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TITLE

Anticancer Drug Resistance in Yeast Translocants

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A chromosomal translocation is caused by rearrangements of chromosomal fragments between two non-homologous chromosomes. These chromosome aberrations are characteristic of many human diseases, including cancer. Recently, the Bridge Induced Translocation technique (BIT) was developed to generate non-reciprocal translocations between any desired loci in *S. cerevisiae* cells, which could serve as a model system for investigating gross chromosomal rearrangements and neoplastic transformation in higher organisms. Besides affecting DNA replication, cell cycle, karyogamy, cytokinesis and producing genetic instability, this event can lead to upregulation of 20 genes involved in response to toxins, including pleiotropic drug resistance transcriptional factor genes, and increased resistance to anticancer chemicals like Doxorubicin and Latrunculin A via endocytic actin network deregulation triggered by over-expression of the PRK1 serine/threonine protein kinase gene. This effect can be further enhanced by the overexpression of PDR1 and PDR3 transcriptional regulators of pleiotropic drug resistance factors. However, when the actin depolymerizing drug Latrunculin A penetrates through the cell wall and membrane barriers, it can kill translocants more efficiently than wild type cells. These observations provide an example of an acquired anticancer drug resistance mechanism and could serve as a lead to how it might be overcome, as any treatment inhibiting genome rearrangements could increase the positive outcome of anticancer therapy by reducing cellular drug resistance.

Biography

Dmitri Nikitin, male, molecular biologist, graduated from biology department, Samara State University in 1993. He worked for Acad. Skryabin's Institution of biochemistry and physiology of microorganisms (Pushchino, Russia) from 1993 to 2005, and International center for genetic engineering and biotechnology (Trieste, Italy) from 2005 to 2009. He obtained his PhD in 1999 at Institute of industrial microorganisms (Moscow, Russia). By now he has published 10 papers and attended 12 international conferences. D. Nikitin trained 12 undergraduate, master and PhD students; participated in 9 international grants and got 6 awards, including award of Russian Science Support Foundation Program "Outstanding scientists. Candidates and Doctors of Science for 2004 year". The awards have been nominated for his success in characterization of different restriction-modification systems, microbial pathogenic factors and description of new microbial taxons. He is member of Russian Biochemical society from 1997 and reviewer of international scientific journals. Recently his research concerns with characterization of molecular and cellular effects of chromosomal translocations on eukaryotic (*Saccharomyces cerevisiae*) cells using proteome, transcriptome and different cellular biology approaches.