系统生物学

天津医科大学
生物医学工程与技术学院

2016-2017 学年上学期（秋）
2013 级生信班

第三章　转录组学

伊现富（Yi Xianfu）

天津医科大学（TIJMU）
生物医学工程与技术学院

2016 年 10 月

教学提纲

1. 转录组学概述
   - 组学概述
   - 转录组学
   - 研究方法
2. RNA-Seq
   - 概述
   - 技术简介
   - 数据分析
   - 应用实例
3. 顺反组
   - 概述
   - ChIP-Seq
     - 技术简介
     - 数据分析
     - 应用实例
4. 表观遗传学
   - 概述
   - 甲基化测序
     - 技术简介
     - 数据分析
     - 应用实例
5. 回顾与总结
   - 总结
   - 思考题


TIANJIN MEDICAL UNIVERSITY


TIANJIN MEDICAL UNIVERSITY


TIANJIN MEDICAL UNIVERSITY

As an example of clinical applications, researchers at the Mayo Clinic used an RNA-Seq approach to identify differentially expressed transcripts between oral cancer and normal tissue samples. They also accurately evaluated the allelic imbalance (AI), ratio of the transcripts produced by the single alleles, within a subgroup of genes involved in cell differentiation, adhesion, cell motility and muscle contraction identifying a unique transcriptomic and genomic signature in oral cancer patients.

Tuch BB, Laborde RR, Xu X, et al. (2010). ”Tumor transcriptome sequencing reveals allelic expression imbalances associated with copy number alterations”. PLoS ONE. 5 (2): e9317.

Novel insight on skin cancer (melanoma) also come from RNA-Seq of melanoma patients. This approach led to the identification of eleven novel gene fusion transcripts originated from previously unknown chromosomal rearrangements. Twelve novel chimeric transcripts were also reported, including seven of those that confirmed previously identified data in multiple melanoma samples.
Berger MF, Levin JZ, Vijayendran K, et al. (April 2010). ”Integrative analysis of the melanoma transcriptome”. Genome Res. 20 (4): 413–27.

Furthermore, this approach is not limited to cancer patients. RNA-Seq has been used to study other important chronic diseases such as Alzheimer (AD) and diabetes. In the former case, Twine and colleagues compared the transcriptome of different lobes of deceased AD's patient's brain with the brain of healthy individuals identifying a lower number of splice variants in AD's patients and differential promoter usage of the APOE-001 and -002 isoforms in AD's brains. Twine NA, Janitz K, Wilkins MR, Janitz M (2011). "Whole transcriptome sequencing reveals gene expression and splicing differences in brain regions affected by Alzheimer's disease". PLoS ONE. 6 (1): e16266.

In the latter case, different groups showed the unicity of the beta-cells transcriptome in diabetic patients in terms of transcripts accumulation and differential promoter usage and long non coding RNAs (lncRNAs) signature.

Ku GM, Kim H, Vaughn IW, et al. (October 2012). ”Research resource: RNA-Seq reveals unique features of the pancreatic β-cell transcriptome”. Mol. Endocrinol. 26 (10): 1783–92.

Morán I, Akerman I, van de Bunt M, et al. (October 2012). ”Human β cell transcriptome analysis uncovers lncRNAs that are tissue-specific, dynamically regulated, and abnormally expressed in type 2 diabetes”. Cell Metab. 16 (4): 435–48.

For example, NGS technology identified several previously undocumented differentially-expressed transcripts in rats treated with AFB1, a potent hepatocarcinogen. Nearly 50 new differentially-expressed transcriptions were identified between the controls and AFB1-treated rats. Additionally potential new exons were identified, including some that are responsive to AFB1. The next-generation sequencing pipeline identified more differential gene expressions compared with microarrays, particularly when DESeq software was utilized. Cufflinks identified two novel transcripts that were not previously annotated in the Ensembl database; these transcripts were confirmed using cloning PCR.

errick B. A.; Phadke D. P.; Auerbach S. S.; Mav D.; Stiegelmeyer S. M.; Shah R. R.; Tice R. R. (2013). ”RNA-seq reveals novel hepatic gene expression pattern in Aflatoxin B1 treated rats”. PLoS ONE. 8: e61768

or example, Han et al. (2011) examined microRNA expression differences in bladder cancer patients in order to understand how changes and dysregulation in microRNA can influence mRNA expression and function. Several microRNAs were differentially expressed in the bladder cancer patients. Upregulation in the aberrant microRNAs was more common than downregulation in the cancer patients. One of the upregulated microRNAs, has-miR-96, has been associated with carcinogenesis, and several of the overexpressed microRNAs have also been observed in other cancers, including ovarian and cervical. Some of the downregulated microRNAs in cancer samples were hypothesized to have inhibitory roles.
Han Y.; Chen J.; Zhao X.; Liang C.; Wang Y.; Sun L.; Jiang Z.; Zhang Z.; Yang R.; Chen J.; Li Z.; Tang A.; Li X.; Ye J.; Guan Z.; Gui Y.; Cai Z. (2011). ”MicroRNA expression signatures of bladder cancer revealed by deep sequencing”. PLOS ONE. 6: e18286.

顺反组

维基百科

顺反组（cistrome）指的是“全基因组尺度下反式作用因子的顺式作用靶点的集合，也可以说是在体情况下转录因子结合位点或组蛋白修饰在全基因组上的位置”。“顺反组”这一术语是 cistron（顺反子）和 genome（基因组）的混成词，最初由达纳-法伯癌症研究所和哈佛医学院的研究者命名。

染色质免疫沉淀等技术结合微阵列分析“ChIP-on-chip”或大规模并行 DNA 测序“ChIP-Seq”极大地方便了对转录因子及其它染色质相关蛋白的顺反组的定义。

百度百科

顺反组 (cistrome) 是由“Dana-Farber 癌症研究所”与哈佛医学院的科学家提出的遗传学术语，用于定义一个反式（trans）调控因子在基因组（genome）范围内的作用对象——一组顺式 (cis) 作用元素。一些技术，例如免疫共沉淀与基因芯片结合的技术 (ChIP-on-chip)，已经被广泛的应用于发现转录因子以及其他染色质相关因子的顺反组。

顺反组

维基百科

顺反组（cistrome）指的是“全基因组尺度下反式作用因子的顺式作用靶点的集合，也可以说是在体情况下转录因子结合位点或组蛋白修饰在全基因组上的位置”。“顺反组”这一术语是 cistron（顺反子）和 genome（基因组）的混成词，最初由达纳-法伯癌症研究所和哈佛医学院的研究者命名。

染色质免疫沉淀等技术结合微阵列分析“ChIP-on-chip”或大规模并行 DNA 测序“ChIP-Seq”极大地方便了对转录因子及其它染色质相关蛋白的顺反组的定义。

百度百科

顺反组 (cistrome) 是由“Dana-Farber 癌症研究所”与哈佛医学院的科学家提出的遗传学术语，用于定义一个反式（trans）调控因子在基因组（genome）范围内的作用对象——一组顺式 (cis) 作用元素。一些技术，例如免疫共沉淀与基因芯片结合的技术 (ChIP-on-chip)，已经被广泛的应用于发现转录因子以及其他染色质相关因子的顺反组。

知识点

-
-

技能

-
-

1.

2.