



29<sup>th</sup> Conference of International Academy of  
Pathology (IAP) – Arab Division  
1<sup>st</sup> Oman Pathology Society Conference



# FATTY ACID SYNTHASE REGULATES THE CHEMOSENSITIVITY OF BREAST CANCER CELLS TO CISPLATIN-INDUCED APOPTOSIS

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*November 16<sup>th</sup>, 2017*

# Background

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- Fatty acids are main form of energy storage and have important roles in many cellular signaling and structural molecules.
- Palmitate; an 18 - carbon saturated fatty acid, and Oleate; a 16 - carbon monounsaturated fatty acid, are the two most abundant fatty acids in the body.
- Fatty acid synthase (FASN) is a 270 kDa, key enzyme in fatty acid synthesis pathway.
- In normal cells, FASN level is sustained low and is controlled by hormonal and nutritional regulatory signals as cells use exogenous dietary lipids for their metabolic processes.
- In highly proliferating cancer cells, fatty acids are synthesized to provide adequate amount of lipid for cell membrane biosynthesis and enough energy.

# Rationale and Aims

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- Synthesis of fatty acids require FASN enzyme up regulation and activity which is seen in cancer cells.
- Changes in certain oncogenic proteins in some cancer cells results in the activation and expression of FASN enzyme, regardless of the dietary circulating fat.
- Although, some studies showed that elevated level of FASN is a marker of poor prognosis for patients with breast cancer, its role as a possible metabolic oncogene still remains unclear.
- Therefore, we aimed to:
  1. Measure fat intensity in both triple-negative and -positive breast cancer cells treated with Palmitate and Oleate.
  2. Examine their effect on the cell ultra-structure, FASN expression and apoptosis induction.
  3. Assess the influence of Palmitate and Oleate on FASN-mediated, Cisplatin-induced apoptosis.

Palmitate significantly increased fat content in both breast cancer cells while Oleate only increased it in TNBC cells

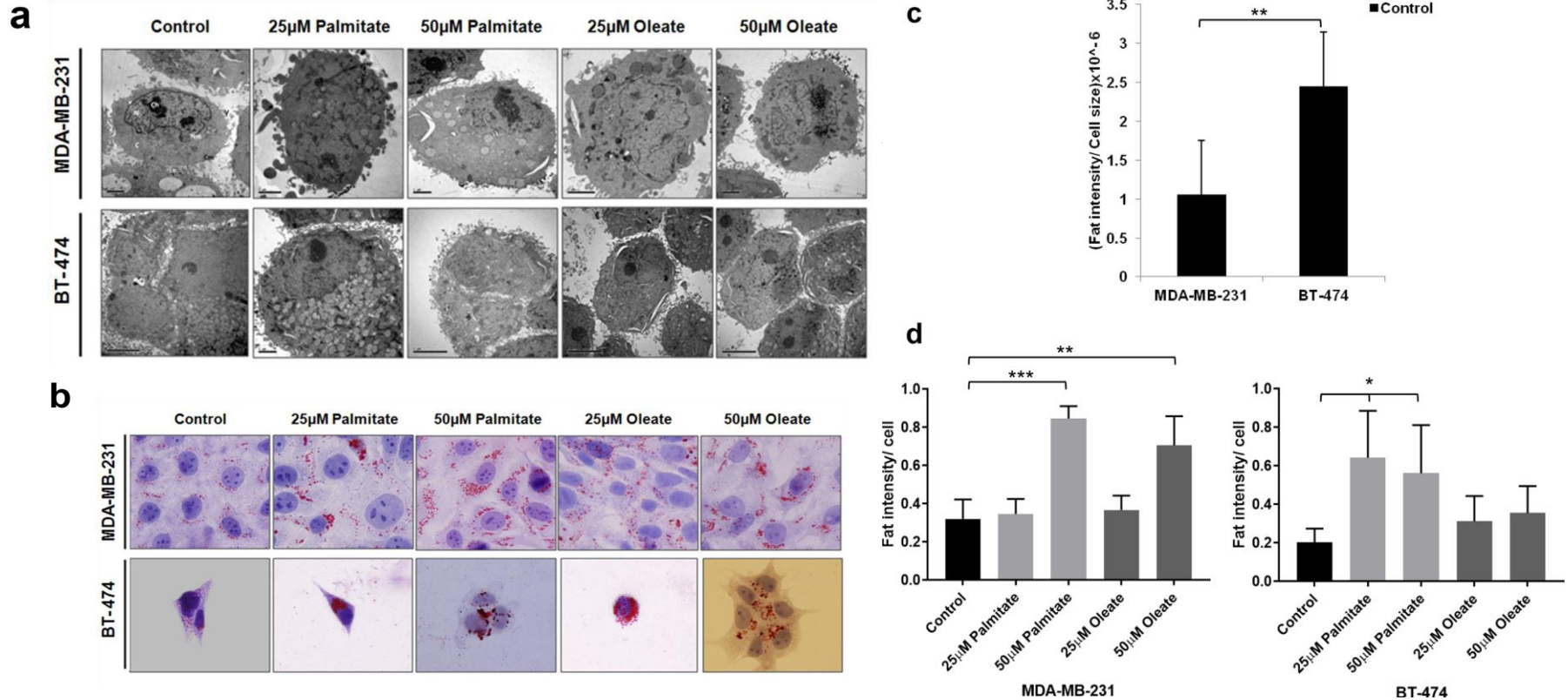


Fig. 1 The effect of Palmitate and Oleate on fat content in MDA-Mb-231 and BT-474 cells. a) Transmission Electron Microscope, b) Oil Red O stain, c & d) Fat intensity/cells

## Palmitate and Oleate had differential effects on FASN expression in breast cancer cells

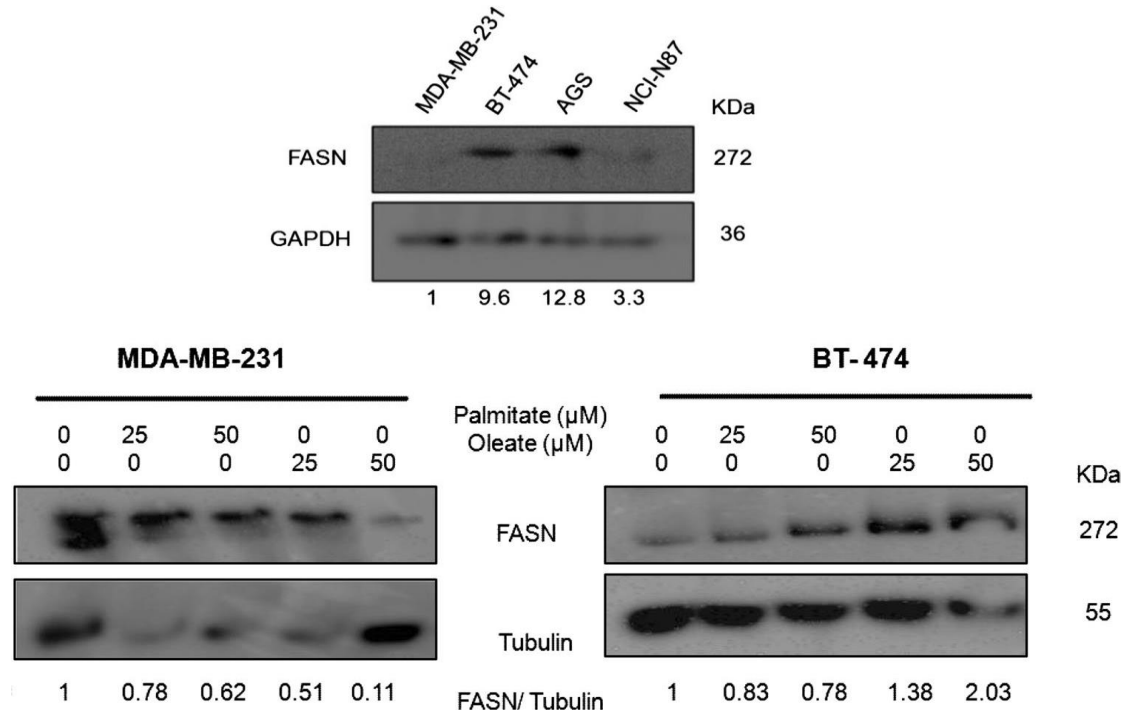


Fig. 2 FASN expression in MDA-MB-231 and BT-474 cells treated for overnight with Palmitate and Oleate. Western Blot was used to measure protein content. Hoechst Stain was used to detect apoptosis

## CDDP decreased FASN expression in Triple-negative and increased it in Triple-positive breast cancer cells

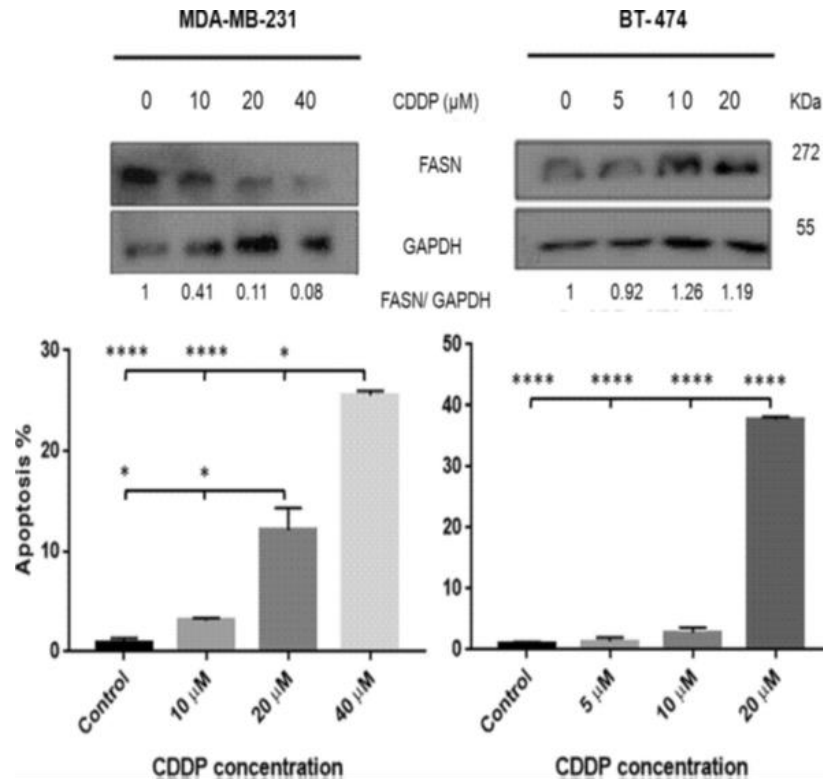


Fig. 3 The effect of CDDP treatment for 24 hours on FASN expression and apoptosis in MDA-MB-231 and BT-474 cells. Western Blot was used to measure protein content. Hoechst Stain was used to detect apoptosis

## FASN contributes to CDDP-induced apoptosis in Triple-positive breast cancer cells

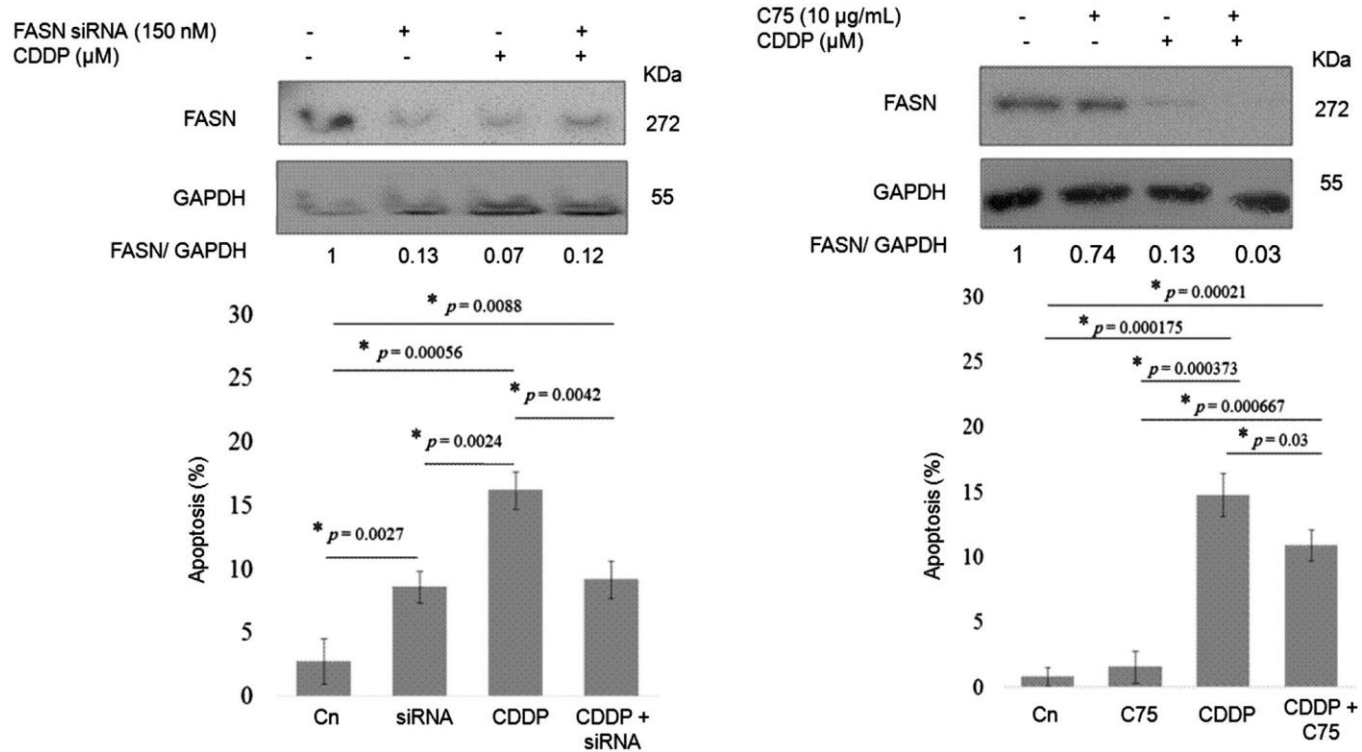


Fig. 4 The effect of FASN inhibition by 24 hours siRNA and 4 hours C75 on CDDP-induced apoptosis in BT-474 cells

## FASN contributes to CDDP-induced apoptosis in Triple-Negative breast cancer cells

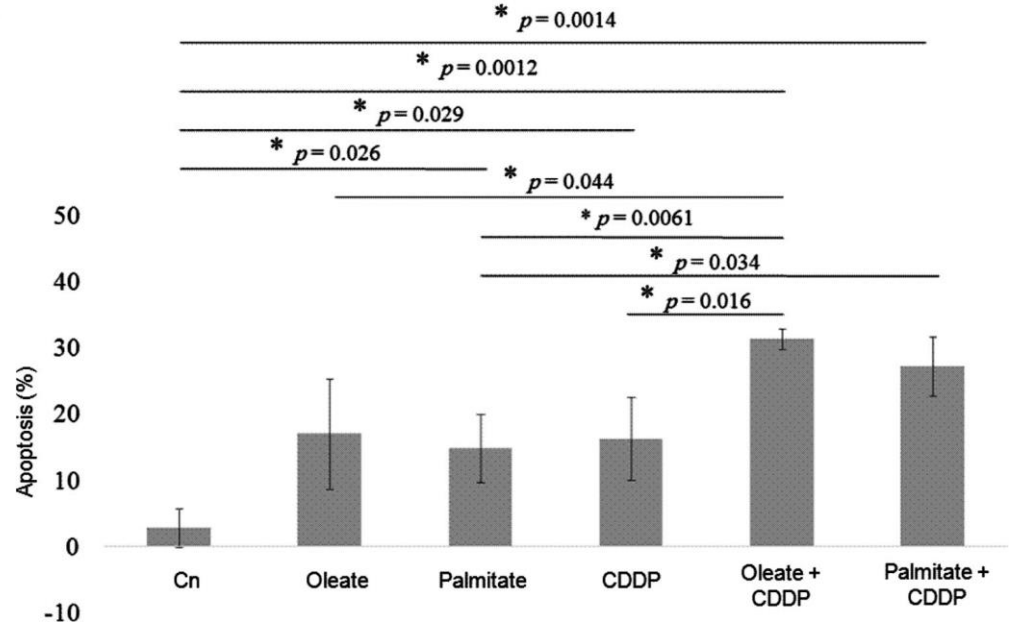
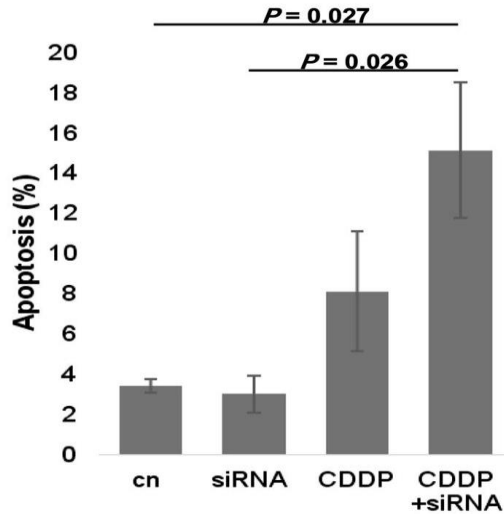
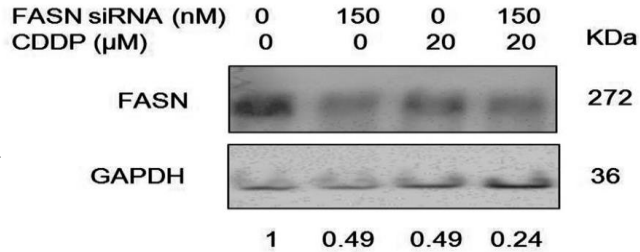


Fig. 5 The effect of siRNA, fatty acids, and CDDP treatment on MDA-MB-231 cells apoptosis



# Summary

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- FASN can modulates chemosensitivity of both cell lines.
- Inhibiting its expression in TNBC can yield promising results in overcoming chemoresistance by enhancing the CDDP-induced apoptosis.
- Understanding the molecular mechanisms of breast cancer might open new insights to overcome its chemoresistance by introducing new targeted therapies.

# Acknowledgement

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Ms. Hanaa Al Lawati

Ms. Moza Al Adawi

Mrs. Nadia Al Abri

Mrs. Buthaina Al Dhahli

Mrs. Kawther Al Adawi

Dr. Ikhlas Ali

Dr. Fahad Al Zidjali