Role of CtBP in Cancer: A Central Hub Connecting Growth, Migration and Death

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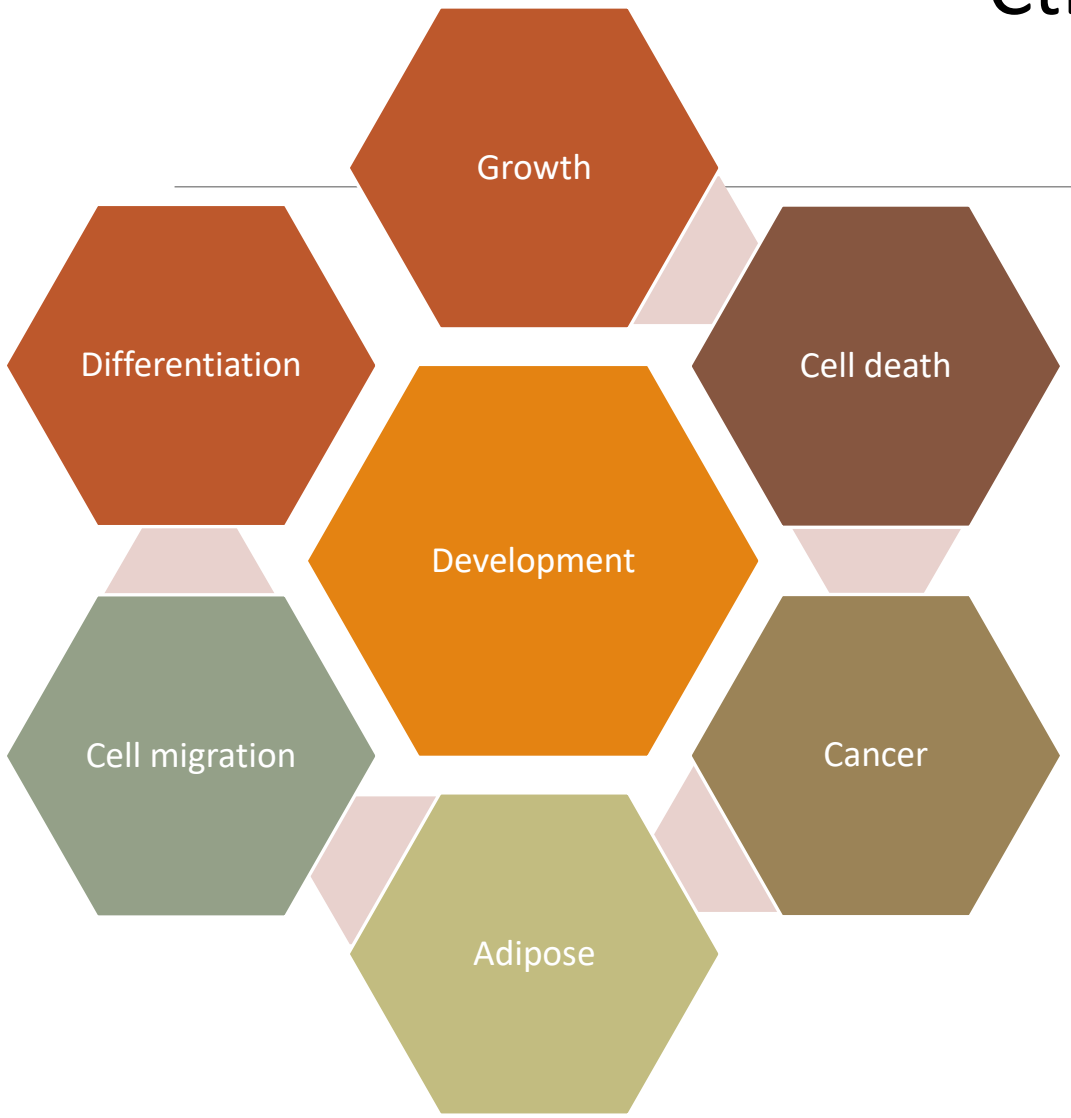
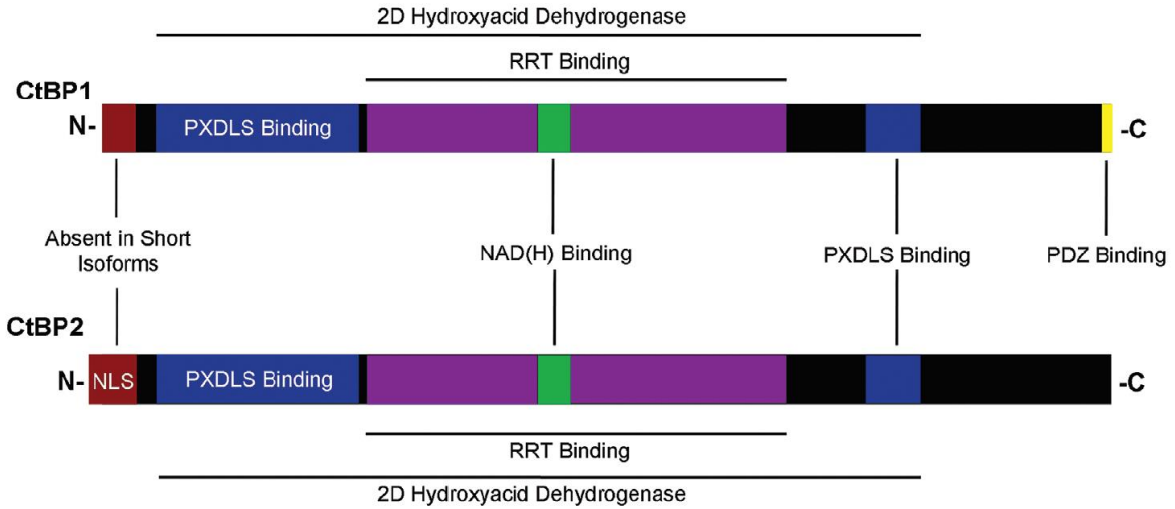
2023,10,28

CtBP is a well-established co-repressor

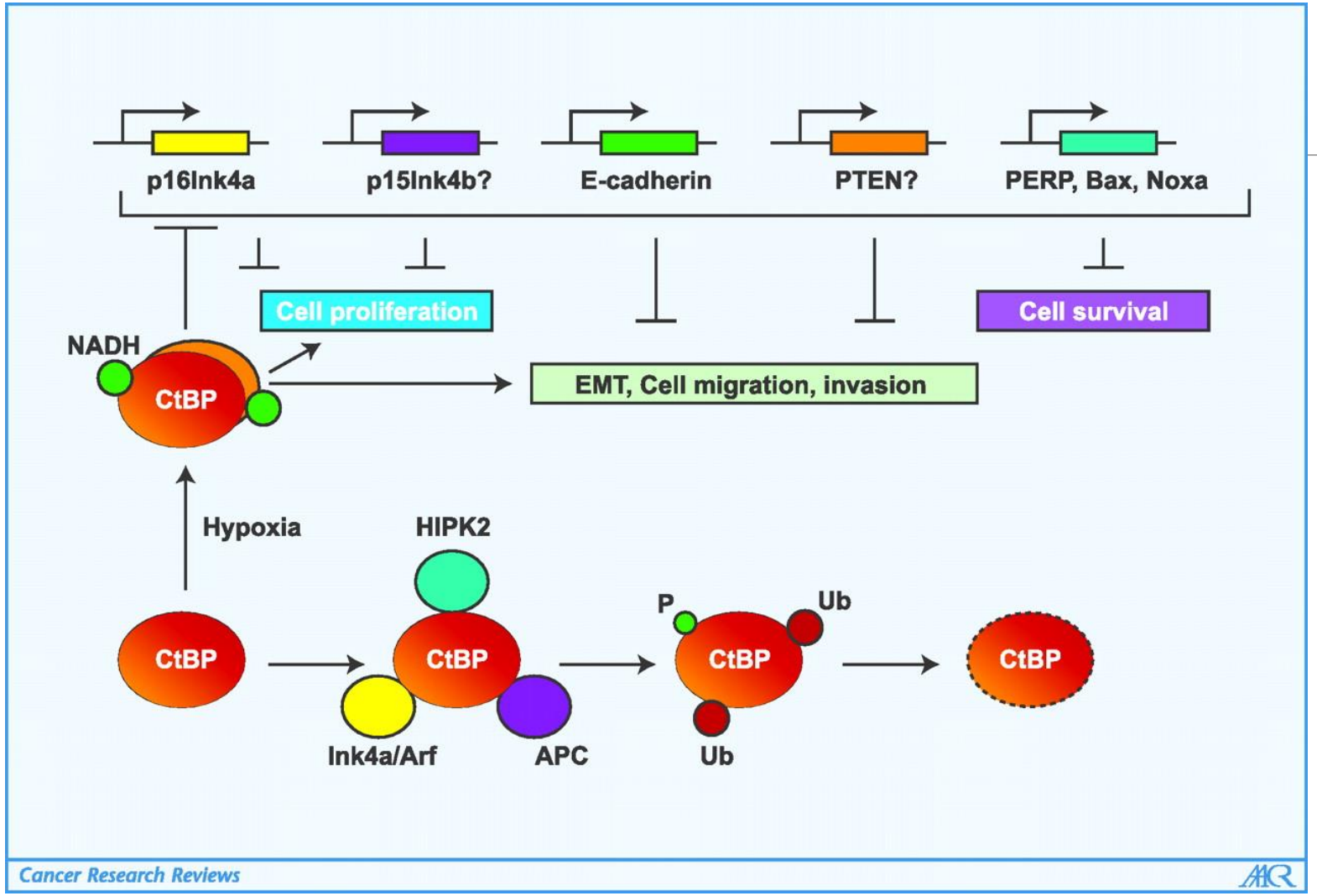




Chinnadurai et al., Mol Cel 2009

Stankiewicz et al., BioMol Concepts 2014

CtBP is a repressor of tumor suppressor genes

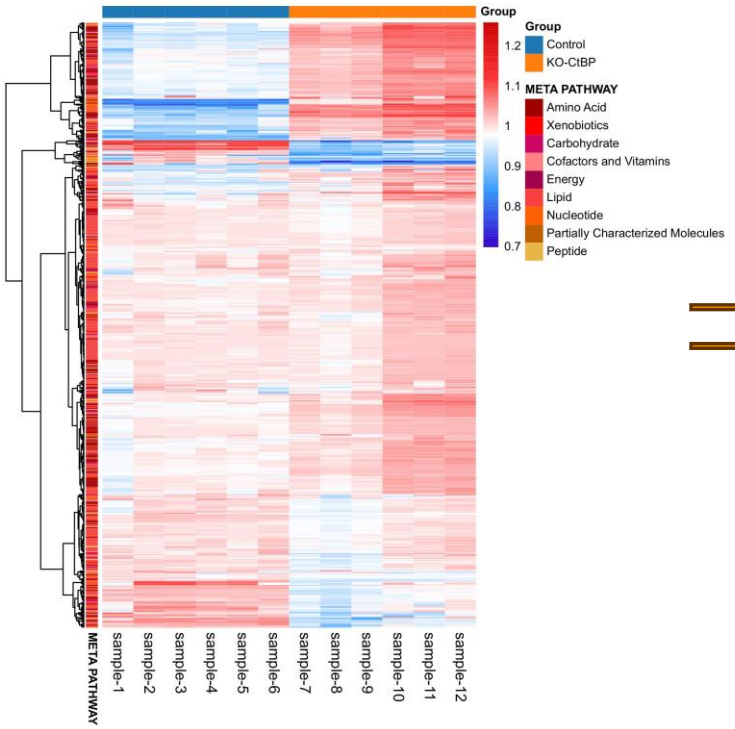


Chinnadurai 2009 Cancer Research

BRCA1,
SIRT4
SREBF2
RAD51
CD24
PALB2
…

Di et al., Nature comm 2013
Di et al., Nature Str Mol Bio 2010
Zhao et al., Oncogene 2019
Hao et al., CCR 2017, 2018
Hao et al., Theranostics, 2019
Wang et al., Cell death Disease 2015
Wang et al., Oncogenesis 2017
Li et al., IJBS 2023

CtBP is a regulator of cell metabolism



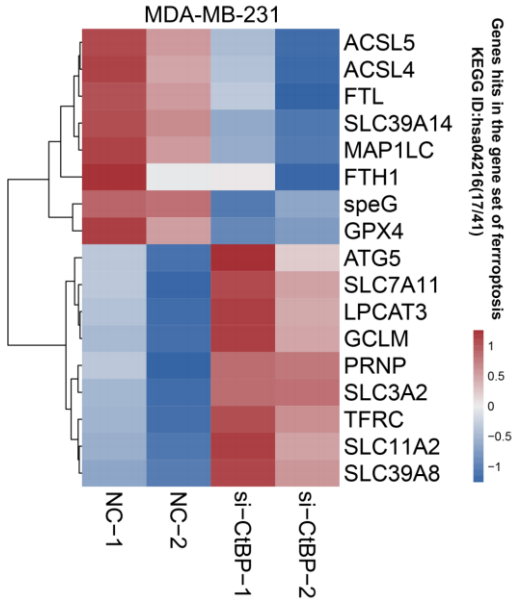
KEGG Mapper Search Result

Pathway (223) | Brite (0) | Module (110) | Network (49) | Disease (0)

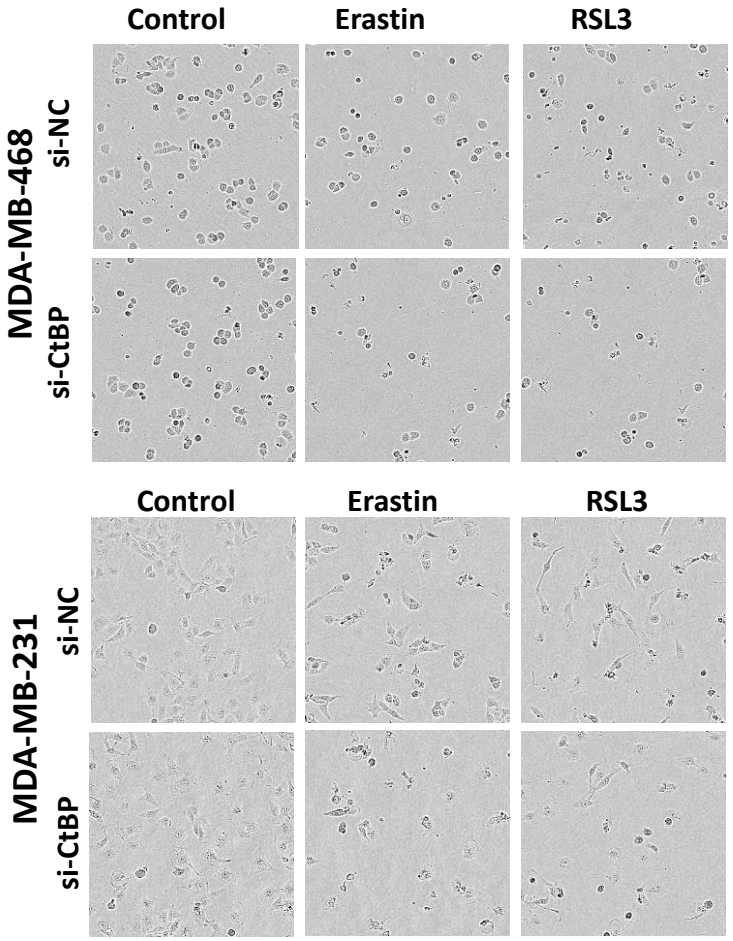
Sort by the Network list

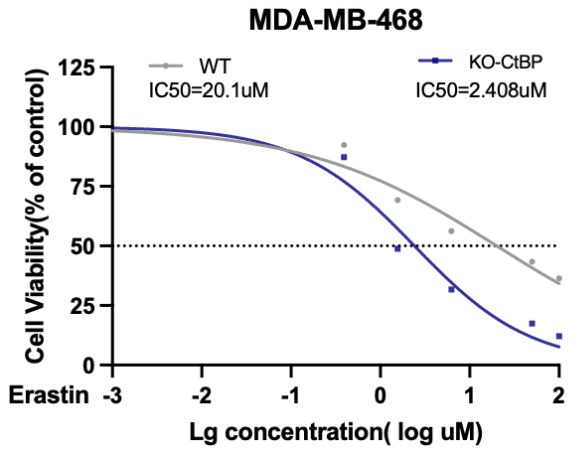
Show matched objects

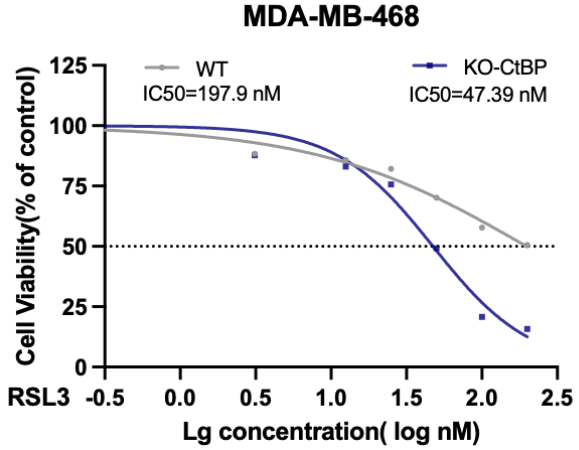
06033 Glycine, serine and arginine metabolism (9)
06024 Valine, leucine and isoleucine degradation (6)
06030 Methionine metabolism (6)
06525 Ferroptosis (6)
06026 Glutathione biosynthesis (5)
06032 Lipoic acid metabolism (5)
06015 N-Glycan biosynthesis (4)
06027 Purine salvage pathway (4)
06010 Urea cycle (3)
06014 Sphingolipid degradation (3)
06016 Phenylalanine and tyrosine metabolism (3)
06020 beta-Oxidation in mitochondria (3)
06036 Lysine degradation (3)
06037 Histidine metabolism (3)
06322 TRH-TSH-TH signaling (3)
06463 Parkinson disease (3)

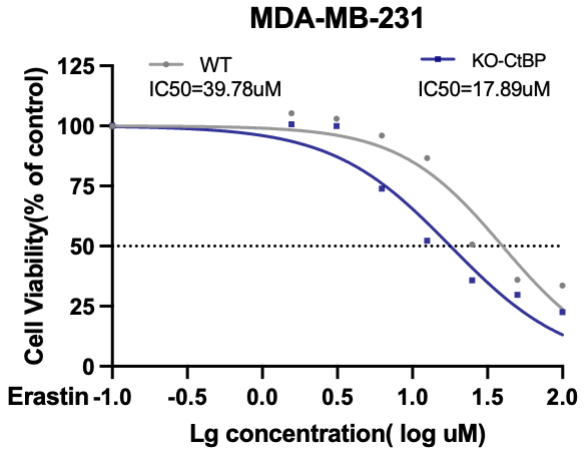


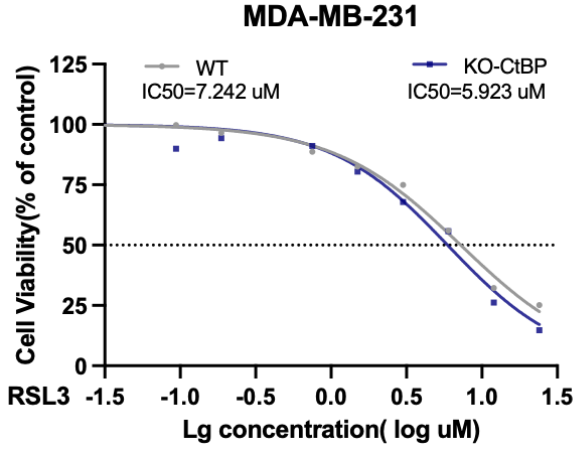
CtBPs deletion enhances ferroptosis sensitivity



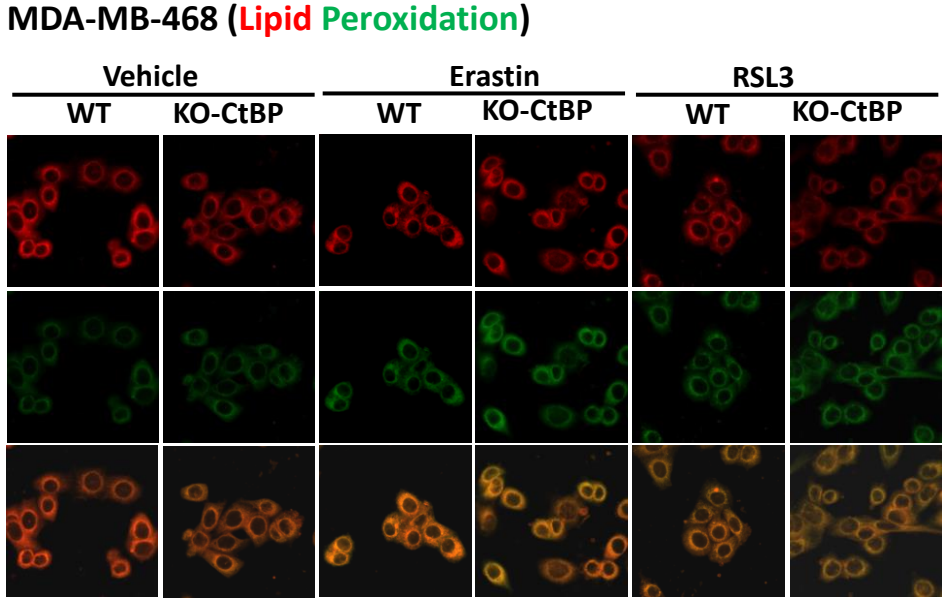




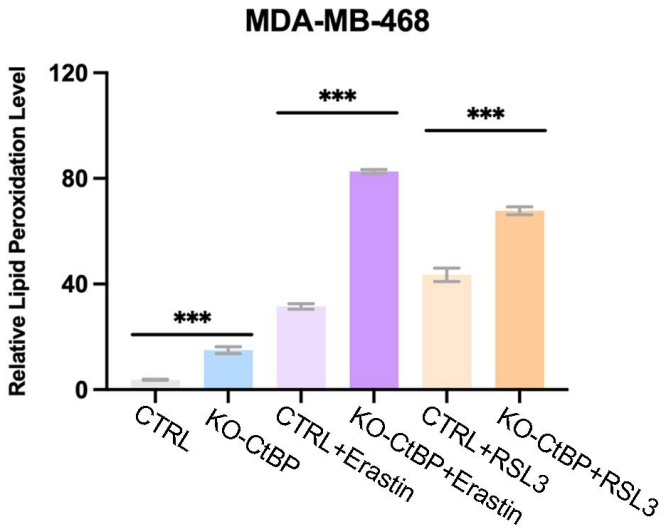


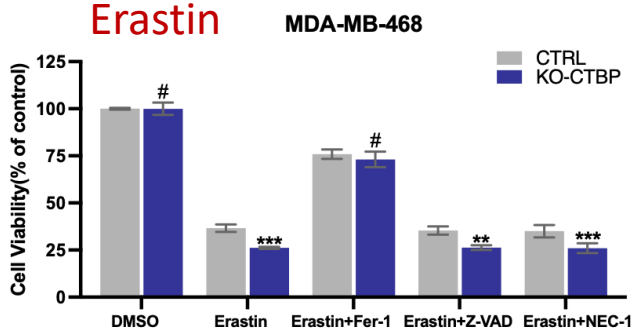


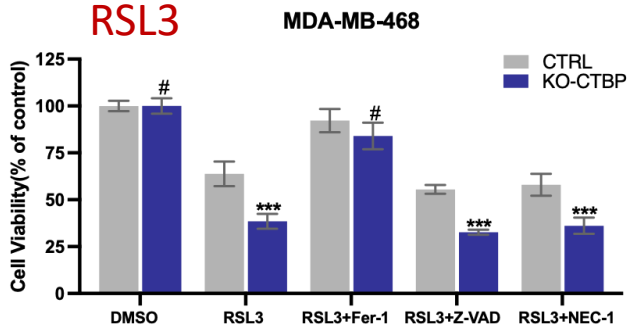
CtBPs deletion enhances ferroptosis sensitivity



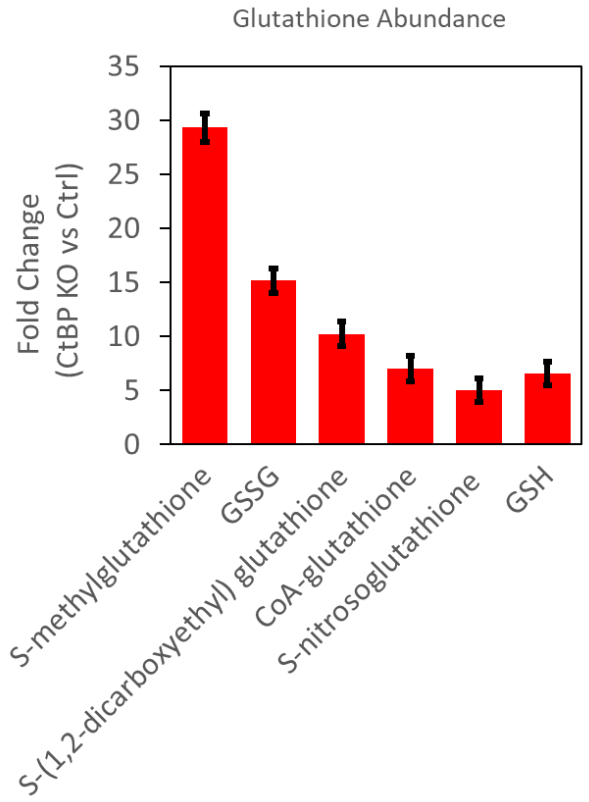
BODIPY® 581/591 C11

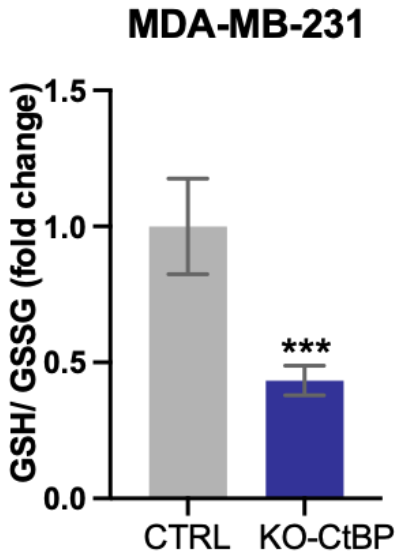


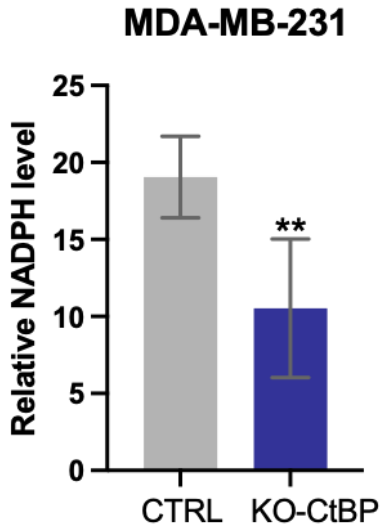


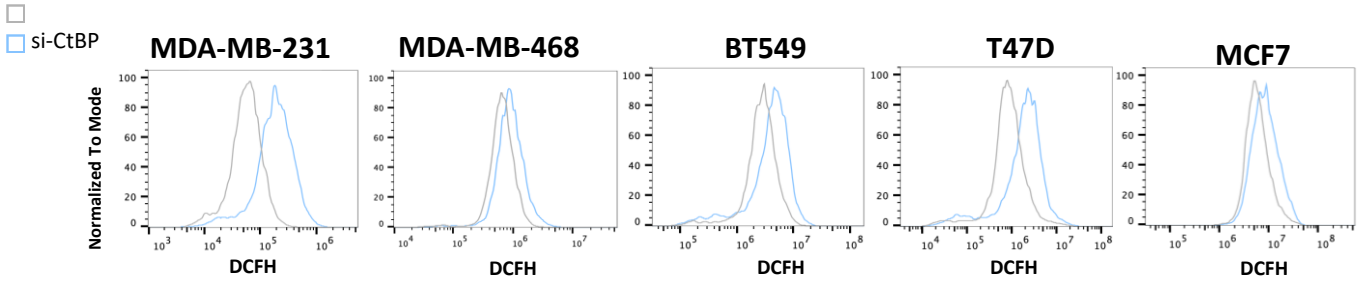


Knockdown CtBP results in the oxidative stress of TNBC

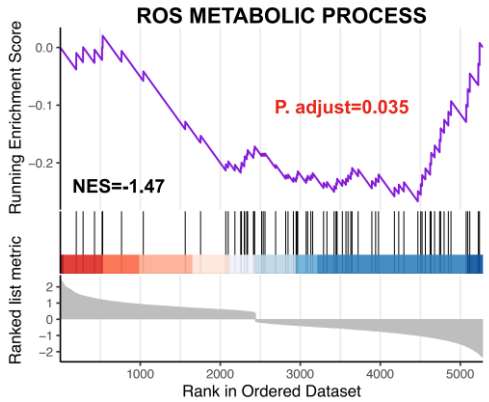


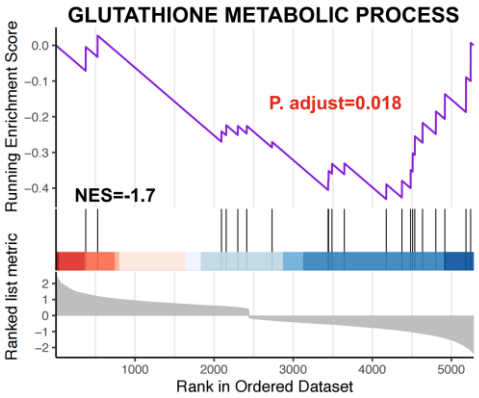


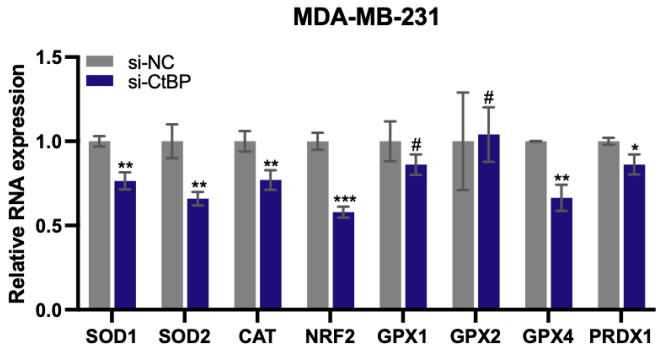


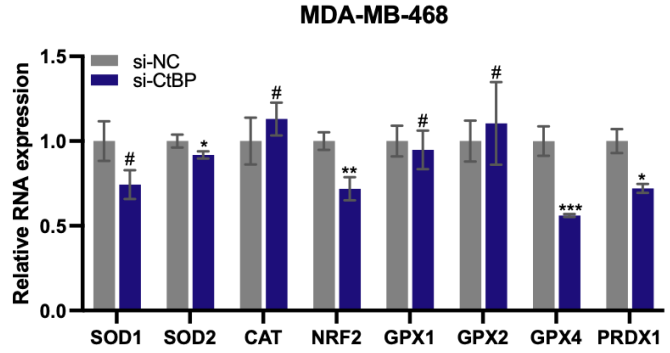


Loss of CtBPs represses anti-oxidative related pathway

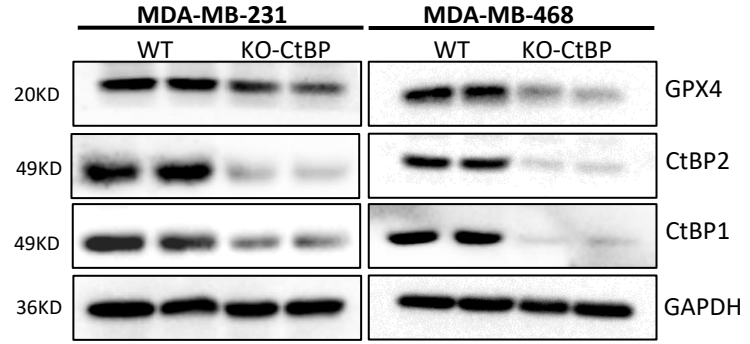


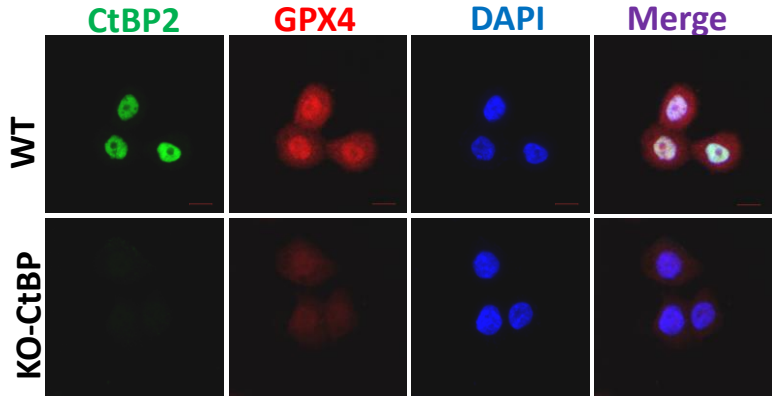






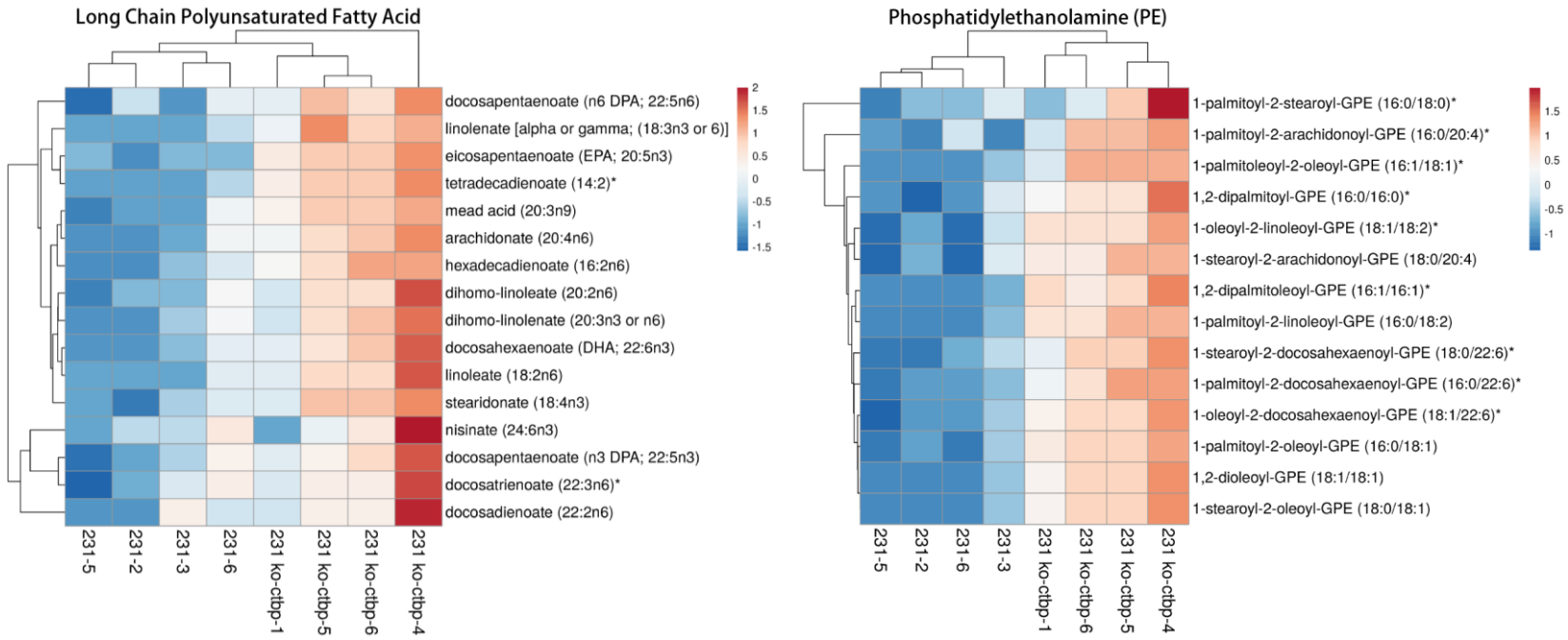
ROS METABOLIC PROCESS





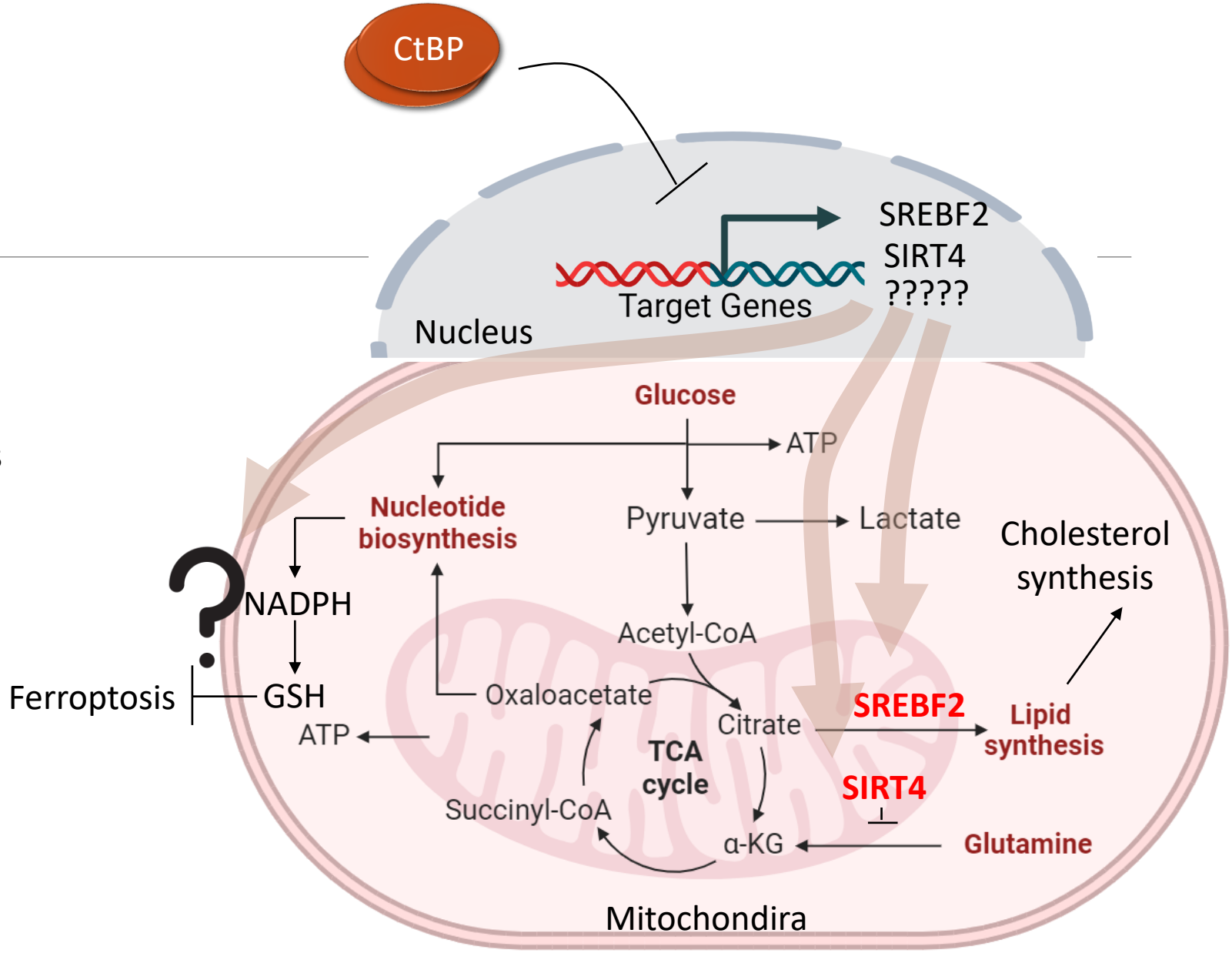
MDA-MB-468

Low CtBP associates with the increased abundance of PUFA and PE

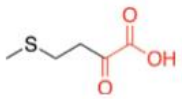
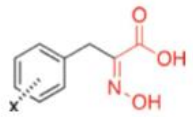
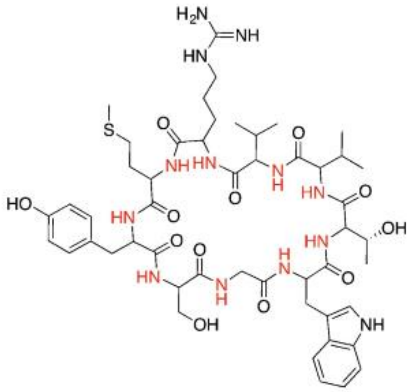
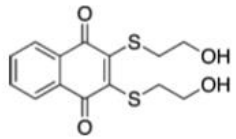


Summary

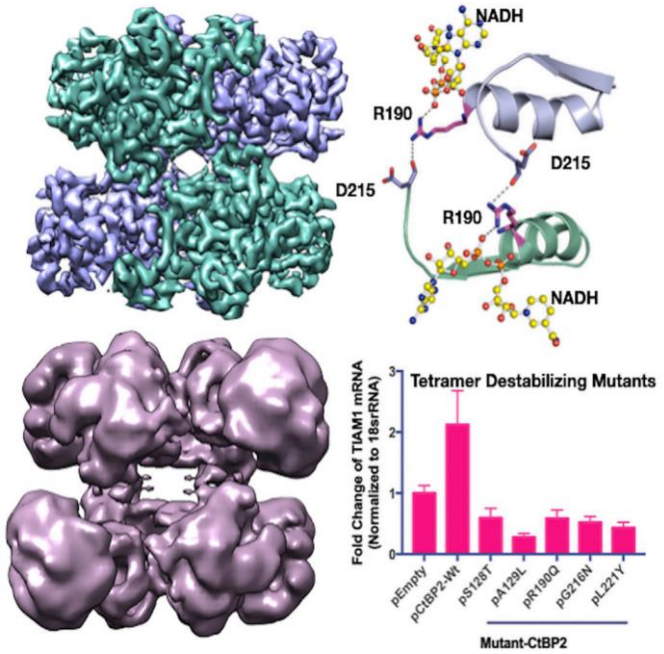
- CtBP represses ferroptosis.
- CtBP increases GSH/GSSG ratio.
- How CtBP regulates the genes involved in ferroptosis regulation is still under investigation.



CtBP, a therapeutic Target?

Name of the compound	Structure of compound	Mode of action
MTOB 2-Keto-4-(methylthio)butyric acid		Substrate at low concentrations, but dehydrogenase inhibitor at high concentrations.[86,88]
HIPP derivatives (2-Hydroxyimino-3-phenyl-propionic acid)		Dehydrogenase inhibitors.[82,89]
Cyclic Peptide CP61 **(cyclo-SGWTVVRMY)**		Inhibitor of homo/ hetero-dimerization of CtBP1 and CtBP2.[92]
NSC95397		Inhibitor of CtBP interaction with partners such as E1A that contain PxDLS sequences.[93]

Cancer Biol Ther. 2017 Jun 3;18(6):379-391.



Bellesis et al. JBC 2018
Jacrois et al. Structure 2021

Acknowledgement

Current lab members

Tai Lixin PhD
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Wang lifen
Tang ping
Zhu Dongliang
Xu Hongxia
Liu Tianyu
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Lab Alumni

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Li jingjing, PhD
Li Peipei, PhD
Wang Yuan PhD

Collaborators

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Shuhai Lin, Xiamen University
Haisheng Zhou, Anhui Medical University
Chuxia Deng, University of Macau

Core Facilities of Faculty of Health Sciences, University of Macau

- Genomics,
- metabolomics,
- small animal facilities etc.