SELECTED OPPORTUNITIES IN ONCOLOGY

Targeting Myeloperoxidase Overcomes Cytarabine Resistance in Human Acute Myeloid Leukemia

TARGETING MYELOPEROXIDASE OVERCOMES CYTARABINE RESISTANCE IN HUMAN ACUTE MYELOID LEUKEMIA

Product factsheet

Preclinical

- **Product:** a MPO inhibitor

- **Rational / POC:**
  - Chemoresistant acute myeloid leukemia (AML) cells have a decreased level of mitochondrial and cytosolic ROS associated with an overexpression of myeloperoxidase (MPO)
  - High MPO-expressing AML cells are less sensitive to AraC *in vitro* and *in vivo*
  - Targeting MPO expression and enzyme activity sensitizes to AraC treatment through triggering a sustained oxidative stress in the high expressing MPO AML cells. This is due to superoxide accumulation in mitochondria that impairs OXPHOS metabolism drives apoptotic death and selective eradication of chemoresistant AML cells *in vitro* and *in vivo*.

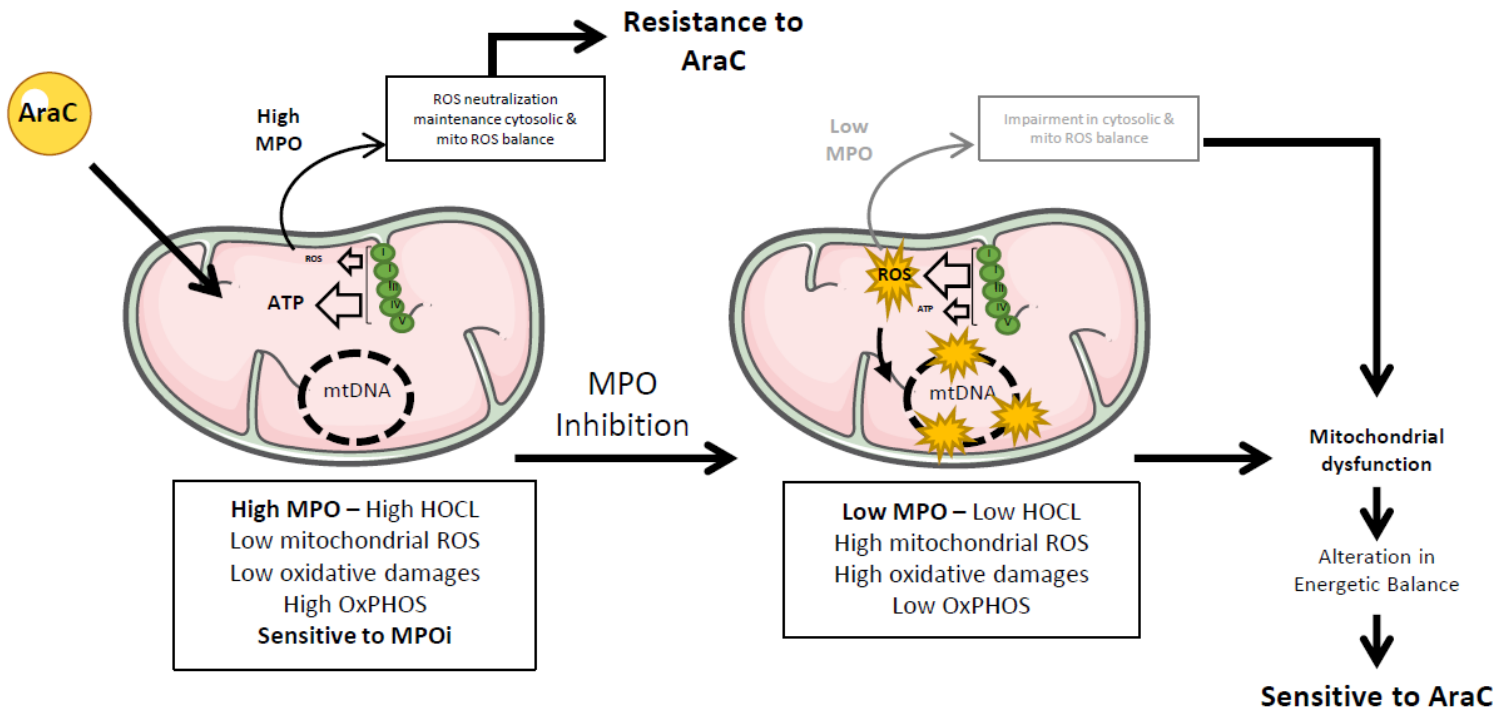
- **Patent and publication:**
  - USE OF MYELOPEROXIDASE (MPO) INHIBITORS FOR THETREATMENT OF CHEMORESISTANT ACUTE MYELOID LEUKEMIA (AML) **PCT/FR2018/051889**
  - Targeting Myeloperoxidase Overcomes Chemoresistance in Human Acute Myeloid Leukemia Hosseini M et al. Submitted for publication

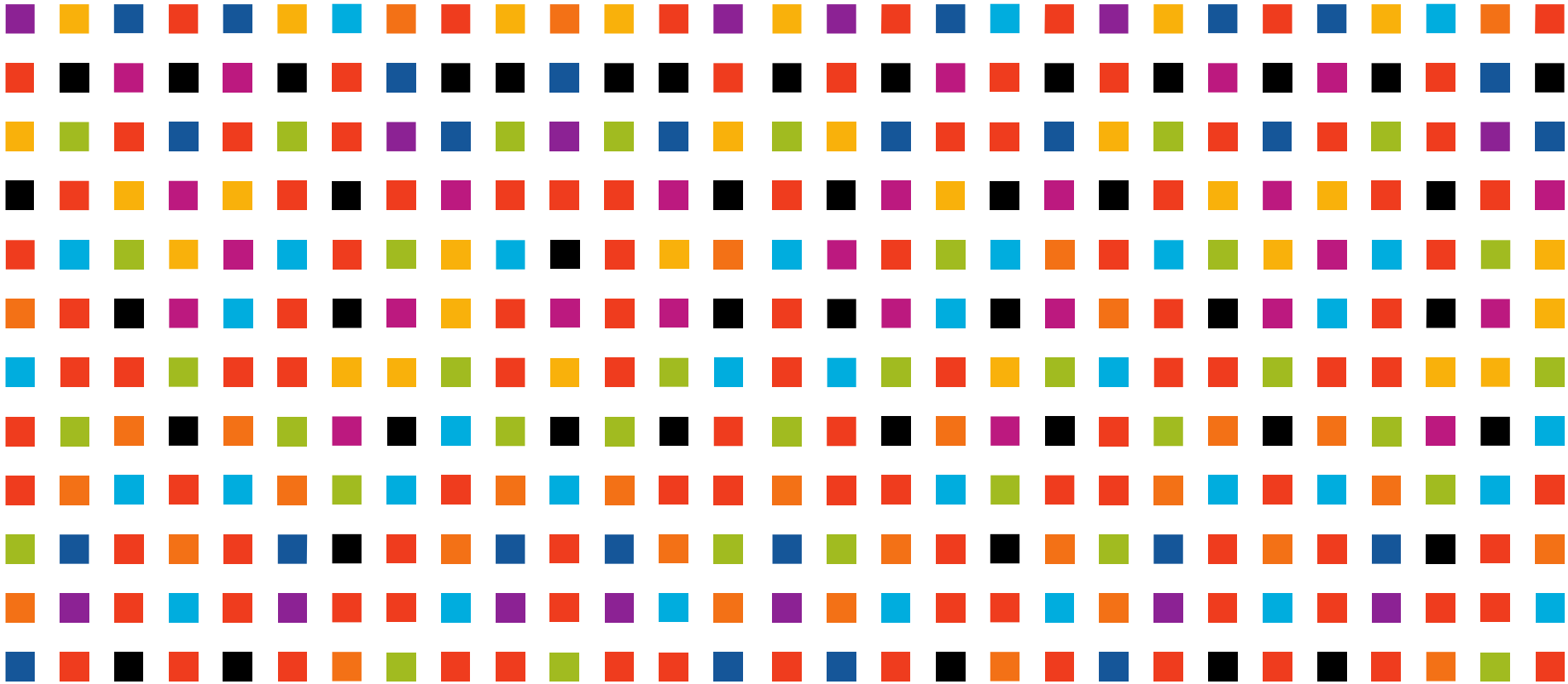
Targeting Myeloperoxidase Overcomes Cytarabine Resistance in Human Acute Myeloid Leukemia

Proof of concept

Preclinical

Schematic diagram of mechanism of action of MPO in AML cells post AraC





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