BIOL463-Fall2015

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In-class assignment

Assigned paper:

Plank, J.L. and Dean, A. (2014) Enhancer function: mechanistic and genome-wide insights come together.

Instructions:

1. Form a group of 4 - 5 people.
2. Take out the assigned paper (can be on your mobile device, laptop, etc).
3. Discuss the questions below and, as a group, formulate (and type up) answers ensuring that everybody's input is taken into account.
4. Designate one group member to type the answers into the assignment. At the end of class:

- type the names of each group member on the assignment;
- email the assignment (as an attachment, one per group) to Pam and cc all group members, so that everybody has a copy;
- keep in mind that this could be one of your top four assignments for your portfolio!

Get to work, * YOU ONLY HAVE - 25 MIN! **

Questions:

1. Take a few minutes to share what was the most confusing thing about the article that you would like to understand. If anyone in the group is able to help out, they should please do so! Then, list all the points that remain confusing and that group members would like to understand.

- We are not familiar with the high throughput techniques of this article (5C, Hi-C etc.), and to us it is an important part to visualize how the conclusions throughout the review were deduced.

- The structure and composition of TADs were not explained in great detail and we would like to know more about how they differ to EPU's, super enhancers, sub-TADs, intra-TAD, and what the active and inactive character of TADs are and how it can change during development with focus on the organizational structure.

2. The authors report on advances in our understanding of how enhancers (or, proteins associated with/bound to enhancers) interact with promoters (or, proteins associated with/bound to promoters). When investigating this topic, why do you think it is important to study a variety of model systems and cell types? What could have happened if people had focused their studies on one particular cell type at one particular developmental stage? (If appropriate, use examples from the article to support your reasoning).

By focusing on a broad number of model systems you study a larger number of enhancers compared to if you only study one specific cell type. Different cell linages also use varied enhancers to recruit certain linage-determining transcription factors. Further, some enhancers are required during development but turned off in a later stage of development. By studying more systems you simply study more enhancers and get a greater picture of enhancers.

3. Some people have argued that by looking at the chromatin structure/packaging, at the combinations of histone modifications, and at the proteins associated with an enhancer element, one can predict quite accurately whether that enhancer element is active, poised, inactive, *etc.* Do you agree or disagree with this view, and why? Use relevant information from the article to support your reasoning.

We agree that is it possible to predict whether a particular enhancer is active by looking on the histone modifications. Acetylation of histone-tails correspond to active genes and gene expression, since the DNA is uncoiled from the nucleosomes.

4. Based on what you have learned by reading the review article, do you expect so see genes localized in the same region of the nucleus in every cell, all the time? Do you expect to see a particular pattern of localization? Explain your reasoning.
5.

When transcription is active, the enhancer is associated in a complex with the promoter. Since different genes are expressed in different cells, you would expect a different pattern of colocalization of enhancers and promoters in the nucleus.

6. *Time permitting:* Using the information in Figure 1, propose a general model for how enhancers interact with promoters to elicit gene expression in eukaryotes.

Different proteins form complexes at both the enhancer and promoter site. These proteins have high affinity for each other which speeds up the initial interaction of the complexes to form a loop in the DNA. Afterwards cohesin binds to form and stabilize the chromatin loop, which then recruit the transcription factor complex.

7. *Time permitting:* How do DNA methylation and eRNAs contribute to enhancer function?

Studies of eRNA suggest that eRNA might have a role in formation and/or stabilization of enhancer-gene loops. It could also be possible the the eRNA are produce just to keep the enhancer available. DNA methylation silence the promoter and inactivate transcription, this could indirectly influence the enhancer function. Studies have also shown that DNA methylation negatively impact enhancer function.