Genome architecture in action: Gene regulation via 3D chromatin organization in human, mouse and malaria parasites

Abstract: The field of regulatory genomics has recently witnessed significantly increased interest in the three-dimensional structure of DNA in the nucleus, catalyzed by the development of chromosome conformation capture techniques (e.g., Hi-C) that profile genomic proximities on a genome-wide scale. Systematic analysis of these proximities is particularly important to identify targets of disease-associated genetic variants more than 90% of which reside in noncoding regions with unknown gene targets. In this talk, I will start with an overview of the diverse uses of conformation capture data and then present two recent projects concerning the interplay between genome form and function. First, I will talk about our study on the dynamic nuclear organization of the deadliest human malaria parasite (*Plasmodium falciparum*). Our study revealed that the parasite has a complex genome architecture shaped around precisely regulating its virulence genes and that this architecture goes through holistic changes in correlation with the parasite’s overall transcriptional activity during its cell cycle in human blood. Next, I will present a novel statistical method, *Fit-Hi-C*, for assigning confidence estimates to chromosome conformation capture data. Applied to Hi-C data from various human and mouse cell lines, *Fit-Hi-C* identified significant interactions that preferentially link expressed gene promoters to active enhancers, confirmed previously validated, cell line-specific regulatory interactions, and revealed that genomic regions with similar replication times prefer to be closer in 3D.