Breast Cancer Diagnostics Based On Interphase Spatial Genome Positioning

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Genomes are non-randomly organized within the three-dimensional space of the cell nucleus. The nuclear position of many genes and genomic regions changes during physiological processes such as proliferation, differentiation and, importantly, disease. We have exploited the changes in gene positioning patterns to develop a novel diagnostic tool in the detection of breast cancer. Using an established human mammary epithelial 3D cell culture model of early breast cancer, we identified several genes which specifically reposition during tumourigenesis. We extended these studies to human tissues and, using an unbiased screening approach, we identified several genes whose nuclear positions are robustly altered in breast cancer as compared to normal tissue. These markers, used either singularly or in combination, are able to detect cancer tissues with high accuracy in a retrospective analysis. The changes in positioning are not the consequence of global spatial genome reorganization in cancer cells since we find a gene-specific repositioning behaviour. Moreover, the repositioning events are specific to cancer and do not occur in non-cancerous breast disease. These results establish spatial genome organization as a novel diagnostic strategy in cancer detection. We are currently validating our marker genes in a larger sample set and are identifying positioning markers to distinguish different cancer sub-types.