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Novel Drugs Targeting for Immunogenic Cancer Cell Death

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Abstract

The unique characteristics of lysosomes in cancer cells, including their number and stability, make them an attractive target for cancer-specific therapies. However, no lysosome-targeting drugs have been approved for clinical use. Here, we describe a novel therapeutic approach utilizing reversible thiol binder 11, which selectively accumulates in the lysosomes of cancer cells. Thiol binder 11 increases lysosomal reactive oxygen species (ROS), leading to lysosomal destabilization, disruption, and subsequent immunogenic cancer cell death—effects that are not observed in healthy cells.

In a murine sarcoma Nemeth-Kellner (NK)/Ly-RB model, treatment with thiol binder 11 significantly extended the lifespan of mice from 21 to 85 days and resulted in complete cures in 40% of the cohort. Remarkably, the cured mice developed tumor-specific antibodies, and a subsequent challenge with NK/Ly-RB cells led to 100% survival, compared to 0% in the control group of naïve mice.

Ex vivo analyses revealed that neutrophils from the spleens of cured animals contributed to the antitumor response by producing neutrophil extracellular traps (NETs), further supporting the immune-mediated effects.

In conclusion, thiol binder 11 exerts a direct antitumor