Clinical and Research Genomics
Lecture 03-04
Chromatin and Nuclear Dynamics

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We knew something was different before we knew exactly why

Waddington’s “Epigenetic Landscape” is a lineage decision metaphor for all cells

Barth and Imhof, 2010
Epi:

From the Greek: ἐπί
over, on top of

Allergy Prevention: Epi-pen

Mind-Body Theory: Epi-phenomenalism
The old model was a simple “ball and stick” for active DNA and inert histones
Now we know much more; closer to a “histone code”

Strahl and Allis, 2000

Barth and Imhof, 2010
Four main histones form an octet holding 147 base pairs
Many modifications of $H(X)(Y)(Z)$

<table>
<thead>
<tr>
<th>Superfamily</th>
<th>Family</th>
<th>Subfamily</th>
<th>Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linker</td>
<td>H1</td>
<td>H1F</td>
<td>H1F0, H1FNT, H1FOO, H1FX</td>
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<td></td>
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<td>HIST1H1A, HIST1H1B, HIST1H1C, HIST1H1D, HIST1H1E, HIST1H1T</td>
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<td>H2AF</td>
<td>H2AFB1, H2AFB2, H2AFB3, H2AFJ, H2AFV, H2AFX, H2AFY, H2AFY2, H2AFZ</td>
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<tr>
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<td>HIST1H2AA, HIST1H2AB, HIST1H2AC, HIST1H2AD, HIST1H2AE, HIST1H2AG, HIST1H2AI, HIST1H2AJ, HIST1H2AK, HIST1H2AL, HIST1H2AM</td>
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<td>H2A2</td>
<td>HIST2H2AA3, HIST2H2AC</td>
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<td>Core</td>
<td>H2B</td>
<td>H2BF</td>
<td>H2BFM, H2BFS, H2BFWT</td>
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<td>HIST1H2BA, HIST1H2BB, HIST1H2BC, HIST1H2BD, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2BH, HIST1H2BI, HIST1H2BJ, HIST1H2BK, HIST1H2BL, HIST1H2BM, HIST1H2BN, HIST1H2BO</td>
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<td>HIST2H2BE</td>
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<td>HIST2H3C</td>
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<td>HIST3H3</td>
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<td>HIST4H4</td>
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http://en.wikipedia.org/wiki/Histone
Many sites for:
methylation, acetylation, phosphorylation, propionylation, butrylation, ubiquitination, formylation, SUMOylation, citrullination, proline isomerization, ADP-ribosylation, crotonylation
NIH Epigenome “RoadMap” is finding the marks in almost all tissues/cells

http://www.genboree.org/epigenomeatlas/index.rhtml
Most frequent mutations in pediatric GBM are histone or regulatory related.

Histone variants also rank severity of breast cancer

Histone marks blossom during development

Mid-Blastula Transition (MBT) at 3.3 hours in zebrafish

Lindeman, Dev. Cell, 2011
Peaks are clear in some cases, not as clear in others. Best to use two antibodies!

Lindeman, Dev. Cell, 2011
We are also still finding all the components of the “Histone Code”

Tan et al, Cell, 2012
67 new marks found so far this year

Tan et al, Cell, 2012
Kcr is close to Kac, but unique

Tan et al, Cell, 2012
Kcr enriched in enhancers

Tan et al., Cell, 2012
Kcr critical for male germ cell development

Tan et al, Cell, 2012
But what is the best way to find the peaks?