ChIP-seq technology and applications

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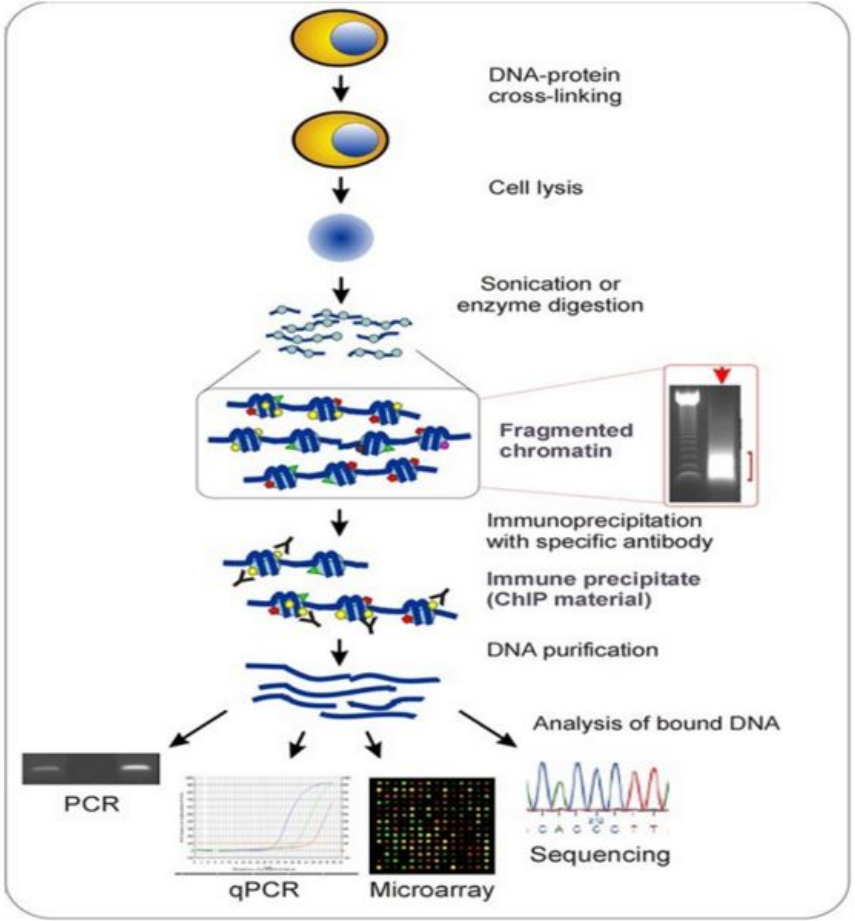
Galaxy Workshop — Cuernavaca, 2017

ChIP-Seq principle

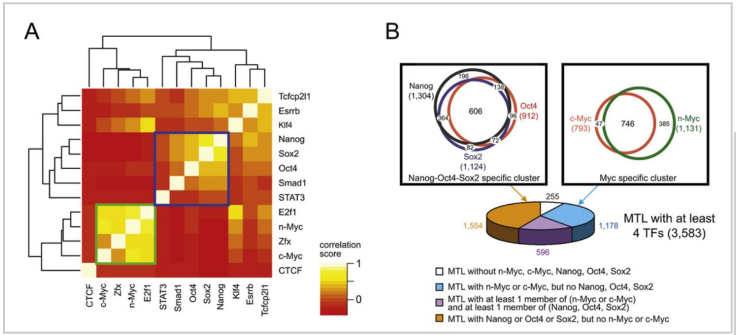
- Used to analyze, at the level of whole genomes:
  - transcription factor binding locations
  - histone modifications

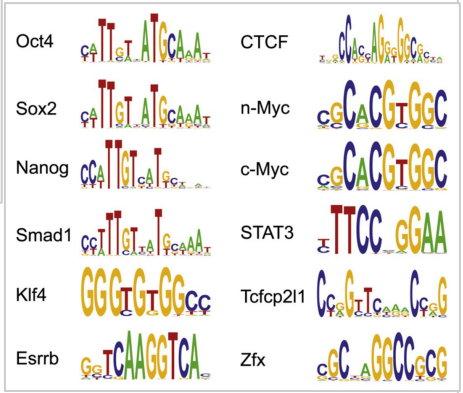


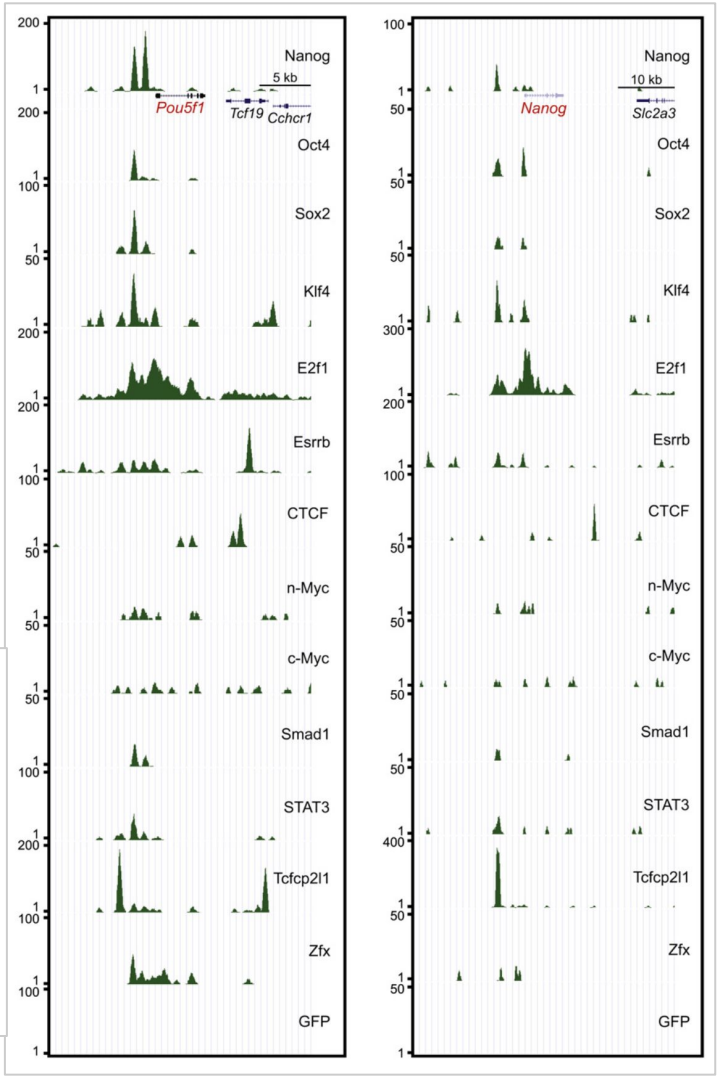
ChIP-seq for 13 TFs in mouse ES cells

Integration of External Signaling Pathways with the Core Transcriptional Network in Embryonic Stem Cells

Xi Chen,[1,2,6] Han Xu,[3,6] Ping Yuan,[1] Fang Fang,[1,2] Mikael Huss,[4] Vinsensius B. Vega,[3] Eleanor Wong,[5] Yuriy L. Orlov,[4] Weiwei Zhang,[1,2] Jianming Jiang,[1,2] Yuin-Han Loh,[1,2] Hock Chuan Yeo,[4] Zhen Xuan Yeo,[4] Vipin Narang,[3] Kunde Ramamoorthy Govindarajan,[3] Bernard Leong,[3] Atif Shahab,[3] Yijun Ruan,[5] Guillaume Bourque,[3] Wing-Kin Sung,[3] Neil D. Clarke,[4] Chia-Lin Wei,[5,*] and Huck-Hui Ng[1,2,*]

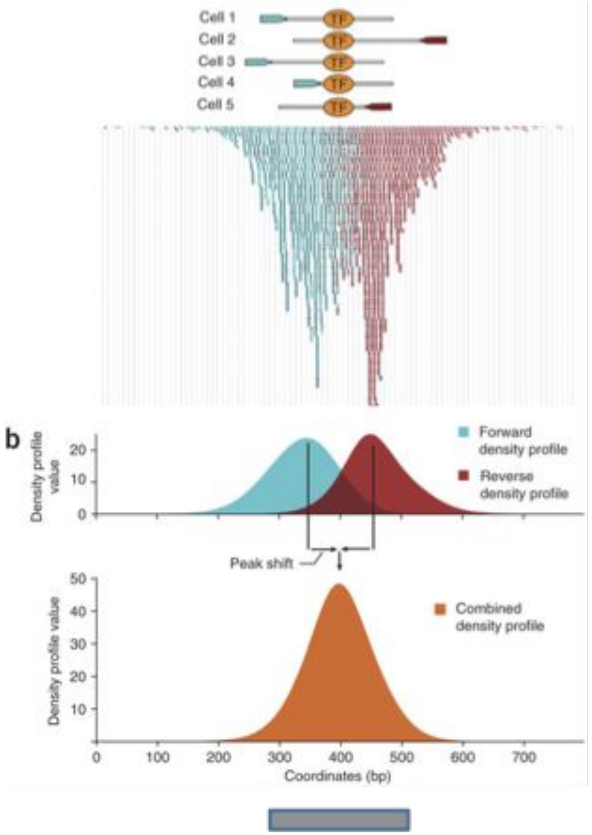






ChIP-Seq analysis in brief

- Fragments (typically ~300bp) cover the region of interest + some pieces on both side.
- We only sequence a short read on one or both extremities
- **The binding site is thus generally not in our reads !**
- Solutions
  - Bioinfo read extension
  - Bioinfo: read shifting
  - Experiment: Exo-ChIP (digest flanks between sequencing).

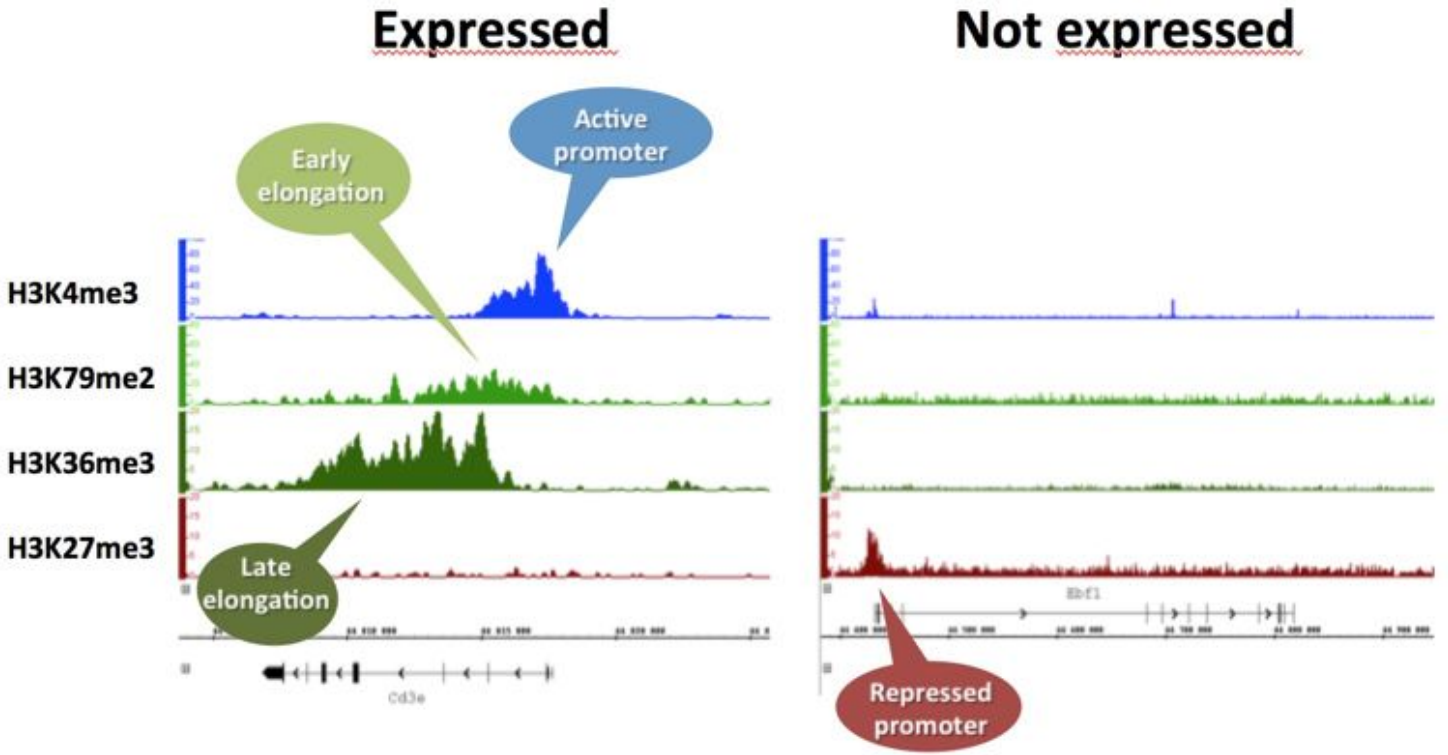


Aligned reads

Binding profile

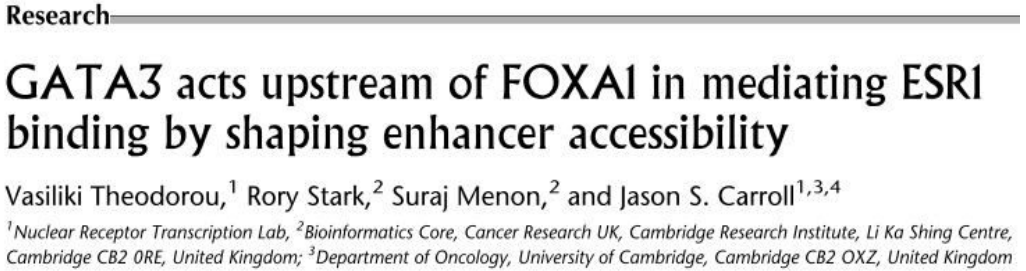
Binding Peak

Epigenetic modifications of histones



Dataset used

- Estrogen-receptor (ESR1) is a key factor in **breast cancer development.**
- Goal of the study: understand the dependency of ESR1 binding on presence of cofactors, in particular GATA3, which is mutated in breast cancers.
- Approaches: GATA3 silencing (siRNA), ChIP-seq on ESR1 in WT vs. siGATA3 conditions, chromatin profiling.



Research

GATA3 acts upstream of FOXA1 in mediating ESR1 binding by shaping enhancer accessibility

Vasiliki Theodorou,[1] Rory Stark,[2] Suraj Menon,[2] and Jason S. Carroll[1,3,4]

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Theodorou,V., Stark,R., Menon,S. and Carroll,J.S. (2013) GATA3 acts upstream of FOXA1 in mediating ESR1 binding by shaping enhancer accessibility. *Genome Res*, **23**, 12–22.