Unravelling Epigenomic Communication through Social Network Science: the influential role of 5hmC in the context of 3D chromatin interaction network

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Abstract

Epigenetic communication through histone and cytosine modifications is essential for gene regulation and cell identity. We have recently proposed the first framework for modelling chromatin communication to get insight on the function of epigenetic modifications in mouse ESCs. The epigenetic communication architecture was inferred from genome-wide location data plus extensive manual annotation. Our analysis of this directional communication network revealed that the elongating form of RNA Polymerase 2 (RNAPII-S2p) receives information from most of the system. We also discovered that 5-hydroxymethylcytosine (5hmC) is the most influential signal and that 5hmC co-localization with specific interactors points to different important processes for ESCs. An evolutionary analysis also showed that 5hmC mediates the co-evolution of proteins involved in 5hmC-dependent communication (Juan et al. 2016).

Intrigued by our findings, we explored these communication hubs in the context of the 3D chromatin network. We have recently developed a powerful method, inspired from social-sciences and denoted as Chromatin Assortativity (ChAs), to identify important epigenetic features in different types of chromatin contacts. Application of this method to state-of-the-art promoter-centred chromatin interaction networks in ESCs showed that RNAPII-S2p plays a prominent role in promoter/active-enhancer contacts (Pancaldi et al. 2016).

Here, for the first time, we are assessing the importance of 5hmC in the 3D chromatin contact network. Extending ChAs to pairs of features, we study how 5hmC's different roles, associated to the presence of specific interactors, might play a role in promoter-promoter and promoter-enhancer contacts. Furthermore, we investigate the relevance of 5hmC in defining specific regulatory states in chromatin communities implicated in distinct functional processes.

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Pancaldi V, et al. Genome Biol., 2016, 17(1):152.