Abstract #7056

Telomir-Zn: A Novel Metal Ion Regulator Affecting Age-Related Disorders and Cancer

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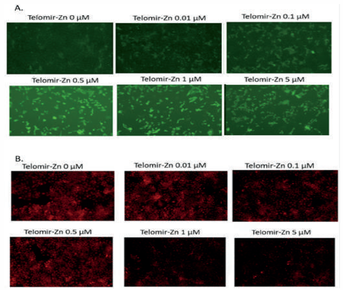
Introduction

Telomir-Zn is a first-in-class small-molecule metal modulator engineered to selectively control intracellular iron and copper homeostasis. It is being developed as a therapeutic candidate for aging-related diseases and cancer, leveraging its dual mechanism of action on metal balance and epigenetic regulation.

Many epigenetic enzymes, including iron- and copper-dependent histone demethylases (KDMs), are overactive in aggressive cancers and require metal cofactors to function. This creates a metabolic–epigenetic dependency where malignant cells rely on elevated iron and copper to maintain a permissive epigenetic state for proliferation and survival.

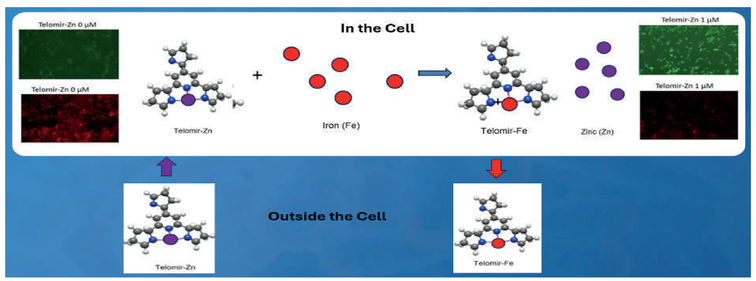
Telomir-Zn targets this vulnerability. By precisely regulating labile intracellular iron and copper pools, it disrupts metal-dependent epigenetic enzymes and reactivates silenced tumor-suppressor programs while simultaneously restricting redox-driven tumor metabolism. This dual mechanism positions Telomir-1 as a novel therapeutic strategy that links metal biology, chromatin control, and cancer cell vulnerability, with potential applications in iron-dependent and epigenetically dysregulated malignancies such as triple-negative breast cancer and prostate cancer.

Mechanism of Action



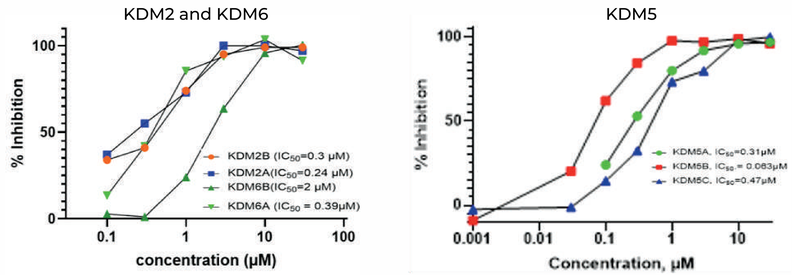
Reciprocal intracellular zinc accumulation and labile iron depletion following metal modulation.

(A) HaCaT cells stained with the zinc-selective probe DA-ZP1
(B) FerroOrange staining demonstrating intracellular labile ferrous iron (Fe^{2+}) levels following 2-hour Telomir-Zn exposure.



Intracellular Ion Exchange
Telomir-Zn enters the cell, captures excess iron or copper, and swaps them for protective zinc — removing toxic metals and restoring healthy cellular balance

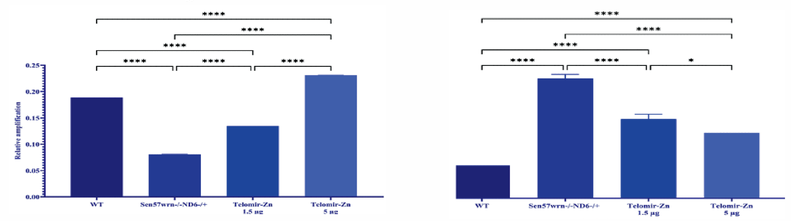
KDMs



Telomir-Zn Potently Inhibits Histone Demethylases (KDMs) - KDM2, KDM5 and KDM6

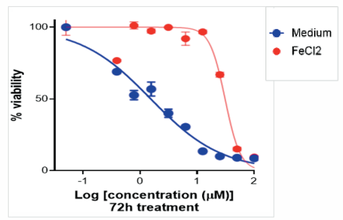
Aging

Telomir-1 Restores ROS and Telomer Length in a Zebrafish Model of Werner Syndrome



Relative telomeric DNA content assessed by PCR-based comparative amplification and brain reactive oxygen species (ROS) levels measured in wild-type (WT), Sen57^wrn−/−^ND6^−/+^, and treated zebrafish.

Cancer in Vitro



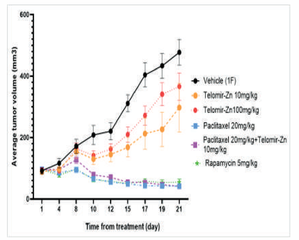
Anti-cancer activity in TNBC cells –
MDA-MB 468 Cells Effect of iron. Viability evaluated by live cell counting at 72 hours. FeCl2 at 10 µM was co-incubated with Telomir-Zn at the indicated concentration

Cell line used	Cancer Type	Telomir-Zn IC_{50} (µM)
HCC 1806	TNBC	0.87
MDA-MB-468		1.5
HCC 70		3.6
HL 60	Leukemia	1.6
PC3	Prostate (Androgen-independent)	14.3
LNCap	Prostate (Androgen-dependent)	21.3
PANC-1	Pancreatic	38.6
HaCat	Normal keratinocytes	>50

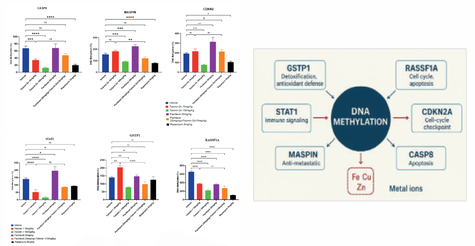
Telomir-Zn reduced cell viability most potently in TNBC and other cells and does not affect viability in normal cells

Cancer in Vivo

Anti-Cancer Activity in Prostate Cancer Xenograft (PC3) Mice Model

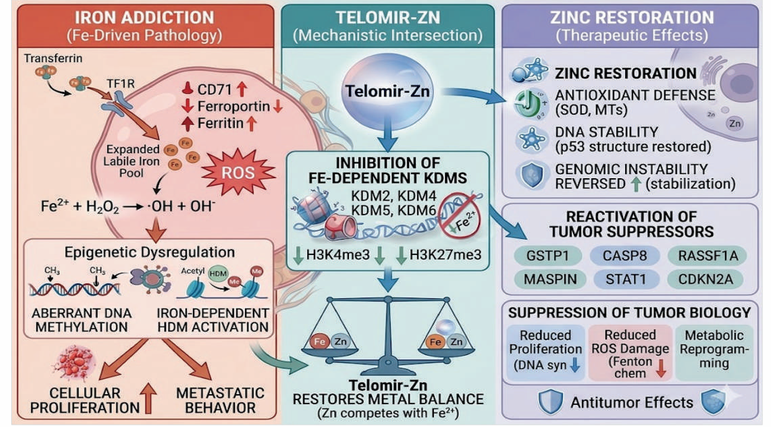


Telomir-Zn Reduces DNA Methylation of Key Proteins



Prostate cancer progression is driven by abnormal DNA methylation that silences key tumor-suppressor genes. Reducing this hypermethylation restores tumor-suppressor gene functions and supports cellular protection. DNA methylation evaluated on tumors on day 21.

Telomir-Zn: Restoring Homeostasis in Iron-Addicted Cancer



Summary

Many cancers exhibit an iron addiction, and expansion of the labile iron pool, promoting ROS generation and activity of Fe^{2+}-dependent lysine demethylases (KDMs).
Telomir-Zn restores metal homeostasis by introducing redox-inert zinc, reducing catalytic Fe^{2+} availability and inhibiting KDM activity.

This leads to accumulation of activating histone methylation marks and reactivation of tumor suppressor genes.

Together, these effects reduce oxidative stress, proliferation, and metabolic signaling, ultimately suppressing iron-driven tumor growth.