MAR11-2010-007297

Abstract for an Invited Paper
for the MAR11 Meeting of
the American Physical Society

Nanotechnology Approaches to Studying Epigenetic Changes in Cancer

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Placing polyelectrolytes into confined geometries has a profound effect on their molecular configuration. For instance, placing long DNA molecules into channels with a cross-section of about 100 nm^2 stretches them out to about 70% of their contour length. We are using this effect to map epigenetic changes on single DNA and chromatin strands. This mapping on single molecules becomes central in the study of the heterogeneity of cell population in cancer, since rapid change of epigenetic makeup, propagated through rare cancer stem cells, is a hallmark of its progression. We demonstrate the basic building blocks for the single-molecule epigenetic analysis of genomic sized DNA. In particular, we have achieved the mapping of methylated regions in DNA with heterogeneous 5-methyl cytosine modification using a specific fluorescent marker. We further show that chromatin with an intact histone structure can be stretched similar to DNA, and that the epigenetic state of histone tails can be detected using fluorescent antibodies.