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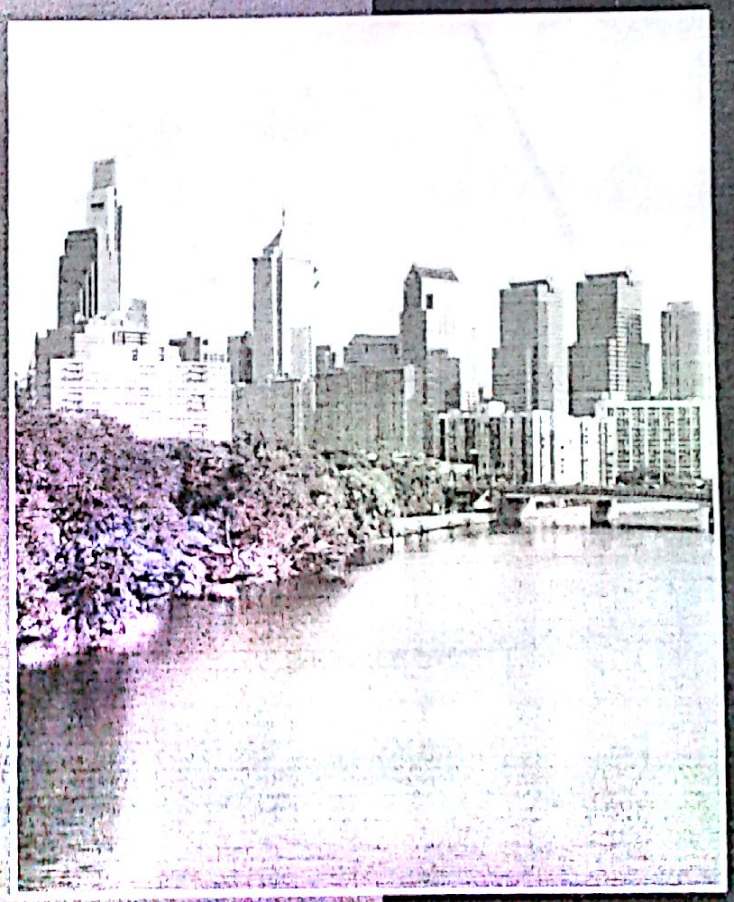

2014 International Symposium on Molecular Medicine & Infectious Diseases

DREXEL UNIVERSITY College of Medicine

ABSTRACT BOOK

2014 International Symposium on Molecular Medicine and Infectious Disease

Drexel University College of Medicine, Philadelphia, PA

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The Annual Symposium of the Institute for Molecular Medicine & Infectious Disease

Contents

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C09

A small-molecule inhibitor of RAD51 recombinase sensitizes human cancer cells to DNA damage.

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The homologous recombination pathway plays a critical role in repair of the most harmful types of DNA lesions, double strand breaks and inter-strand cross-links. RAD51 is a key protein of homologous recombination. RAD51 carries out the essential steps of homology searching and strand exchange between broken and intact DNA molecules. Recently we developed a DNA strand exchange assay to screen a 202,556-compound library for inhibitors of the RAD51. We indentified a specific RAD51 small molecule inhibitor B02. In vitro B02 efficiently inhibits the strand exchange activity of RAD51, but not of its ortholog EcRecA. We demonstrated that B02 binds to RAD51 directly with Kd ~ 5.6 μM. The mechanism of B02 inhibition of RAD51 includes disruption of RAD51 binding to ssDNA and also inhibition of dsDNA binding by the RAD51-ssDNA filament. In vivo, B02 suppresses IR-induced RAD51 foci formation, reduces gene conversion and increases cell sensitivity to cross-linking agents, cisplatin and mitomycin C. We found that B02 significantly enhances killing of human breast cancer cells MDA-MB-231 by cisplatin both in cell culture and in mouse xenografts.

C10

High-throughput single molecule whole genome mapping in nano-channels

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Despite recent advances in high throughput DNA sequencing, de novo assembly of short sequencing reads remains a significant technical challenge. The presence of structural variation and repetitive elements with near-identical sequence motifs makes sequence assembly extremely difficult. Long-range haplotypic information often needs to be bioinformatically inferred, and experimental validation is labor-intensive. Therefore, we have developed an nano-mapping approach that can provide scaffolds for sequence assembly and complement analysis of structural variation. Long DNA molecules (up to several hundred kb) labeled at sequence-specific sites are linearized in silicon-based nano-channels. High-resolution imaging of individual labeled DNA molecules allows us to measure inter-marker distances to generate nano-maps of distinct haplotypes.

C11

Effects of electrically generated non-thermal plasma on metabolism of metastatic prostate cancer cells

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Metastatic cancers, including prostate cancer, currently remain incurable diseases. There is an urgent need for novel medical approaches to treat metastatic tumors, which tend to be resistant to chemo- and radiation therapy. Non-thermal plasma discharges and electrical fields have been studied for a variety of biomedical applications, including their ability to induce apoptosis as a possible method of cancer eradication. The cellular intrinsic apoptotic pathway is mediated by mitochondria, therefore the mitochondria energetics is a plausible target for cancer therapy. This work aimed to explore the effects of microsecond electrical plasma discharges on bioenergetic processes in metastatic prostate cancer cells. Earlier we demonstrated that, different from some other tumors, prostate cancer cells have very actively