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Anti-GD2 antibody dinutuximab inhibits triple-negative breast tumor growth by targeting GD2+ breast cancer stem-like cells

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Anti-GD2 antibody dinutuximab inhibits triple-negative breast tumor growth by targeting GD2+ breast cancer stem-like cells

Ly S, Anand V, El-Dana F, et al.

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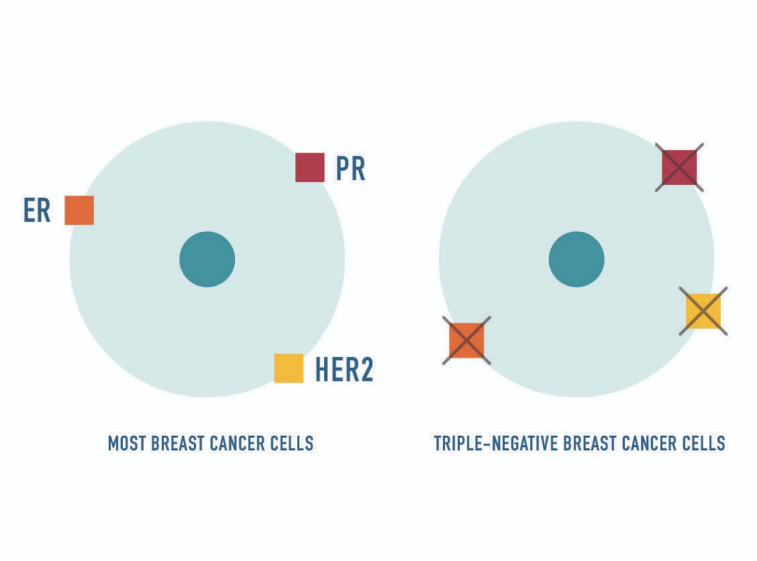
Introduction

Cancer is a disease caused by uncontrolled cell proliferation that spreads to and damages surrounding body tissues

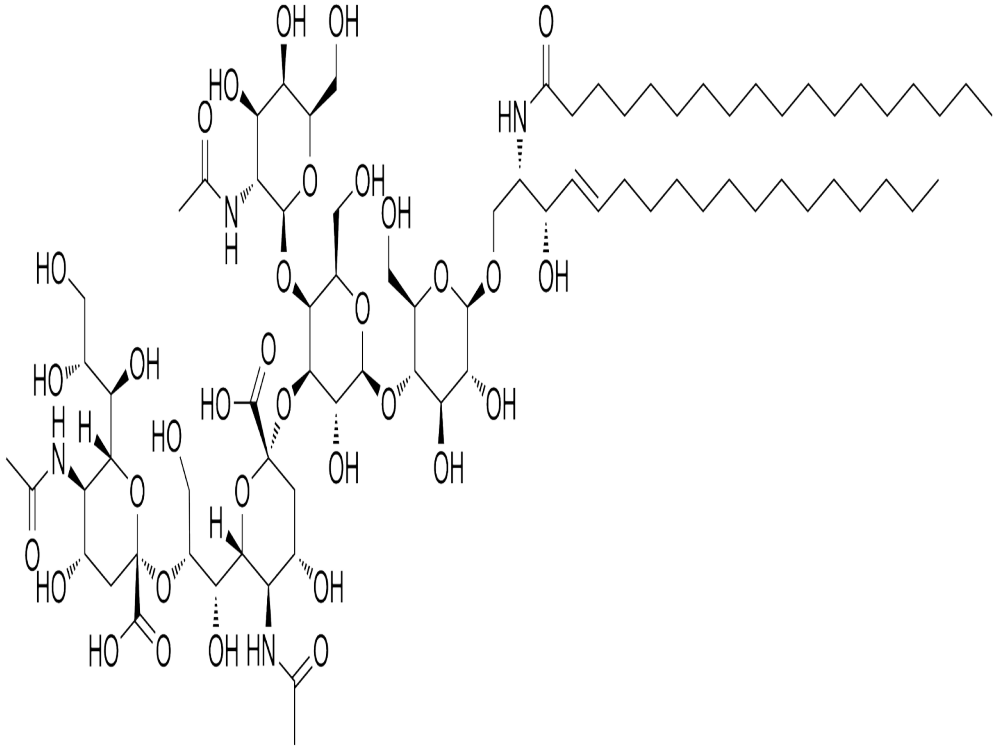
Triple Negative Breast Cancer (TNBC) is an aggressive subtype of breast cancer that often has worse prognosis (outcome). It is characterized by its lack of three markers..



What is GD2?

GD2 is a disialoganglioside (glycolipid) found on the cell surface of TNBC cells

They have a role in cell adhesion, migration, and cell signaling.



Abstract abstracted

- A fraction of cells in TNBC are thought to have stem-cell like properties. They are called Breast cancer stem-like cells (BCSCs)

- The BCSCs in primary TNBC are responsible for metastasis (spread of tumor from its primary origin to a different tissue) ***and*** chemotherapy resistance

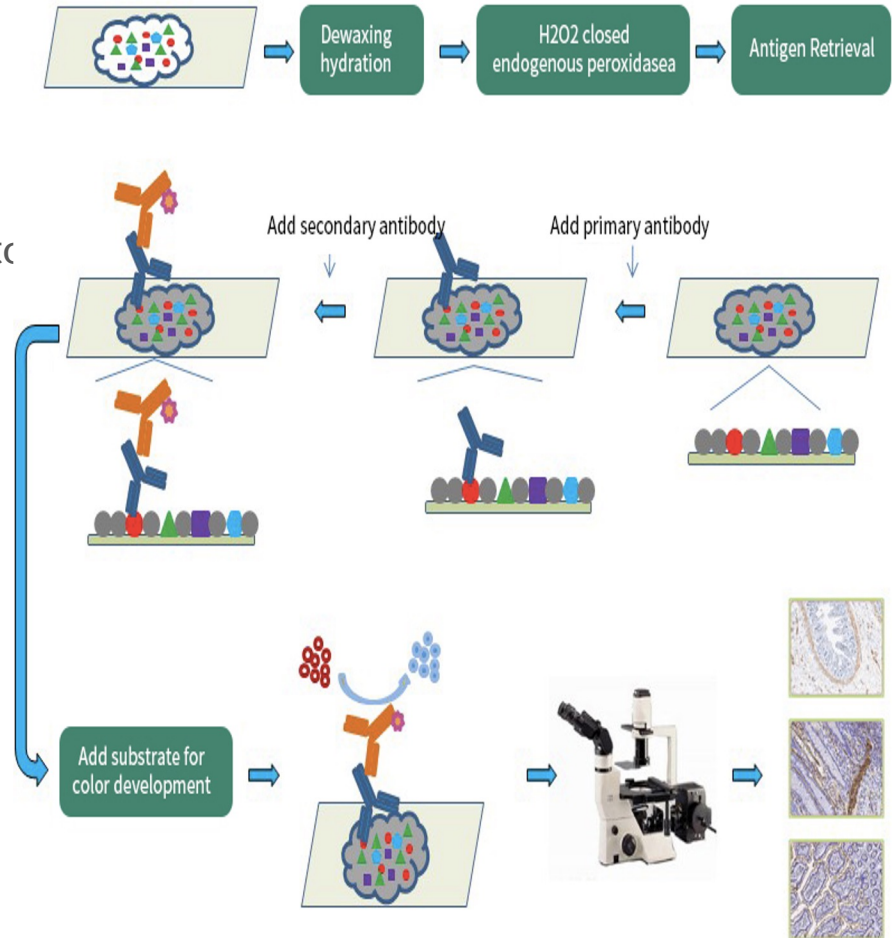
- This article shows that GD2 is highly expressed in the BCSC population and targeting them can be an effective way to inhibit breast cancer growth and metastasis

Method

The researchers conducted a series of experiments but I summarized the most important ones that lead to the conclusion

-Immunohistochemistry of frozen primary tumor tissues

- Effect of dinutuximab (anti GD2 chemotherapy) on TNBC patient-derived xenograft growth



Immunohistochemistry of frozen primary tumor tissues

Goal is to analyze GD2 expression in TNBC

Steps:

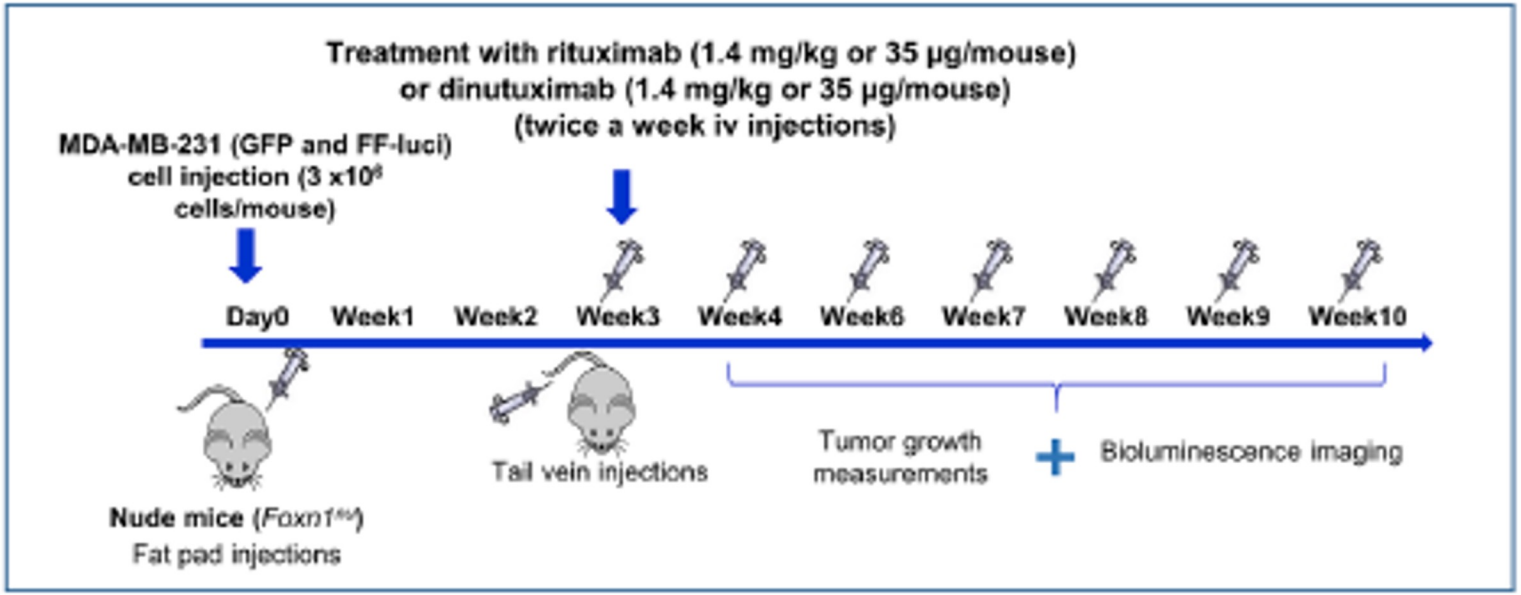
1- TNBC tissue was obtained and sectioned 7-10 µm in thickness using a cryotone

2- A series of fixative chemicals were added to preserve and maintain the tissue

3- The slides were incubated with an anti-GD2 primary antibody for an hour

4- The tissue was then stained with DAB and hematoxylin to enhance tissue contrast allowing us to analyze the slide under a microscope

Effect of dinutuximab (anti GD2 chemotherapy) on in vivo tumor growth in a TNBC cell line xenograft model



Results

GD2 is upregulated in TNBC cell lines, PDX (patient derived xenograft) models and TNBC tissues

Table 1 Percentages of GD2$^+$ cells among breast cancer cell lines and in TNBC PDX models

Serial number	Cell line/PDX model	Breast cancer type	Median (± standard dev.) percentage of GD2+ cells*
1	Hs 578T	TNBC	99.10 ± 0.20
2	SUM159	TNBC	15.20 ± 0.60
3	MDA-MB-231	TNBC	10.40 ± 0.20
4	HIM3	PDX-derived TNBC	7.96 ± 0.52
5	MDA-MB-453	TNBC	0.28 ± 0.05
6	BT-549	TNBC	6.22 ± 0.87
7	HCC1395	TNBC	99.70 ± 0
8	HCC1806	TNBC	0.69 ± 0.05
9	DU4475	TNBC	0.97 ± 0.07
10	HCC70	TNBC	9.85 ± 0.75
11	BT-20	TNBC	0.44 ± 0.15
12	HCC38	TNBC	22.30 ± 1.10
13	MDA-MB-468	TNBC	4.14 ± 0.15
14	HCC1599	TNBC	0.42 ± 0.07
15	MDA-MB-436	TNBC	27.55 ± 1.35
16	SUM149	Inflammatory breast cancer/TNBC	0.22 ± 0.10
17	ZR-75-1	ER+	2.87 ± 0.51
18	MCF7	ER+PR+	5.99 ± 0.37
19	SKBR3	Her2+	1.38 ± 0.17
20	MDA-MB-361	ER+PR+	0.87 ± 0.24
21	T47-D	ER+PR+	8.90 ± 0.42
22	BT-474	ER+PR+Her2+	0.23 ± 0.08
23	PA14-0421-29	TNBC PDX	11.9
24	PIM-001	TNBC PDX	3.4

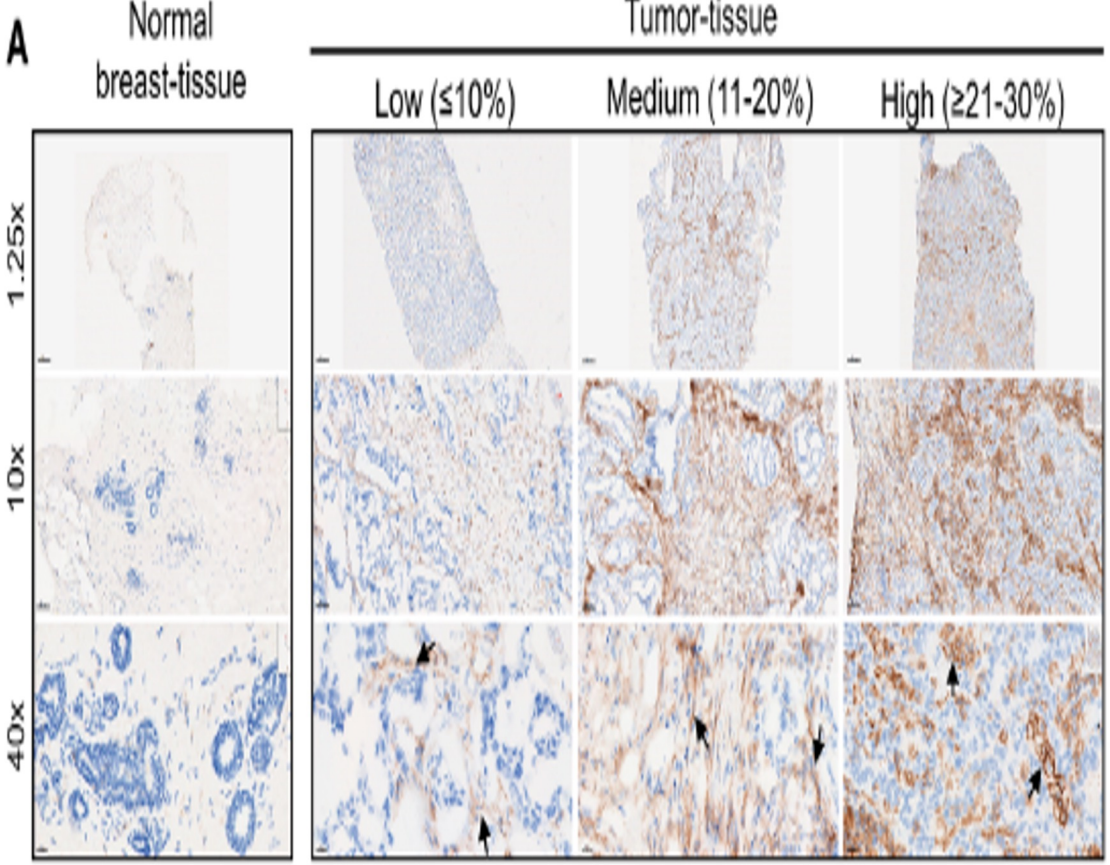


Figure A compares GD2 expression in normal breast tissue and tumor tissue in immunohistochemical analysis. Black arrows indicate GD2 staining.

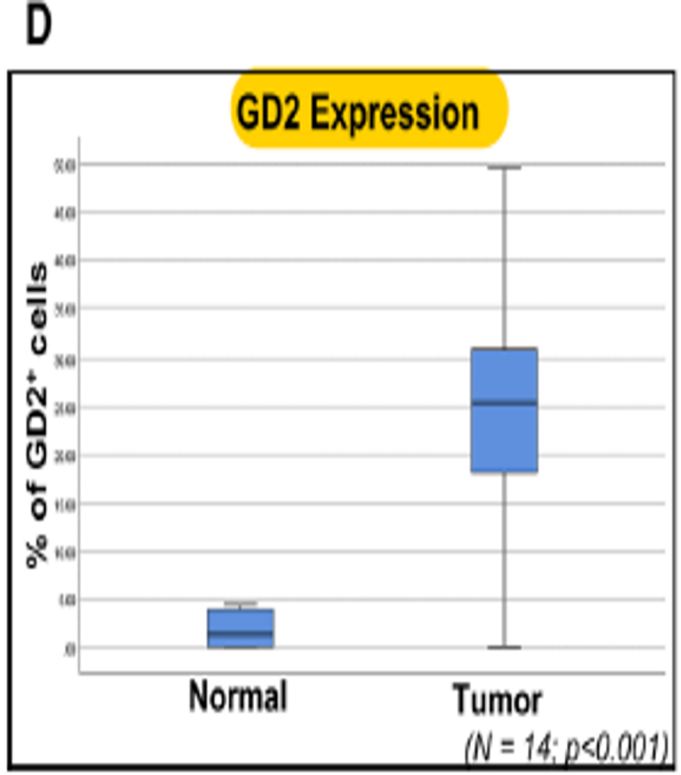
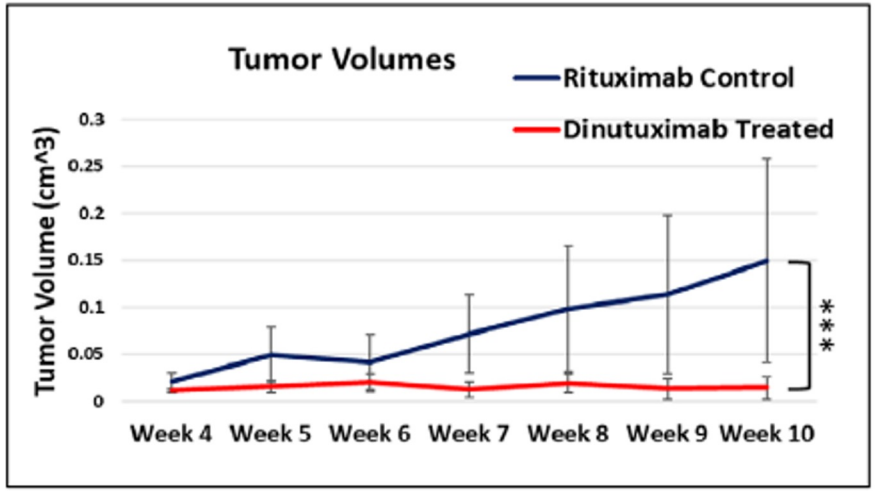


Figure D compares GD2 expression in tumor tissue and adjacent normal tissue. We can see a significant increase in expression in tumor tissue

Results

B



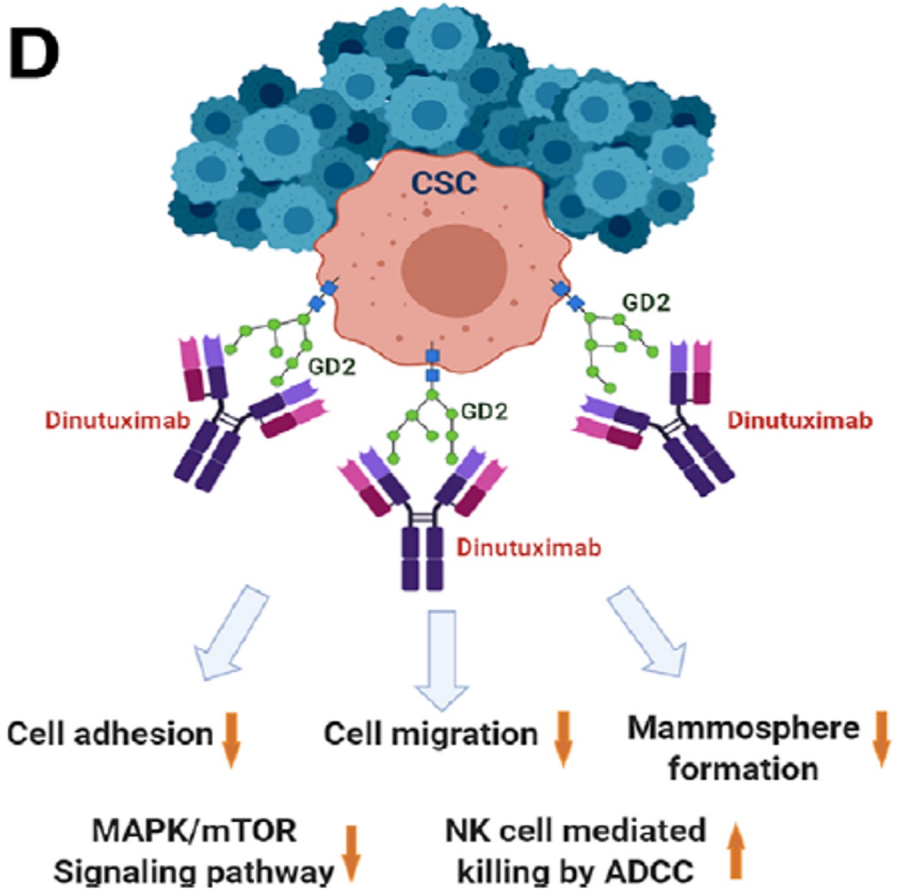
-Results from the dinutuximab vs. rituximab (control) treatment in TNBC xenograft model

-Results clearly show that dinutuximab is a significantly effective treatment in TNBC

Conclusion

-The study demonstrated that GD2 is a therapeutic target in TNBC

-The chemotherapeutic agent dinutuximab targets GD2^{+} cells and inhibits cell adhesion, migration, and mammosphere formation by regulating the mTOR pathway involved in cell proliferation and migration



Reference

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Discussion Questions

1- Sometimes in cancer, we do not know the exact reason behind tumor initiation and progression. Do you think that we should spend our time researching the details of cancer and its development or to develop treatments even when we do not know how the treatments work and if they will work in different patients?

2- Do you see a potential in understanding and targeting cancer stem cells ?

3- Do you have any thoughts or concerns or see any limitations in today's approach to cancer research?