Introduction :

Contrary to conventional illustrations, genomic DNA is not linear, but is folded into compact chromosomal structures that likely impact gene expression of the embedded genes. On a global scale, regions with a high degree of compaction are classified as heterochromatin while uncondensed regions are called as euchromatin. These are respectively associated with lower and higher expression levels. Locally, areas where frequent DNA-DNA interactions occur as a results of their close proximity within the cellular nuclear space are called topologically associated domains (TADs). These domains are largely conserved across cell lines and they frequently contain smaller loop structures that promote contact between different genetic regulatory elements such as enhancers and promoters. Such chromatin loops are often found at TAD boundaries (Rao et al, 2014). They are enriched in binding sites of architectural proteins, including CTCF and cohesin (Pope et al, 2014) which are both thought to function in the delimitation of TADs since the boundaries of TADs represent genomic insulators by preventing DNA-DNA interactions across domains. In addition to modulating regulatory interactions between genomic elements, TAD boundaries are also found to be gene-dense and are enriched in highly transcribed genes (Ong et Corces, 2014).

CONNECT THOSE § WITH A SMOOTH TRANSITION

A large proportion of the mammalian transcriptome does not code for proteins and to date, the number of known noncoding genes is more than 3 times that of protein-coding genes (Iyer et al, 2015). Among noncoding RNAs, long noncoding RNAs (>200bp) that do not overlap protein-coding genes are the most abundant (long intergenic noncoding RNAs, lincRNAs). Functional roles of the characterized lincRNAs are diverse. For example **[…]** (READ Howard Chang and John Rinn 2013)

Discuss more on elincRNAs:

-Most active enhancer are associated with transcriptional activity (FANTOM papers)

-enhancer-associated are often transcribed bidiretionally, i.e. no selection on the direction of transcription, and these transcripts are often unstable and rapidly degraded.

- some lincRNAs have been associated with enhancer activity and are likely transcribed in a preferred direction (uni-directional transcription), these are called elincRNAs.

LincRNAs promoters are enriched in enhancer marks (Popadin et al, 2013), which suggest a role in transcriptional regulation. LincRNAs might also play a role in the control of nuclear architecture as they have been shown to mediate promoter-enhancer interactions and are enriched in TAD-boundaries (Chen et al 2016). LincRNAs whose promoter region is associated with enhancers (elincRNAs) are therefore good candidates for studying their involvement in the regulation of DNA-DNA contacts.

In this work, we study the role of elincRNAs in the organization of TADs using bioinformatics tools and publicly available data from the ENCODE project. We investigate the properties of these elincRNAs and their frequence in different elements of the genome. In general, the study of elincRNAs is of particular interest as they have been linked to various disease phenotypes (Ounzain et al, 2014).

**Results**

* (?)Used bins instead of TAD boundaries to avoid arbitrary thresholds
* elincRNAs enriched at TAD boundaries compared to nelincRNAs ?

→if TRUE: Possible role in TAD organization.

* Insulator proteins binding sites enriched in elincRNAs ?

→ if TRUE: Role as insulator ?

**Methods :**

* TAD definition:

TADs used in the computations come from [ENCODE?] the large encompassing TADs were removed to avoid hiding the smaller ones inside.

* TAD boundaries definition:

Instead of using an arbitrary threshold for defining TAD boundaries, TADs were split into 10 bins of 10% of their length.

enrichment test:

GAT  parameters

\*conservation

Computed phastCons score (Siepel et al, 2005)

\*tissue specificity

Computed taus based on method from Kryuchkova-Mostacci et al 2016

\*expression levels

\*data

TADs: ENCODE ?

Pcgenes and lincRNAs expressed in LCL: ENCODE

Raw Hi-C data: aidenlab.org, data from Rao et al, 2014

ChIP-seq data: ENCODE

**Discussion:**

Found/didn’t found association between elincRNAs and….

 Although these results suggest a role for elincRNAs in TAD organization, they provide no information on their exact function of mechanistic role.

**Tools :**

- GAT 1.2

- BEDtools 2.26

- R 3.3.1