4DN Steering Committee Meeting
July 16th, 2019
8am - 9:30am PT, 10am-11:30am CT. 11am-12:30pm, ET

Play recording

Discussion Leader: Clodagh O'Shea

APPROVED: 6/18/2019 MEETING MINUTES [TIMESTAMP – 00:00:00]

Reminders:

1. DCIC have contacted PIs and requested to provide Year 1-5 data submission plans. If you have not received a request, please let DCIC know.
2. Contact Nils or Leonid if you have any issues with policies.

Last SC meeting (Clodagh) [TIMESTAMP – N/A]

1. Look at the portal and Wiki and register for the meeting.

Announcements from NIH (Olivier) [TIMESTAMP – N/A)

1. There are 13 that we will support for sure and 1 pending depending on the availability of funds at the end of this year. This will not be made public but we will email people individually this week about their supplement and they should work with the program director to make this happen.

OH update (Kate/Riccardo/Sheng) [TIMESTAMP – N/A]

1. **Annual meeting logistics: as of 7/15/19**
    a. Total number of registrants: 28
    b. Total number of hotel reservations: 13 guests
2. **Outreach meeting (Thursday, July 11th)**
    a. 4DN brochures are printed and ready to be sent out to PIs who request them. Due to changes in the number of data and upcoming meetings/conferences, the brochure will be revised every 6 months to reflect the most current information.
    b. Spreadsheet with PI mailing address for sending brochures.
3. Thank you to all the TCPA PIs who have provided their annual reports. If any TCPA awards are ending, they are still welcome to attend the annual meeting. We hope that they stay a part of the 4DN (Olivier/Judy).

DCIC update (Burak Alver) [TIMESTAMP – N/A]

1. Slides
    a. Updates:
        i. 72 new 4DN experiment sets have been released since June 18.
            1. Including data from Steve Henikoff's lab, Van Steensel's lab and Lin Chen's lab have been made public.
    b. Data Generation Plans
        i. We have collected responses from most of the centers. Please fill them out if you have done so already.
    c. Reminder - Curating 4DN Experimental Assays

i. Updates on EFO (experiment factor ontology)
    1. Released in this month's EFO updates.
ii. Encyclopedia of assays
    1. This is already public facing and available to all. It is not highlighted as much at the moment because we don't feel it is complete. If one knows the way to the experiment type search page of the portal, they can then drill down on the experiment they are interested in, they can find this encyclopedia. In the next version of the data portal homepage, we will highlight this even more by the end of this year. Features such as protocol descriptions and data analysis tools will be highlighted.
    2. Integrating data sets: There are places where we have collections, one is the JA page. Another one is in the 4DN data portal visualization workspace.
    3. It is a little difficult to track access by 4DN or outside traffic. There is not enough statistics for us to track.
iii. Three-tier hierarchy
iv. Let us know if you have any feedback.
    1. Any introductory materials on your assays.

Omics (Bing Ren) [TIMESTAMP – N/A]

1. **Protocol:** There is one meeting in the Omics WG, Dr. Yijun Ruan's group presented their latest version of chia-pet. They presented this protocol and compared that with Hi-chip. The data shows the in-situ chia-pet is very similar to previously published Hi-chip or plaq-seq protocol with minor variations in experimental procedure performed very well if not better in picking up loops from CDCF binding site. The conclusion was that the in situ chia-pet is a valuable and solid protocol for use to generate chromatin interaction maps centered on certain antibody targeted region such as CDCF binding sites or cohesin binding site. The addition of in situ chia-pet and the previously Omics group discussed hi-chip and plaq-seq procedures, we have three variations of a common protocol that is a combination of chia-pet and hi-c to interrogate chromatin interactions inside the nuclei. The protocol will be released along with other protocols that the subworking group discussed (hi-chip and plaq-seq) with extensive comparison and QC procedures. It will be released this week. We plan to have another discussion in next week's Omics call. I encourage everyone who is interested in adopting this protocol or examine the methods in more detail to come to the next Monday's Omics WG call.
    a. Sub working group primarily worked on hi-chip and plaq-seq in the past because we did not yet have the latest protocol. We examined different variations of the protocol between hi-chip and plaq-seq and the differences among them. We are not commenting on the relative advantages and flaws of the procedure but rather come up with a quality matrix. To evaluate the enrichment of the chromatin loops that's centered on the protein that we're interested in investigating using this procedure. I believe this quality control matrix will be more useful for people to use and to select the optimal protocol for their own experiments.

We also provided in this protocol how to compute this quality matrix and how to determine intermediate steps where the experiments are working. In addition, we have tested different antibodies corresponding to the CDCF, K4me3, k27ac, RNA polymerase, and comparing their performances using such matrix. We will make that antibody list available to use.

2. Protocol approval: We are hoping through this Omics WG extensive discussions to get general endorsement from the group and then recommend to the 4DN consortium. The SC will then consider that recommendation and approve it or not. Once it is approved, this protocol will become public.
    a. Judy: Is this the kind of comparison study that you plan to publish to make it broader to the community? - Bing: We have not thought about it in terms of publication. In the context of this sub working group, we have done extensive comparison between the hi-chip and plaq-seq protocols. The difference boils down to a really minor experimental procedure such as how you make a DNA library and fragment size that you sonicate doing the fragmentation process. Through our own analysis, we have come to certain conclusions. This protocols are robust and will give you good data. Where the performance differs depends on the antibody quality and details of washing and optimization of the antibody concentration and immunoprecipitation procedures. It is difficult to recommend a gold standard procedure when we know that the larger biological variables are coming from antibody sources and the optimization of the chip conditions, including temperatures of immunoprecipitations. All these factors we discussed extensively. We plan to release to Nature protocol publication. In terms of comparison, we have not done extensive cross platform comparisons. If there is a demand from the consortium that we should conduct extensive comparisons and making a final recommendation, we can do that. We will send the current document by the end of this week.
    b. Job Dekker: Given that the comparison of the different methods and presenting the outcome of such comparisons to the community is the mission of the JAWG, several active members of that WG are working very hard to do such comparisons which can be done because data have been obtained in Tier 1 cell lines, maybe a dozen of these methods, and a comparison is being done in the working group. My view, the Omics WG has always been focused on agreeing and discussing how to do an Omics experiment and get protocols worked out. JAWG does not do that, it looks at the data that comes out of this methods and asks how do they compare. This week, the chia-pet group will present some analyses they are doing comparing chia-pet to hi-c. These analyses are ongoing and does not necessarily deal with the experimental protocols in a way that Bing just talked about. In the JAWG, there is an emphasis in producing guidelines, if this is what you want to learn about the 3D genome, and if these are the kinds of experiments you can do. To address what Ananda was saying is a service to the community, such as here is the direct comparative output from the consortium, with a description of the different methods, their strengths and weaknesses and what we would

recommend you do based on your questions. The JAWG are gearing up to get these together given that it has been the year 5.

c. John Lis: It would be nice to have data sets where that comparison is done using the same cell line, antibody and amount of antibody. Bing: We will make that data that we generated available potentially through his Nature protocol publication process.
d. Clodagh: There was a discussion with a group that was generating antibodies against different epigenetic marks. Is this something that can be incorporated here? Ananda: We did not get any traction between the 4DN group and protein capture reagents group to have any joint projects at this point. The protein capture group is pushing forward with the validation of these reagents. Currently, we have 115 antibodies have been tested. We have setup a pipeline where a list of antibodies are looking at chip-seq. A subset of these antibodies, and also using crispr-cas to knock out the particular target to have a better validation and control. They are hoping that within the next six months, we will have a highly evaluated sets of antibodies. The group is preparing to publish these results and we will keep you informed as to where they are. We have not made the website public yet as we are still waiting for all the data to be incorporated. The idea is that this is going to be a website containing the full set of validation data. It will be shared once it is completed and will be a very valuable resource.
e. Sheng: Process of approved protocols and releasing it: Each working group develop and suggest/recommend the particular protocol. When approved by the WG will then go to the SC. The chairs of the WG will then give a brief presentation about the protocol and reasons for the recommendation. When the SC gives the approval, that protocol would be released through the 4DN Web portal. Starting in 2017, there have been a total of 7 experimental protocols recommended by the Omics WG and approved by the SC. One Data Analysis protocol and one Data Standard protocol, for a total of 9 protocols. Recent update to this process is utilizing not only a PDF format but also using the protocol io, which is a line platform that will enable you to categorize reagents in every step and run the experiment virtually as you do the actual report and record and report progresses. It also gives DOI to the protocol that you can also release through the 4DN web portal through the preprint format. Through protocols io, there are version controls so that the lab can update and have multiple versions just like updating through the biorx.
f. Suggestion (Clodagh): It would be a good idea to deliver the set of PDFs that we have produced and make it available or publish it online as a booklet with links to various data so that it is all there for a downloadable resource for the community.

Imaging (David Grunwald) [TIMESTAMP – N/A]

1. Slides
    a. IWG focus: Metadata & Calibration standards for Imaging
        i. ELMI meeting lead to new collaborations with:
            1. GermanBioImaging for the German MetaData Standard
            2. French Imaging Facilities Metrology Group

ii. Industry inclusion via IEEE rather than publication of standards
iii. MetaMax turns out to be of key importance
iv. MetaMax 3.0 in works
v. Metadata Collection Tools is working in OME with bioformats library

b. Ongoing and Upcoming Outreach
i. Field test is now at Harvard Nikon Imaging Center and Rockefeller
ii. UNC has asked if we can visit (limited resources right now)
iii. Conference invitations:
1. EMBL-EBI
2. GlobalBioImaging
3. Seeing is Believing

New/Other Business (Clodagh) [TIMESTAMP - N/A]

1. None.

Action items [TIMESTAMP – N/A]

1. None.