核酸生物学重点实验室学术报告

Elucidating the complexity of the mammalian m6A epitranscriptome

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【报告摘要】 N6-methyladenosine (m^6A) is a widespread reversible chemical modification of RNAs, implicated in many aspects of RNA metabolism. Little quantitative information exists as to how many transcript copies of particular genes are m^6A modified ("m^6A levels"), or the relationship of m^6A modification(s) to alternative RNA isoforms. To deconvolute the m^6A epitranscriptome, we developed m^6A level and isoform-characterization sequencing (m^6A-LAIC-seq). We found that cells exhibit a broad range of non-stoichiometric m^6A levels with cell type specificity. At the level of isoform characterization, we discovered widespread differences in use of tandem alternative polyadenylation (APA) sites by methylated and nonmethylated transcript isoforms of individual genes. Strikingly, there is a strong bias for methylated transcripts to be coupled with proximal APA sites, resulting in shortened 3' untranslated regions (3'-UTRs), while nonmethylated transcript isoforms tend to use distal APA sites. m^6A-LAIC-seq yields a new perspective on transcriptome complexity and links APA usage to m^6A modifications.

研究成果

1.Molinie B.*, Wang J.*, Lim KS., Hillebrand R., Lu ZX., Wittenberghe NV., Howard BD.,Daneshvar K., Mullen A., Dedon P., **Xing Y**.+, Giallourakis C.+ (2016) m6A level and isoform characterization sequencing (m6A-LAIC-seq) reveals the census and complexity of the m6A epitranscriptome. ***Nature Methods***. 13(8):692-8. (+ joint corresponding authors).
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2. Park JW.+, Chung S., Rouchka E., Tseng YT., **Xing Y**.+ (2016) rMAPS: RNA map analysis and plotting server for alternative exon regulation. ***Nucleic Acids Research***. 44(W1):W333- 8. (+ joint corresponding authors).

3.Damianov A., Ying Y., Lin CH., Lee JA., Tran D., Vashisht AA., Bahrami-Samani E., **Xing Y**., Martin KC., Wohlschlegel JA., Black DL. (2016) Rbfox splicing regulators are recruited to pre-mRNA as part of a novel multi-protein complex, LASR***. Cell.*** 165(3): 606-619. PMCID: PMC4841943

4. Cieply B.*, Park JW.*, Nakauka-Ddamba A., Bebee TW., Guo Y., Shang X., Lengner CJ., **Xing Y**.+, Carstens RP.+ (2016) Multiphasic and dynamic changes in alternative splicing during induction of pluripotency are coordinated by numerous RNA binding proteins***. Cell Reports***. 15(2):247-255. (+ joint corresponding authors).