

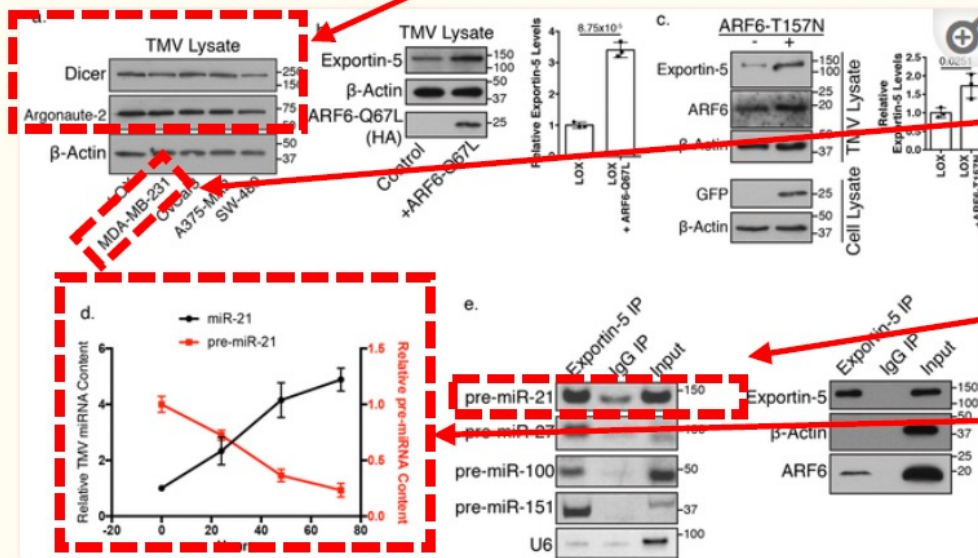
**The data in the identified issues in the  
Cancer Cell manuscript (2014) was  
independently validated and  
reproduced by other researcher  
groups in published papers**

# Example 1

Nat Cell Biol. 2019 Jul; 21(7): 856–866.

doi: 10.1038/s41556-019-0345-y

Identification of **Dicer** and **AGO2** in breast cancer vesicles.



Same exosomes used as in the Cancer Cell 2014 manuscript (**MDA-MB-231**).

Demonstration of **pre-miR21** and **miR21** in exosomes.

Demonstration of **precursor microRNA 21** processing in exosomes.

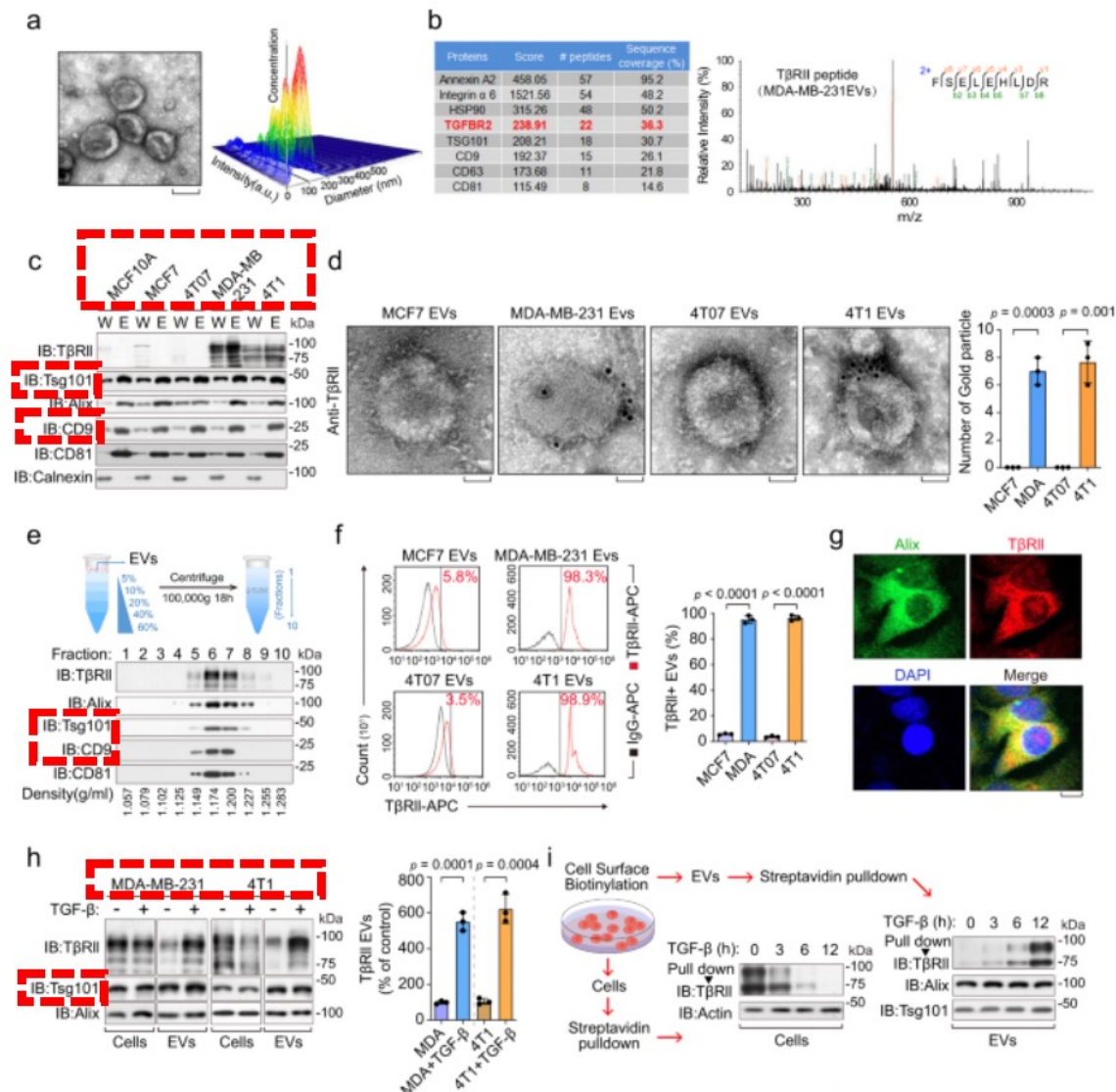
Figure 3:

pre-miRNA processing machinery is contained in shed TMVs.

# Example 2

Nat Commun 2022, 13, 4461; Xie, F., Zhou, X., Su, P. et al. Breast cancer cell derived extracellular vesicles promote CD8+ T cell exhaustion via TGF- $\beta$  type II receptor signaling.

**Fig. 1: Extracellular expression of T $\beta$ RII on malignant breast cancer cell-derived EVs and its regulation by TGF- $\beta$ .**



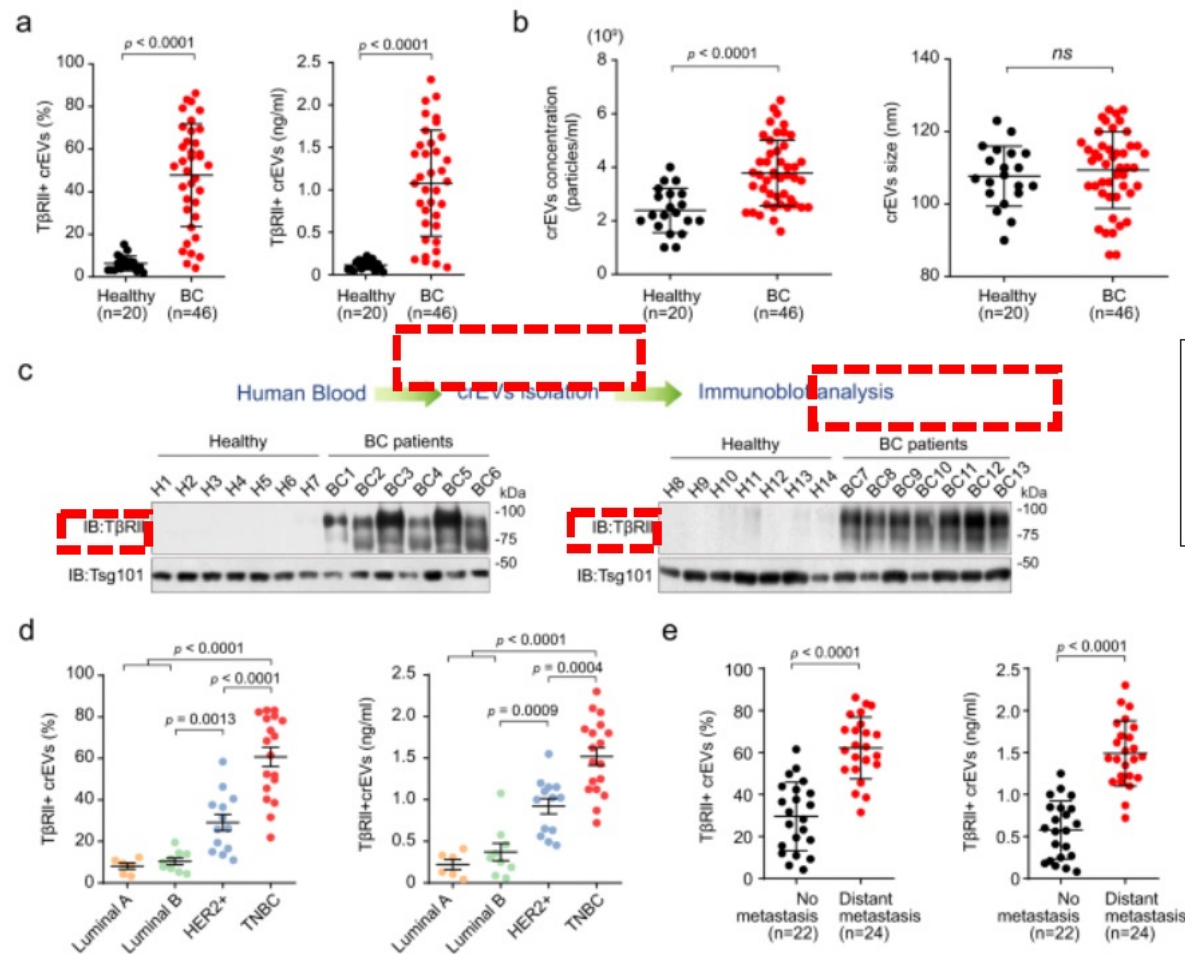
Same cell lines used in Cancer Cell 2014 manuscript: **MCF10A, MCF7, MDA-MB-231 and 4T1.**

Demonstrates presence of the **exosomes markers TSG101 and CD9.**

# Example 2

Nat Commun 2022, 13, 4461; Xie, F., Zhou, X., Su, P. et al. Breast cancer cell derived extracellular vesicles promote CD8+ T cell exhaustion via TGF- $\beta$  type II receptor signaling.

**Fig. 3: The amount of T $\beta$ RII on circulating EVs distinguishes patients with breast cancer from healthy donors.**

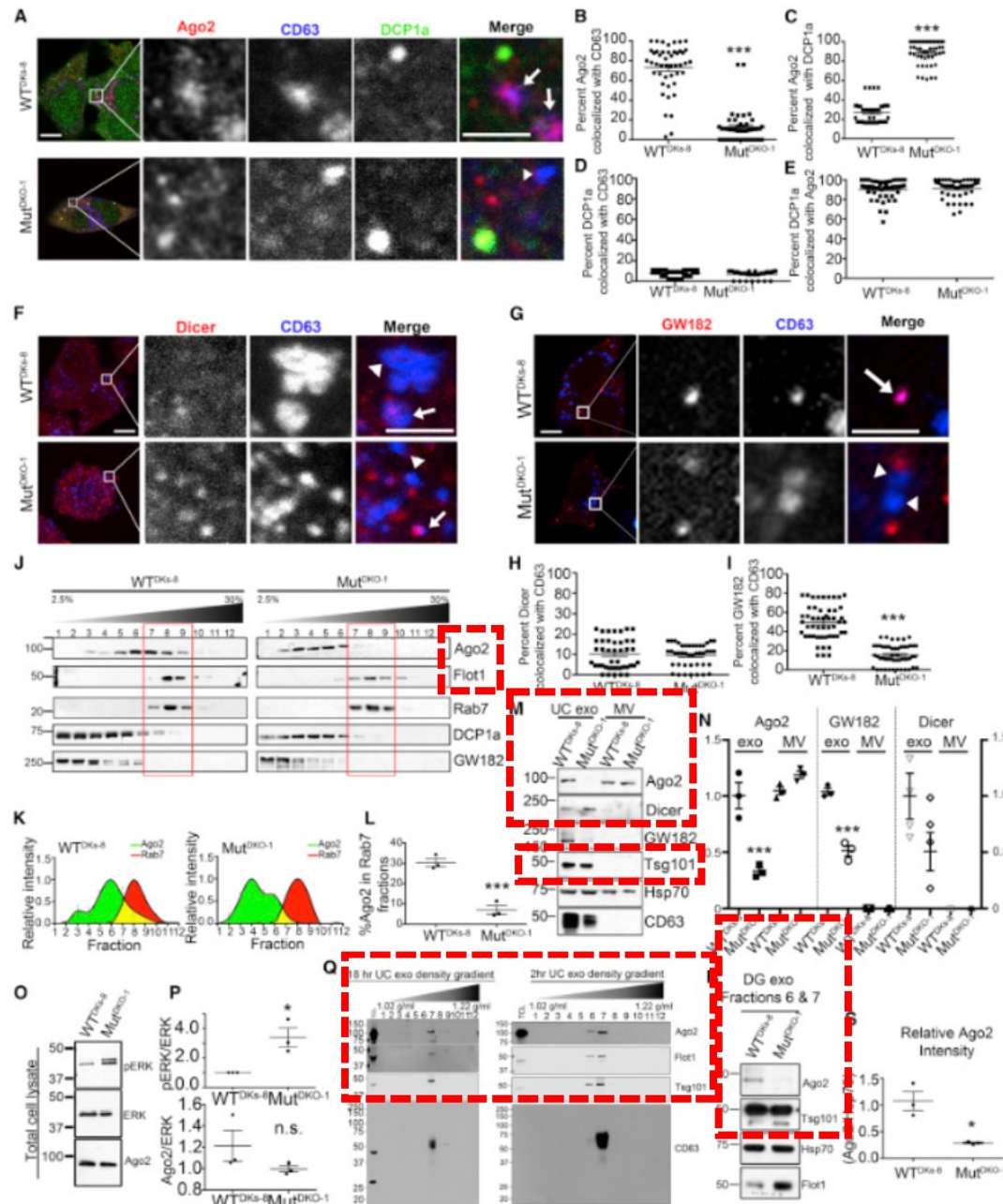


Demonstrates presence of the **exosomes marker TSG101** in exosomes from the serum of breast cancer patients.



# Example 3

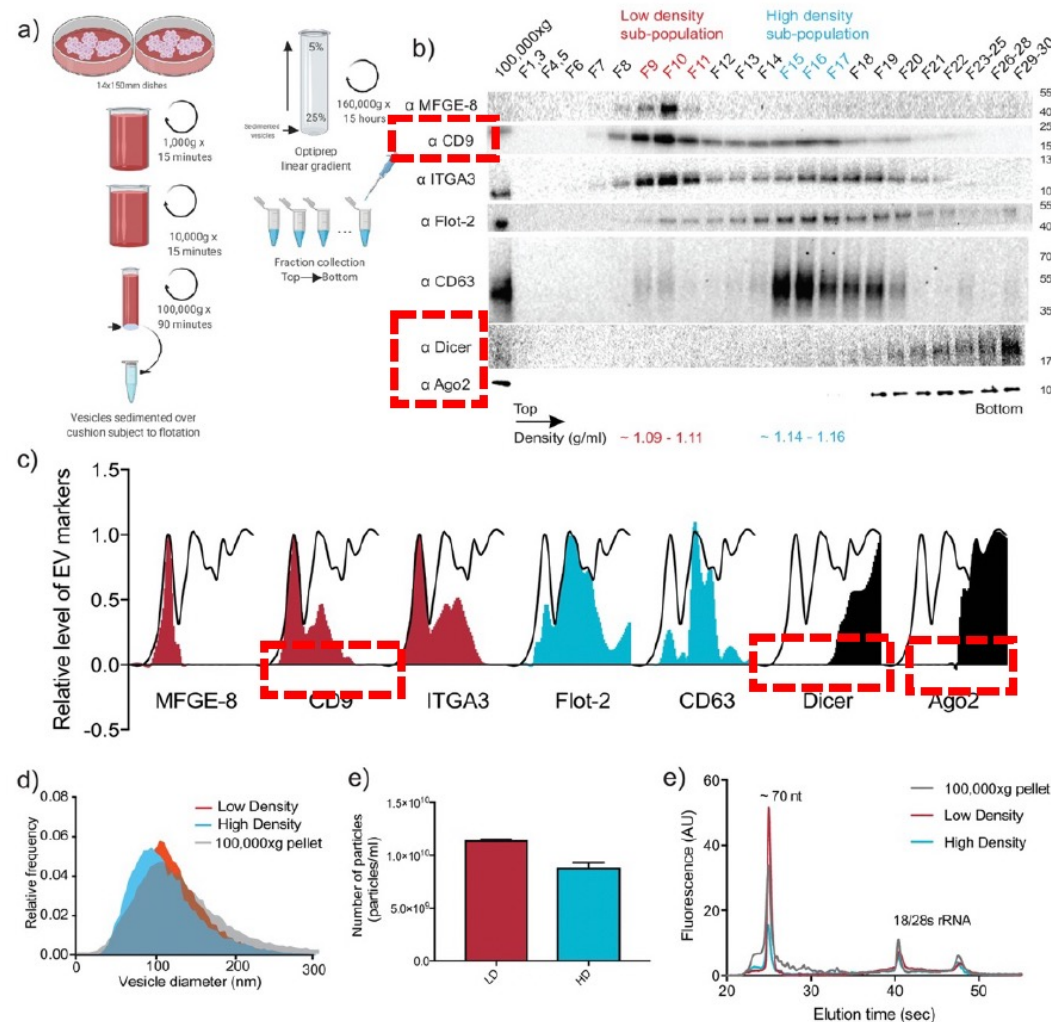
Cell Rep. 2016 May 3;15(5):978-987. doi:  
10.1016/j.celrep.2016.03.085



Demonstrates presence of  
**AGO2, Flotilin 1, Dicer, and  
TSG101** in exosomes.

# Example 4

**eLife 2019 8:e47544** Morayma M et al... Randy Schekman. Distinct mechanisms of microRNA sorting into cancer cell-derived extracellular vesicle subtypes.

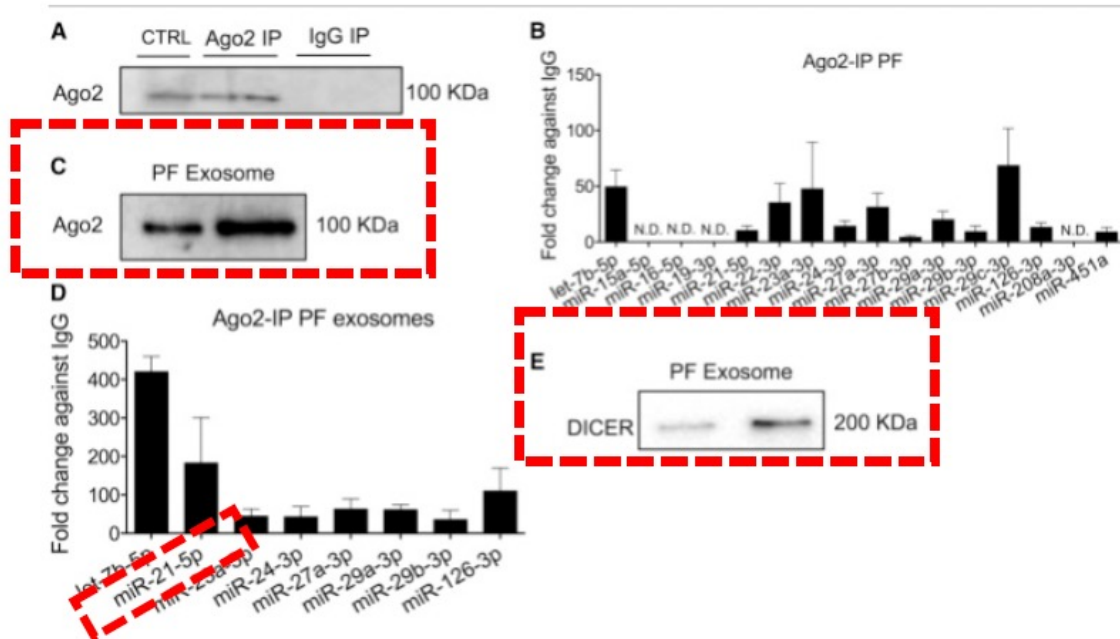


Demonstrates presence of **CD9, Dicer, and AGO2** in exosomes.

**Two biochemically distinct sEV sub-populations are released by MDA-MB-231 cells.**

# Example 5

Mol Ther. 2017 Mar 1;25(3):679-693. doi: 10.1016/j.ymthe.2016.12.022.



Demonstrates presence of **AGO-2, Dicer, and miR-21** in exosomes.

[Download : Download high-res image \(403KB\)](#)

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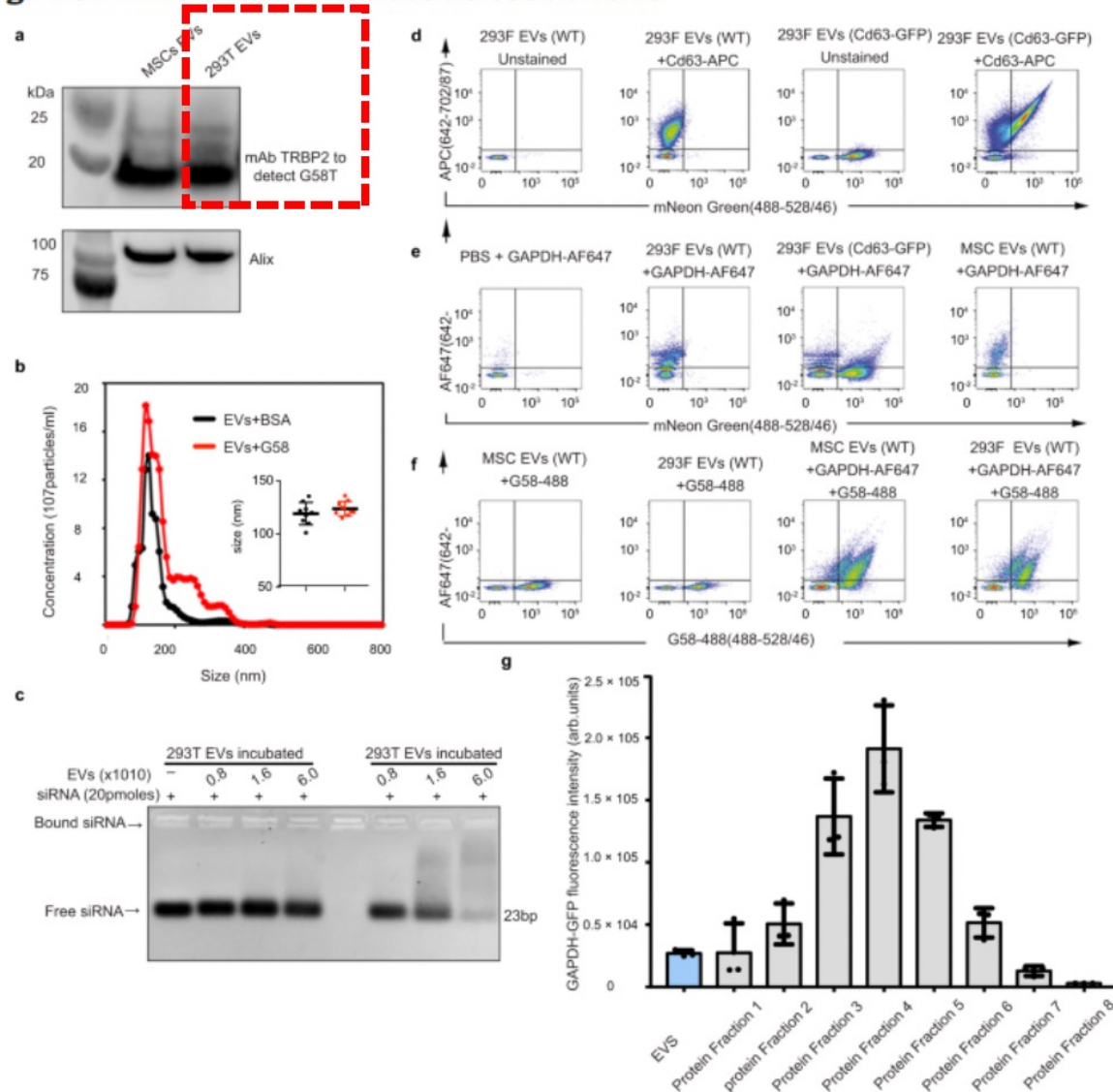
**Figure 4. PF Exosomes Contain DICER and AGO-2 Protein**

(A) Validation by immunoblotting of AGO-2 immunoprecipitation (IP) performed on human PF samples using AGO-2 antibody. Mouse non-specific IgG antibody was used as control for the IP. ECs were used as positive control (CTRL). (B) The miRNA expression after AGO-2 IP is presented as fold enrichment relative to IgG; mean+ SEM; n= 5. (C) AGO-2 in exosomes enriched from PF samples (representative western blot images). (D) AGO-2 IP was performed on exosomes enriched from PF samples. miRNA expression is expressed as fold enrichment in the AGO-2 IP relative to IgG; mean+ SEM; n= 2. (E) Representative western blot images of DICER protein incorporated in the exosomes.

# Example 6

Nat Commun 2021, 6666; Dar, G.H. et al. GAPDH controls extracellular vesicle biogenesis and enhances the therapeutic potential of EV mediated siRNA delivery to the brain.

**Fig. 2: GAPDH binds to EV surface via G58 domain.**



Demonstrates presence of **TRBP2** in extracellular vesicles.



# Example 7

J Biol Chem. 2013 Jul 5; 288(27): 20014–20033 doi: 10.1074/jbc.M112.438895

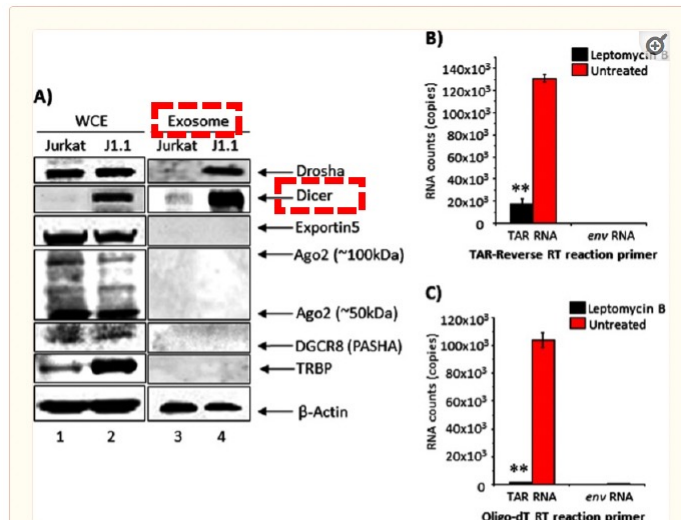


FIGURE 5.

J1.1-derived exosomes contain components of the RNAi machinery. *A*, Jurkat- and J1.1-derived whole cell extracts and exosomes were separated on a 4–20% Tris-glycine gel and analyzed by Western blot using antibodies against Dicer, Drosha, exportin, Ago2, DGCR8, TRBP, and β-actin. Total RNA isolated from J1.1-derived exosomes with and without leptomycin B treatment (10 nM) was subjected to qRT-PCR with TAR-reverse primer (*B*) and oligo(dT) primers (*C*). cDNA was then quantified by SYBR Green real time PCR with the primer sets specific for HIV-1 TAR and env sequences. Error bars show the standard deviation from three independent RNA preparations. Double asterisk indicates  $p \leq 0.01$ .

Demonstrates presence of **Dicer** in exosomes.

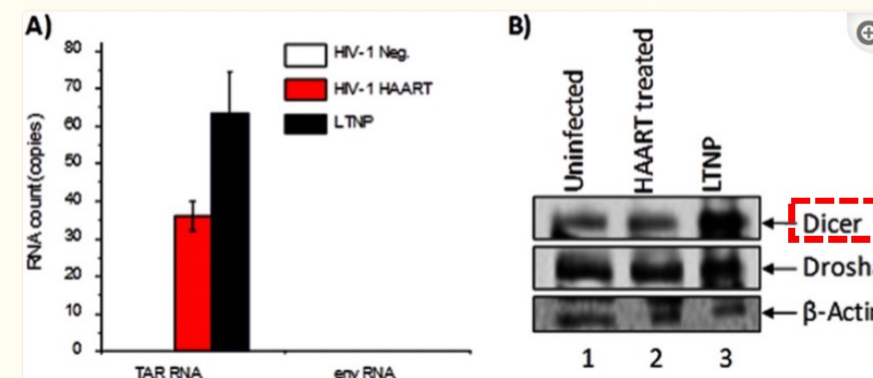


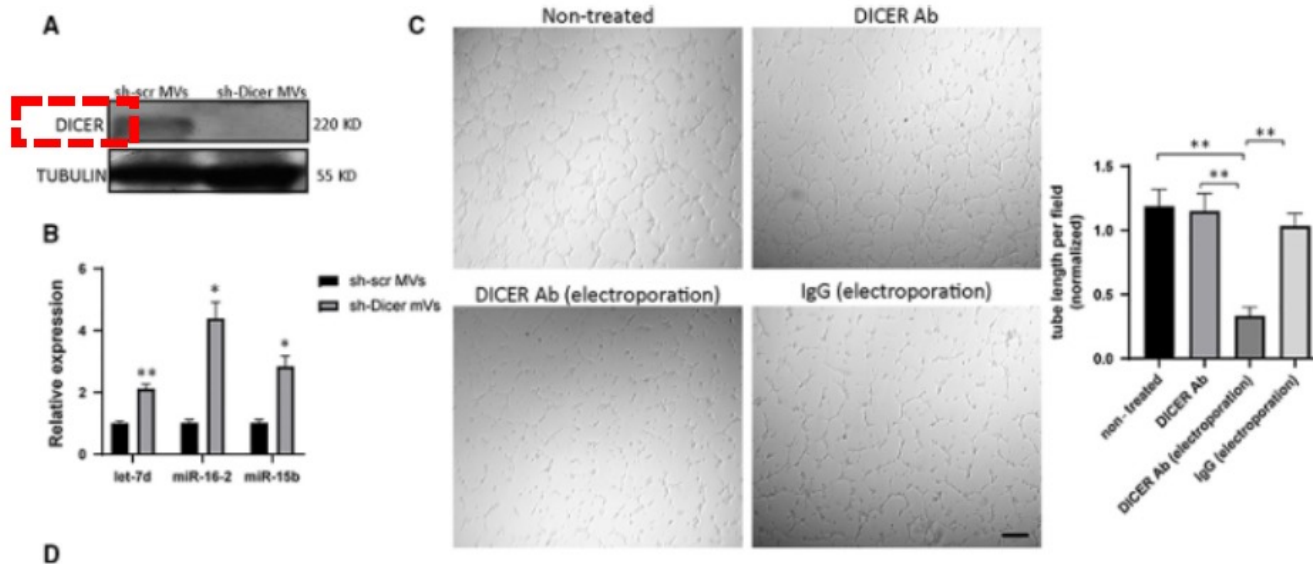
FIGURE 10.

TAR RNA, Dicer, and Drosha can be detected in serum exosomes. *A*, exosomes were isolated from pooled sera obtained from uninfected (control), HAART-treated, and LTNP HIV-1-infected patient groups and analyzed by qRT-

Demonstrates presence of **Dicer** in exosomes.

# Example 8

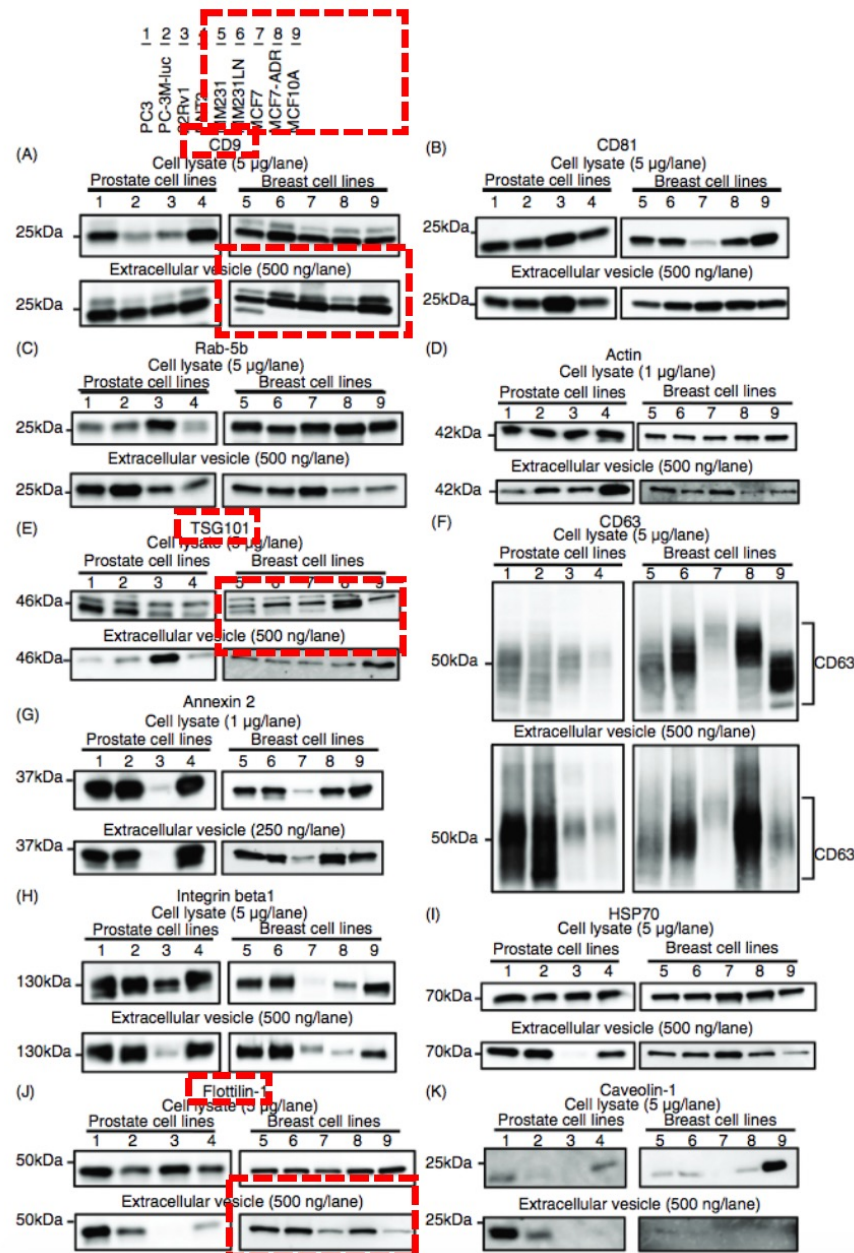
J Cell Mol Med. 2020 May;24(9):4915-4930. doi: 10.1111/jcmm.14917



Demonstrates presence of **Dicer** in exosomes.

# Example 9

Journal of Extracellular Vesicles 2013 Yusuke Yoshioka et al. Comparative marker analysis of extracellular vesicles in different human cancer types.



Same cell lines used in Cancer Cell 2014 manuscript: **MCF10A, MCF7, and MDA-MB-231.**

Demonstrates presence of the **exosomes markers TSG101, CD9, Flotillin-1.**

# Example 10

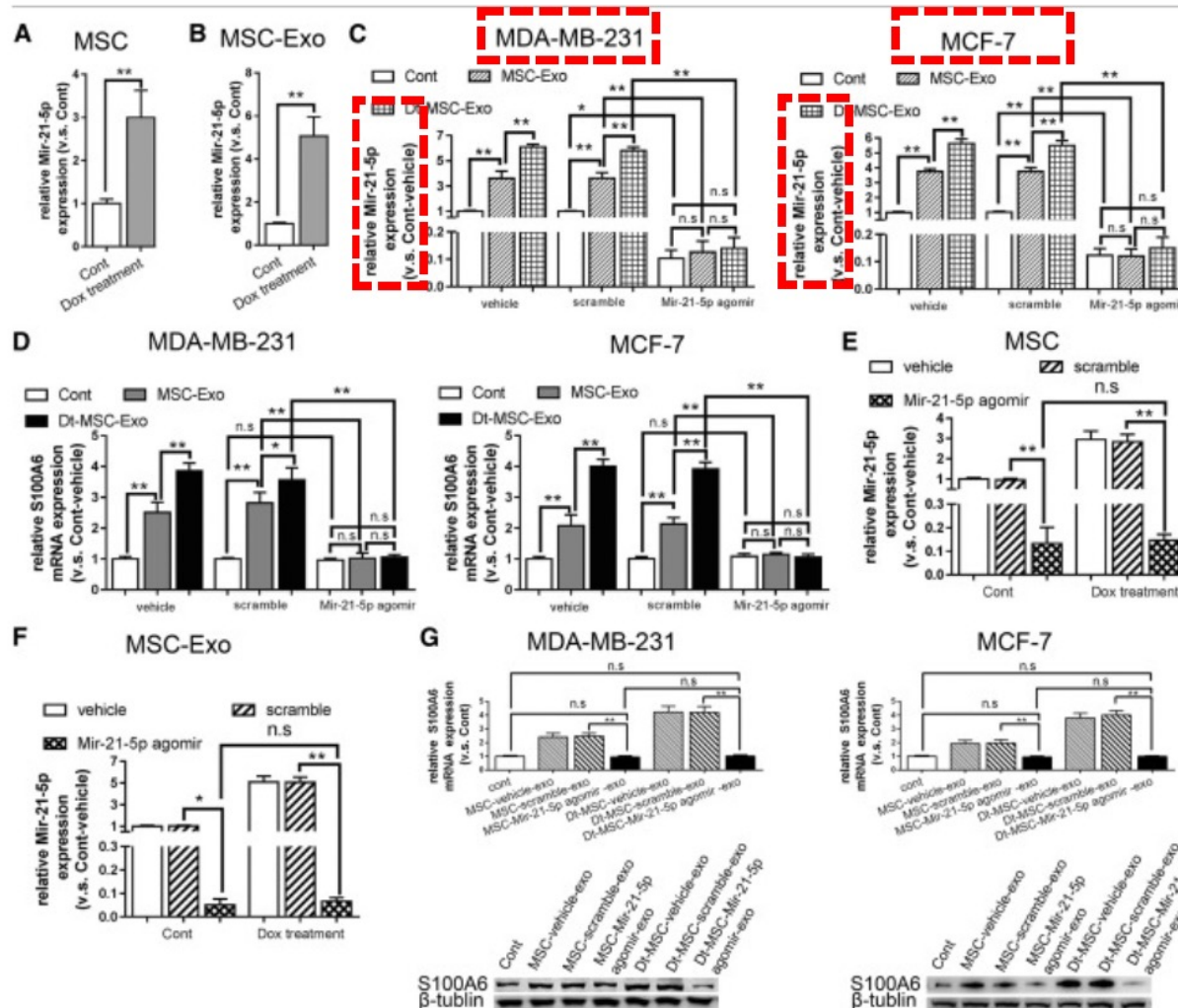
Digestion. 2021;102(4):640-649. **Serum Exosomal Dicer** Is a Useful Biomarker for Early Detection of Differentiated Gastric Adenocarcinoma.

Relates to **Figure 7I** of Cancer Cell 2014 manuscript demonstrating breast cancer serum exosomal Dicer.



# Example 11

**Molecular Therapy - Oncolytics, 2020** Tao Luo et al. Mesenchymal Stem Cell-Secreted Exosome Promotes Chemoresistance in Breast Cancer via Enhancing miR-21-5p Mediated S100A6 Expression.



Same cell lines used in Cancer Cell 2014 manuscript: **MCF7 and MDA-MB-231.**

Demonstrates presence of the **microRNA 21.**

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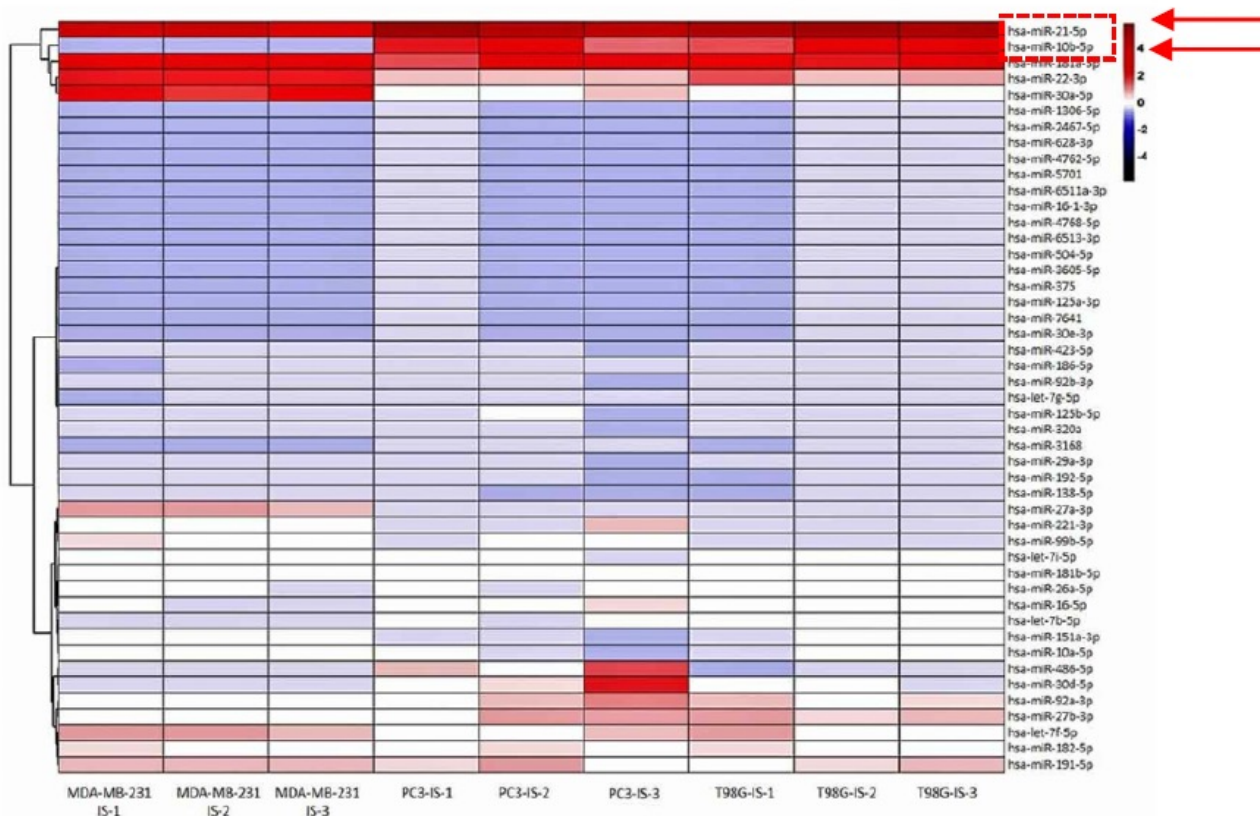
Figure6. MSC-exo and Dt-MSC-exo Promote the Expression of S100A6 in BCs by Delivering miR-21-5p

# Example 12

Cell Adhesion & Migration 2021 Francesca Lessi et.al. Analysis of exosomederived microRNAs reveals insights of intercellular communication during invasion of breast, prostate and glioblastoma cancer cells. 15:1, 180-201.

Figure 4 of 12

Figure 4. Exosomes-derived differentially abundant miRNAs. Heatmap generated with R showing the statistical significant differentially abundant exosomes-derived miRNAs in all three replicates (1, 2 and 3) of the cell lines subjected to the IS



**MicroRNA 21 and microRNA 10b** detected as the **most abundant** microRNAs in **exosomes of MDA-MB231 cells** (the same used in the Cancer Cell 2014 manuscript).