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Short Communication

The Budding Yeast *Saccharomyces cerevisiae* as A Model System for Anti-Cancer Drug Screening

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1. Short Communication

The yeast Saccharomyces cerevisiae is widely used as a model organism to investigate many aspects of eukaryotic cell biology. It has a high level of conservation between its cellular processes and those of mammalian cells with advantages such as simple growth requirements and rapid cell division. Moreover, it is a genetically tractable organism, amenable to modifications such as gene disruption, gene marking and protein-protein interaction with the yeast two-hybrid system. Up to now, yeast has maintained its role as a useful model system for fundamental studies related to disease processes. Indeed, some studies revealed the presence of a regulatory network on apoptosis in yeast that encompasses many of the crucial events that occur in mammalian cells [1]. Comparison of the yeast and human genomes, reported in 1997, revealed that 30% of known genes involved in human diseases have yeast orthologs (i.e. functional homologs) [2]. Yeast models have been employed to study numerous molecular aspects directly related to cancer development, as well as to determine the genetic contexts associated with anticancer drug sensitivity or resistance. Using the available collections of yeast deletion mutants, many different genome-wide screens have been conducted. For example, some of the genome-wide studies identified new mechanisms of resitance to several anti-cancer drugs such as cisplatin, oxaliplatin, mitomycin C, camptothecin and bleomycin-A5, all of which act by damaging the DNA [3-5]. In the screen performed to identify yeast deleted genes that conferred resistance to cisplatin, a chemotherapeutic drug used for treating a variety of cancers, revealed that the uptake of this anticancer drug is mediated by the *CTR1* gene, which encodes a high-affinity copper transporter [6]. The same group has identified the human gene *CTR1* (*SLC31A),* the functional homolog of the yeast CTR1, which also encodes a cisplatin transporter *[6].* Likewise, the genome-wide screen performed with blemoycin-A5, another potent chemotherapeutic agent that can mediate cell killing by attacking the DNA and used in combination therapy for treating various cancers including testicular carcinomas, revealed that Agp2, a plasma membrane protein of the amino acid transporter family, is involved in the high-affinity uptake of this anticancer drug, as well as various substrates including L-carnitine [3]. This observation in yeast led us to uncover that the human L-carnitine transporter hCT2 encoded by the SLC22A16 gene is involved in bleomycin-A5 uptake [7]. We showed that the human NT2/D1 testicular cancer cells, which highly express hCT2, were extremely sensitive to bleomycin-A5, whereas the human HCT116 colon carcinoma cells devoid of detectable hCT2 expression, or the human MCF-7 breast cancer cells that only weakly expressed this permease, showed striking resistance to the drug [7]. Collectively, it is clear that studies from the yeast genome-wide screens have demonstrated the tremendous potential of this organism as a model system for anticancer drug discovery. We believe that this system will continue to hold great promises in genome-wide screening analyses, and to identify novel molecular mechanisms from which lead compounds can be derived that have the potential to become marketable drugs for cancer treatment.

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