КРАТКИЕ СООБЩЕНИЯ

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A SUPPRESSOR LINE-1: PROTECTS CANCER CELL FROM THE DRUG

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The maintenance of phenotypic heterogeneity in the cell population is a mechanism of evolutionary conservatism, which is a mechanism for population survival stress exposure. The researchers found that the genome of the cancer cell subpopulation survived the next one when using other lethal drugs (DTPS) and showed a suppressed chromatin state characterized by histone H3 lysine 9 and 27 (H3K9 and H3K27) increasing degree of methylation.

Key words: Line-1, cancer, heterogeneity, drug resistance.

LINE-1 was first reported what on breast ductal carcinoma by the Astrin teams from the United States, through activation of the proto-oncogene MYC. Four years later, the Nakamura group in Japan reported that the last exon of the APC inserted by the LINE-1 transposon, inactivated the APC gene and eventually resulted in colon cancer case. This is the first case to prove that the LINE-1 can cause cancer by inactivating tumor suppressor gene, but limited by technology. There hasn't been some new progress in the study of LINE-1 over the next decade. In recent years, the development of molecular biology technology has opened a new chapter in LINE-1 research.

In the evolutionary process, activation and propagation of TEs allow the organism to adapt to the changing conditions by generating genomic diversity, but can also result in reduced fitness. Thus, the organism has established complex mechanisms to control their activation. In the context of heterogeneous cancer cell drug reactions, activation of TEs can provide the benefits of adaptation during drug exposure, but their activation may also damage the health of cancer cells. Therefore, apparent genetic inhibition of TEs can provide a resistant population with a reversible genetic protection mechanism to ensure cell survival during lethal drug exposure.

Content

Recently, an article in the journal “Cancer cell” has reported that repression of stress-induced LINE-1 expression protects cancer cell subpopulations from lethal drug exposure. Drug tolerance is a huge obstacle in the subsets of different cells in a variety of pathologies, including bacterial infections and cancer. In bacteria, a relatively quiescent subpopulation of antibiotic-resistant cells, referred to as ‘‘persisters’’, exhibits reversible and transient drug-tolerant properties. And these properties in the face of potentially harmful fluctuations in the environment, this mechanism eliminates the requirements of a wide range of genomic mutations, which are irreversible and may reduce “fitness” that has been implicated in a ‘‘bet-hedging’’ strategy that ensures population survival. In the context of cancer, innate and acquired drug resistance remains the main limitation of all the therapies (Fig. 1).

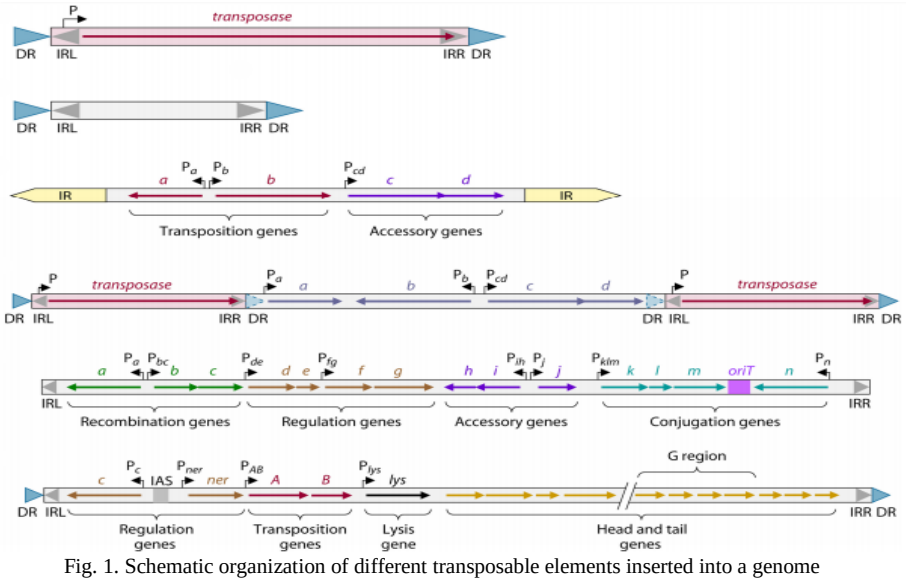

Fig. 1. Schematic organization of different transposable elements inserted into a genome

Researchers have previously discovered a largely metastatic cancer cell subpopulation that survives in fatal drug contact, drug-resistant persistence (DTPs) (Fig. 2). These cells as a founder of the disease recurrence can occur through mutations and non-mutational mechanisms. DTPs are derived from a dynamically fluctuating cancer stem cell population showing characteristic and metabolic changes, DTP reversible characteristic states, which involve the table view of the genetic mechanism in their survival. The epigenetic regulatory mechanism plays a vital role in many aspects of biology and allows cellular response signals to determine the fate of the norm and the stability of the genome during development, and to provide a mechanism for biotic adaptation to environmental changes (Fig. 3).

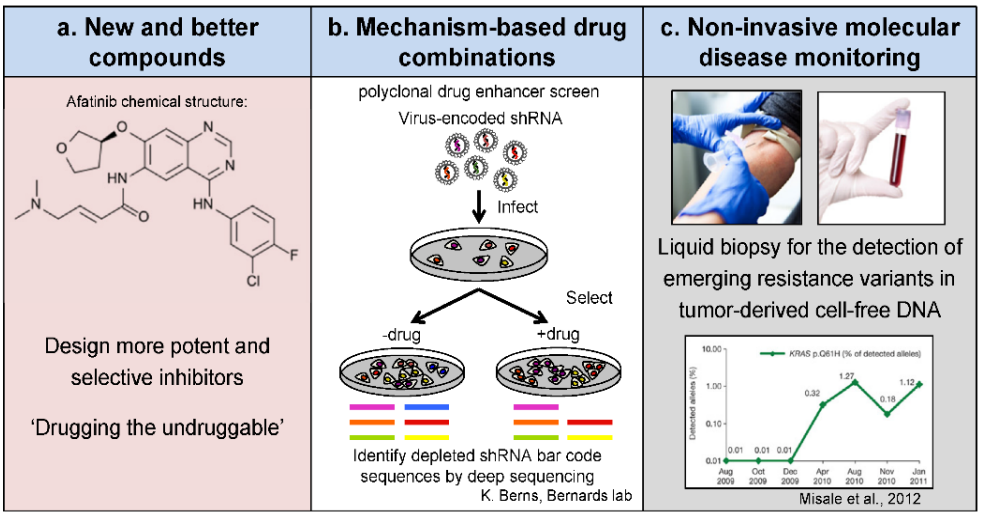

Fig. 2. Strategies to overcome intrinsic resistance and delay acquired resistance

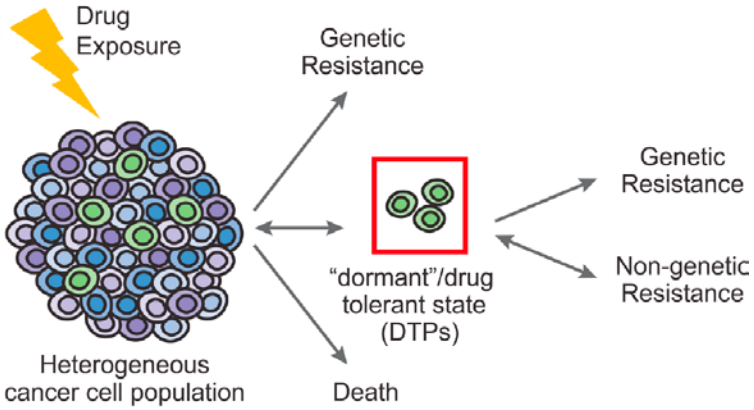

Fig. 3. Schematic representation of heterogeneous responses to drugs in cancer cells

Maintenance of phenotypic heterogeneity within cell populations is an evolutionarily conserved mechanism that underlies population survival upon stressful exposures. Researchers have found that the genome of the cancer cell subpopulation survived the use of other lethal drugs (DTPs) and exhibits a repressed chromatin state characterized by increased methylation of histone H3 lysine 9 and 27 (H3K9 and H3K27). We also show that the survival of DTPs is maintained by H3K9me3-mediated regulators of heterochromatin formation, whereas the increase in H3K9me3 observed in DTPs is most pronounced for long-term cross-repeat elements 1 (LINE-1). In DTPs, the destruction of LINE-1 by oppressive chromatin resulted in DTP ablation, partly by reducing line-1 expression or function.

Conclusion and Significance

The drug-resistant cell population in heterogeneous tumors can serve as a major cause of the recurrence of disease, which remains a major obstacle to successful cancer treatment. Our findings establish a paradigm that a high degree of apparent repression of repetitive genomic elements contributes to the survival of the "resistant" subgroups of cancer cells as a drug-induced elements. Balance of the antiviral defense contributes to the genomic stability and fitness of cancer cell subpopulations. These observations reveal a potential chance of disrupting drug resistance in order to more effectively inhibit the acquired drug in clinical trials often observed for antimicrobial resistance.

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INTENSE PULSED LIGHT AS A NEW TREATMENT FOR BLEPHAROKERATOCONJUNCTIVITIS: A CASE REPORT

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Blepharokeratoconjunctivitis (BKC) refers to a series of conjunctival and corneal disease secondary to blepharitis. Intense pulsed light (IPL) devices contain high-intensity light sources, which emit polychromatic light from 515 nm to 1200 nm. We report the effect of IPL in three cases of BKC.

The first case presented eyelid congestion; crusting and scaling at the eyelash root; meibomian gland obstruction and conjunctival hyperemia in both eyes. The left eye presented old central corneal scarring with neovascularization. BKC was diagnosed. The male patient was treated with three times of IPL and traditional treatment. The second case presented scaling and sleeve-form crusting at the eyelash root; meibomian gland arranged irregularly with opening obstruction; marked conjunctival hyperemia in both eyes. The left eye presented opacities with much neovascularization. In vivo confocal microscopy and optical microscopy examination of eyelid lash showed there were lots of Demodex folliculorum mites in the eyelash follicles. Demodex folliculorum mitesin festation and BKC were diagnosed. The female patient was treated with once of IPL and traditional treatment. The third case presented eyelid congestion; meibomian gland pouting and capping; conjunctival hyperemia and marginal infiltrates of cornea with pannus formation in both eyes. BKC was diagnosed. The female patient was treated with twice of IPL and traditional treatment.

The first case recovered within 17 days. The second case recovered within 23 days. The third case recovered within 14 days. And their ocular surfaces were stable at 1-month follow-up.

Compared with topical medicine treatment of BKC requiring at least 1 month, IPL treatment shortened the course of BKC.

Key words: blepharokeratoconjunctivitis (BKC); treatment; intense pulsed light.

Blepharokeratoconjunctivitis (BKC) refers to a series of conjunctival and corneal disease secondary to blepharitis. Intense pulsed light (IPL) devices contain high-intensity light sources, which emit polychromatic light from 515 nm to 1200 nm. We report the effect of IPL in three cases of BKC [1].

Case report

The first case was a 10-year-old boy. He presented eyelid congestion; crusting and scaling at the eyelash root; meibomian gland obstruction and conjunctival hyperemia in both eyes (Fig. 1).

The left eye presented old central corneal scarring with neovascularization. BKC was diagnosed. He was treated with three times of IPL and traditional treatment. The corneal scarring and neovascularization reduced after first IPL treatment and he recovered within 17 days (Fig. 2).