NEW COMPOUNDS AGAINST CANCER STEM CELLS

Novel iron chelators efficient in triple negative breast cancer thanks to an original mechanism of action allowing the disruption of cancer stem cells iron homeostasis

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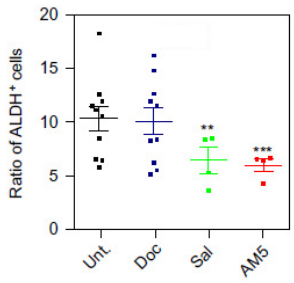
PRESENTATION

The concept of cancer stemness is largely known and based on the hypothesis that a rare population of cells (cancer stem cells) is able to promote tumour growth, metastasis formation and recurrence after therapy. Triple negative breast cancers (TNBCs) are largely treated with broad-based chemotherapies, such as taxanes and anthracyclines while no specific compound is available. TNBC patients, representing 10 to 15% of all breast cancer cases, often encounter tumour recurrence and metastasis formation, including in brain. The present offer proposes a new family of 25 Salinomycin derivatives that was created to improve the original product profile and then evaluated against TNBC cancer stem cells in vitro and in vivo for the best one. Preliminary administration and toxicities studies were performed. The demonstrated mechanism of action is original. The hit compound is able to disrupt, both in vitro and in vivo, cancer stem cell iron homeostasis leading to reactive oxygen species production and lysosomal cell death. It also strongly reduces cancer stem cell population and its seeding capacity in two PDXs (patient-derived xenografts) models during in vivo limiting-dilution assays.



The remaining cancer stem cell population was quantified (using ALDH marker) from previously treated PDX-tumours implanted in mice. AM5 compound is more potent that Sal (Salinomycin) and Doc (docetaxel) for targeting cancer stem cells ® Mai et al. Nat Chem 2017.

Cancer stem cells - Iron homeostasis - Salinomycine derivatives - Triple negative breast cancer - Reactive oxygen species

COMPETITIVE ADVANTAGES

- New mechanism of action
- Targeted therapy
- Prevention of recurrence and metastasis development
- Hit molecule crossing the blood-brain barrier to potentially target brain metastases

APPLICATIONS

- Treatment of cancer, preventing recurrence and metastasis development, in triple negative breast cancer
- Potential treatment for other cancers

PUBLICATIONS

Mai et al. *Nature Chemistry* 2017 Oct.9:1025

DEVELOPMENT PHASE

- *In vivo* efficacy demonstration of the hit in PDXs (patient-derived xenografts) from triple negative breast cancer patients

INTELLECTUAL PROPERTY

International patent application No. WO2016/038223 filed on September 14, 2015

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