

Soluble E-Cadherin and Regulation of ROS in Inflammatory Breast Cancer

Yair Romero, Xiao Ding Hu, Bisrat Debeb

Department of Breast Medical Oncology Research, MD Anderson Cancer Center.

The Problem

IBC (Inflammatory Breast Cancer) is the most aggressive type of Breast Cancer, and disproportionately causes more deaths than any type. There is limited treatments for IBC.

Although only making up around 1-4% of all breast cancer cases, IBC disproportionately causes 8-10% of all breast cancer deaths.

Understanding the molecular mechanisms of IBC biology is needed to develop effective therapies.

Soluble E-Cadherin

- Soluble E-cadherin is an extracellular fragment of full-length E-Cadherin
- E-Cadherin has been shown to lead to reduced progression of cancer, but in IBC there is overexpression of E-Cadherin and it promotes tumor growth.
- Role of soluble E-cadherin IBC tumor progression is unknown.

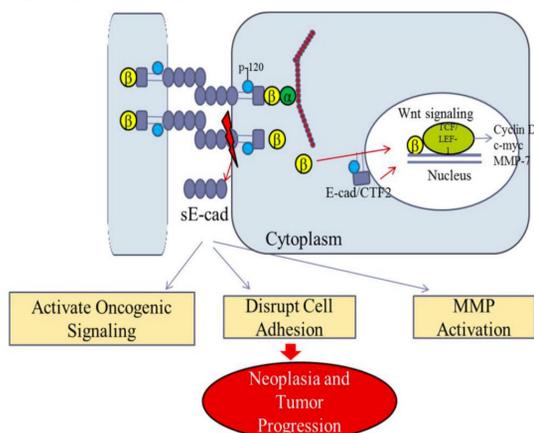


Fig.1. Soluble E-Cadherin that escapes into the cell can lead to activation of Oncogenic Signaling, Disruption of Cell Adhesion and MMP Activation which all lead to Tumor Progression

ROS

ROS is

- a highly reactive chemical produced from Oxygen.
- It causes apoptosis in cancer cells
- It damages cells by a positive chain reaction and can signal the death of cancer cells.
- ROS has both positive and negative effects on cells.

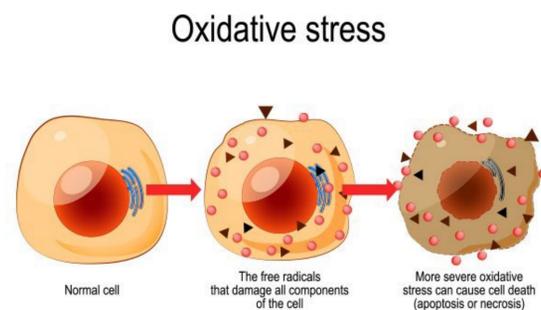


Fig.2. Normal cells going through oxidative stress, and the effects of high ROS on cells.

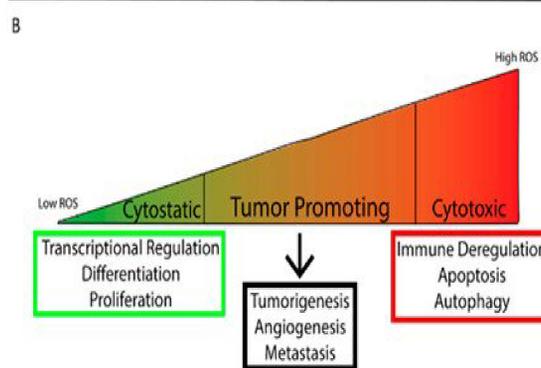


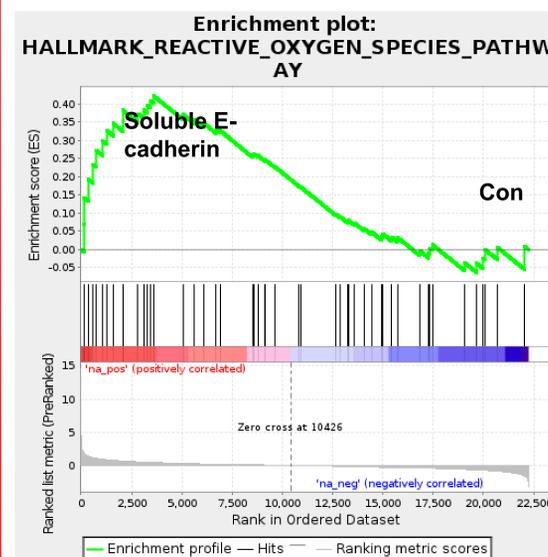
Fig.3. Different levels of ROS. Cytostatic promotes cell growth, The tumor promoting stage causes tumor growth and metastasis, while Cytotoxic causes apoptosis due to the high levels of ROS

Hypothesis

Soluble E-Cadherin promotes survival by inhibiting ROS in IBC.

Reasoning/Rationale.

- We have found that Soluble E-Cadherin promotes tumor growth in IBC.
- We also found that Soluble E-Cadherin inhibits apoptosis and ROS signaling pathways was enriched in the Soluble E-Cadherin group.



SUM149

Methodology

Cell culture: (Used IBC3 & SUM149)

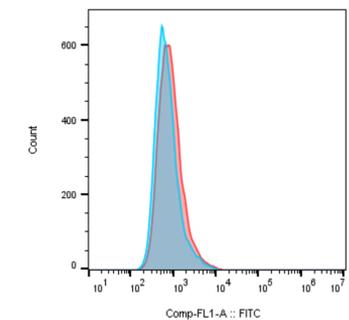
- We incubated 3 plate of control and Soluble E-Cadherin overexpressing IBC cells each for 30 minutes at 37 degrees °C
- Stained cells with DCFDA which labels H2O2.
- Wash with PBS and are then trypsinized.
- We then use a flow cytometer to quantify the total amount of ROS.

Flow cytometer quantification

- We used DCFDA which when exposed to oxygen become fluorescent.
- The cells were then quantified by using a flow cytometer machine.

Results

A



B

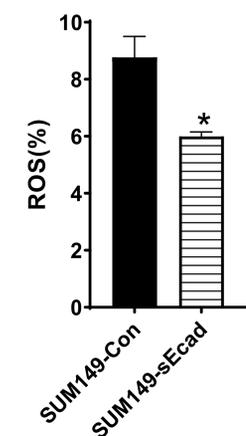


Fig.4. Measurement of ROS in SUM149 cells. (A) Histogram shows ROS level in Soluble E-Cadherin group shifts to the left indicating lower ROS levels than that of control group. (B). A bar graph from two independent experiments. ROS levels are significantly reduced in soluble E-cadherin compared to control SUM149 cells.

Conclusion

- Our results show that Soluble E-Cadherin inhibits the total amount of ROS in SUM149 cells.
- Soluble E-cadherin may promote IBC cancer survival by reducing ROS.

Acknowledgement

I am grateful to the Partnership in Cancer Science and Medicine (PCCSM) program and UT MD Anderson for supporting and funding this research. I would like to thank Dr. Debeb for his guidance and support in conducting this research. I would also like to thank Drs Xiao Ding Hu for her guidance and mentorship throughout this program.