes can also occur by the action of ten-eleven translocation (TET) proteins that successively oxidize 5mC to oxidized methylcytosines (oxi-mCs), including 5-hydroxymethylcytosine (5hmC), 5-formylcytosine (5fC), and 5-carboxylcytosine (5caC). Of these, 5hmC can be deaminated to 5-hydroxymethyluracil (5hmU); 5fC, 5caC, and 5hmU are replaced by an unmodified cytosine via thymine DNA glycosylase (TDG)-mediated base excision repair (BER).

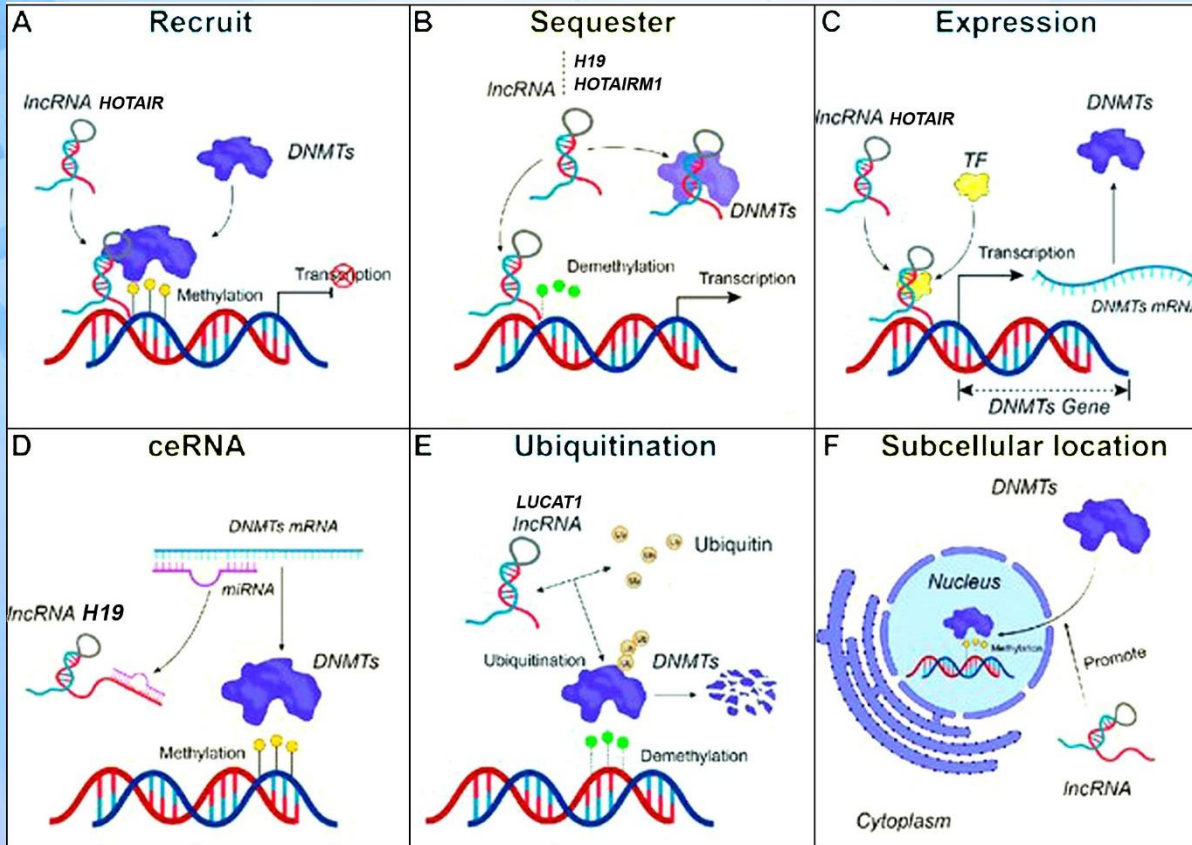
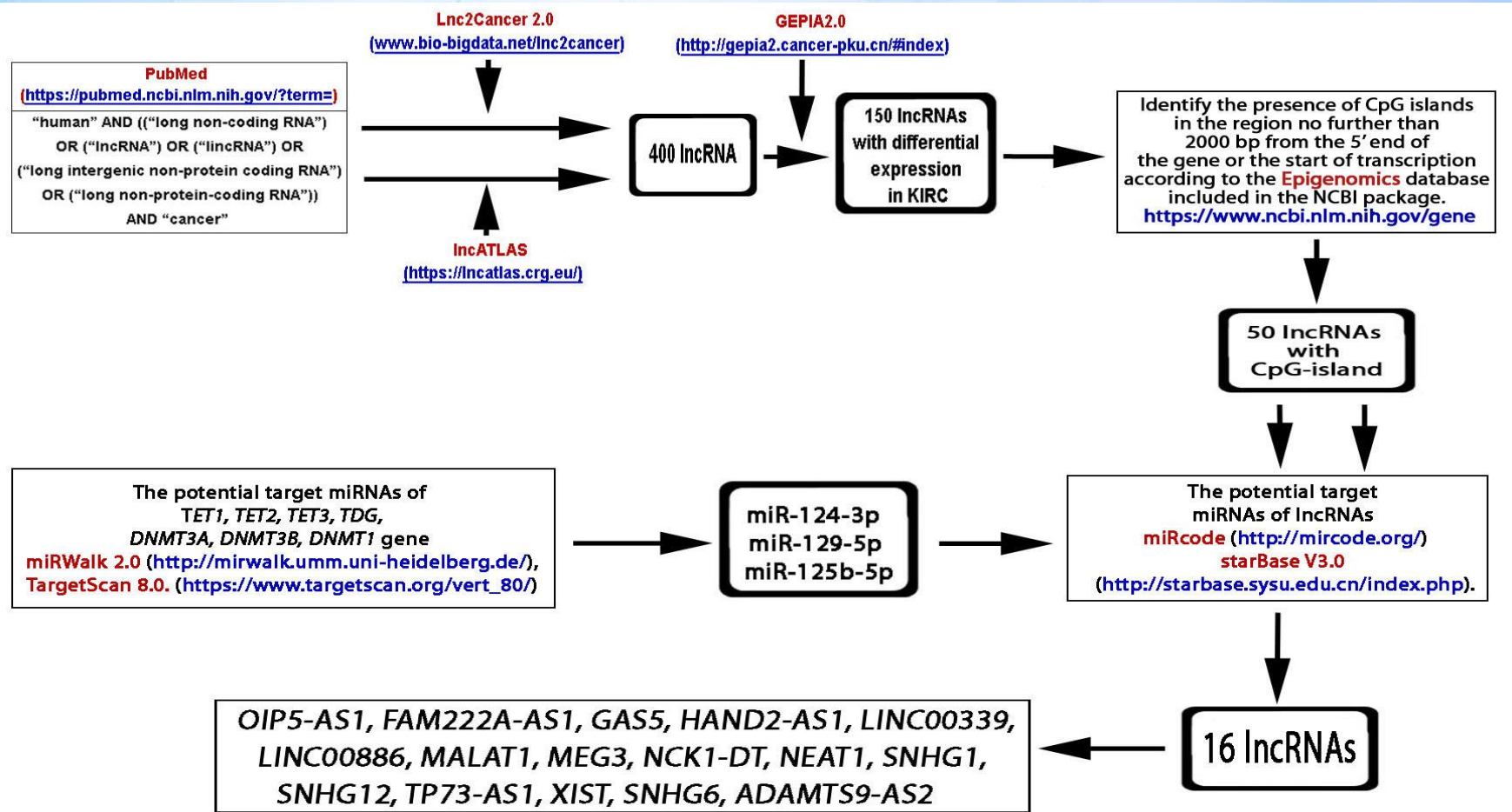
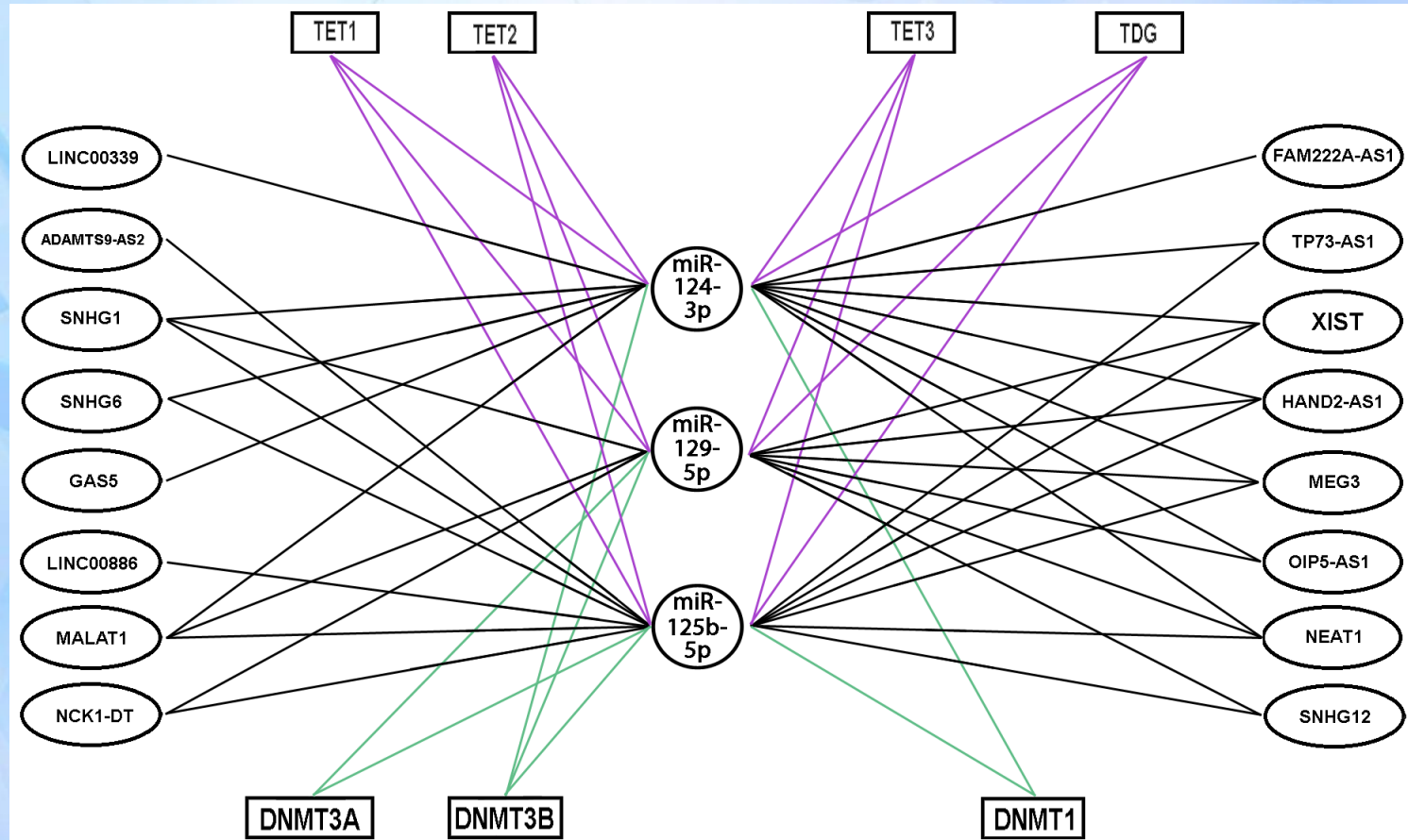


FIGURE 2. Detailed mechanism for DNA methylation regulation by lncRNAs in direct mode. (A). LncRNAs recruit DNMTs to genome loci; (B). LncRNAs sequester DNMTs from genome loci; (C). LncRNAs regulate expression level of DNMTs; (D). LncRNAs function as ceRNA to regulate DNMT expression level; (E). LncRNAs influence the ubiquitination of DNMT proteins to affect the degradation. (F). LncRNAs promote subcellular location of DNMT proteins. It is worth noting that similar mechanisms also applies to TET family members.

The flow chart of the methodology of work.



The lncRNA-mRNA-miRNA ceRNA network.



Conclusion: As a result of the complex analysis, 16 lncRNAs (*OIP5-AS1*, *FAM222A-AS1*, *GAS5*, *HAND2-AS1*, *LINC00339*, *LINC00886*, *MALAT1*, *MEG3*, *NCK1-DT*, *NEAT1*, *SNHG1*, *SNHG12*, *TP73-AS1*, *XIST*, *SNHG6*, *ADAMTS9-AS2*), 3 miRNAs (miR-124-3p, miR-129-5p, miR-125b-5p) and 7 protein-coding genes (*TET1*, *TET2*, *TET3*, *TDG*, *DNMT3A*, *DNMT3B* and *DNMT1*). The probability of their interaction has been estimated. Theoretical data have been obtained on the combination of triplets (axes) possibly involved in the development of ccRCC.