Translating Chromatin Interactions towards the Clinic through Machine Learning and CRISPR-based Methods

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Precision medicine raises the enticing possibility that one day, we can develop individualized medicine by obtaining individual data. To make this a reality, we need to better characterize genomic elements and features of our genome. In the first project, we found that super-enhancers are highly associated with chromatin interactions, and testing of individual chromatin interactions in patient samples showed differences between different individuals. We then used machine learning to predict chromatin interactions from clinical cancer datasets of open chromatin regions and identified chromatin interactions that vary between different individuals, and chromatin interactions distinguished between different subsets of leukemia. In the second project, we used CRISPR excision to interrogate the function of several genomic regions that loop to target gene promoters in order to better understand the roles of chromatin interactions in cells, and found that while super-enhancers are involved in upregulating the gene expression of genes to which the superenhancers loop, certain highly H3K27me3-occupied regions may behave as silencers and barrier regions in the human genome. Taken together, our results raise the possibility of using chromatin interactions as biomarkers, and help to further the development of new "personalized" therapies such as CRISPR-based therapies.