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REACT Redox disruption against circulating tumor cells

Introduction

Metastatic disease is a dynamic process in which established metastases can release metastasis-derived circulating tumor cells (mCTCs), promoting lesion reseeding and further metastatic spread. Survival in circulation requires transient cellular adaptations that remain poorly characterized.

Unmet Medical Need

Current neoadjuvant and adjuvant therapies are primarily designed to reduce tumor burden and eliminate residual disease, rather than directly interfere with metastatic dissemination. No approved therapy specifically targets CTCs or the transient cellular states that enable their survival in circulation. Moreover, the rarity of CTCs and the limited availability of matched primary, metastatic, and circulating tumor-cell populations have hindered the identification of actionable CTC-specific vulnerabilities. New therapeutic strategies capable of selectively targeting tumor cells during vascular dissemination therefore represent an important unmet medical need.

Solution

A distinctive metabolic state has been identified in mCTCs, characterized by restrained mitochondrial respiration, limited respiratory reserve, and increased redox stress. This phenotype is rapidly reversed upon re-adhesion, indicating a transient adaptation associated with the circulating state. While supporting cellular fitness during vascular transit, this adaptation creates a selective vulnerability to pharmacological disruption of redox homeostasis. Targeting this vulnerability increases mitochondrial oxidative stress, selectively reduces mCTCs viability in vitro and decreases circulating tumor-cell and pulmonary metastatic burden in vivo.

Advantages

- Dissemination-focused: acts on the circulating phase of metastatic progression rather than tumor bulk, preferentially targeting mCTCs.
- Mechanistically supported: validated through integrated molecular, metabolic, and functional analyses.
- Preclinically validated: supported by both in vitro and in vivo proof-of-concept.
- Complementary: potentially compatible with existing tumor-directed therapies.

Opportunity

Istituto Europeo di Oncologia is seeking **industrial partners** (license or co-development opportunities)

Inventors



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IP asset: Patent application IT-102026000026008; co-owned by IEO and University of Milan.

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