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High-order chromatin architecture shapes the landscape of chromosomal alterations in cancer[1] GEOFFREY FUDENBERG, Harvard, GAD GETZ, MATTHEW MEYERSON, Broad Institute, LEONID MIRNY, MIT — The rapid growth of cancer genome structural information provides an opportunity for a better understanding of the mutational mechanisms of genomic alterations in cancer and the forces of selection that act upon them. Here we test the evidence for two major forces, spatial chromosome structure and purifying (or negative) selection, that shape the landscape of somatic copy-number alterations (SCNAs) in cancer (Beroukhim et al, 2010). Using a maximum likelihood framework we compare SCNA maps and three-dimensional genome architecture as determined by genome-wide chromosome conformation capture (HiC) and described by the proposed fractal-globule (FG) model (Lieberman-Aiden and Van Berkum et al, 2009). This analysis provides evidence that the distribution of chromosomal alterations in cancer is spatially related to three-dimensional genomic architecture and additionally suggests that purifying selection as well as positive selection shapes the landscape of SCNAs during somatic evolution of cancer cells.

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