



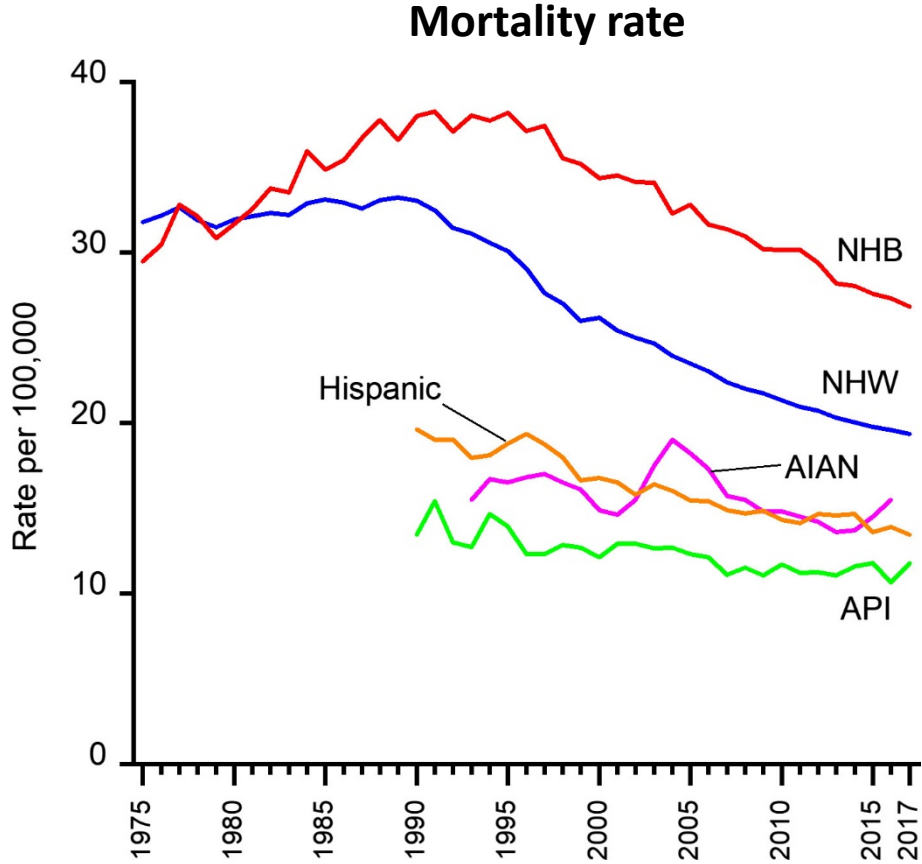
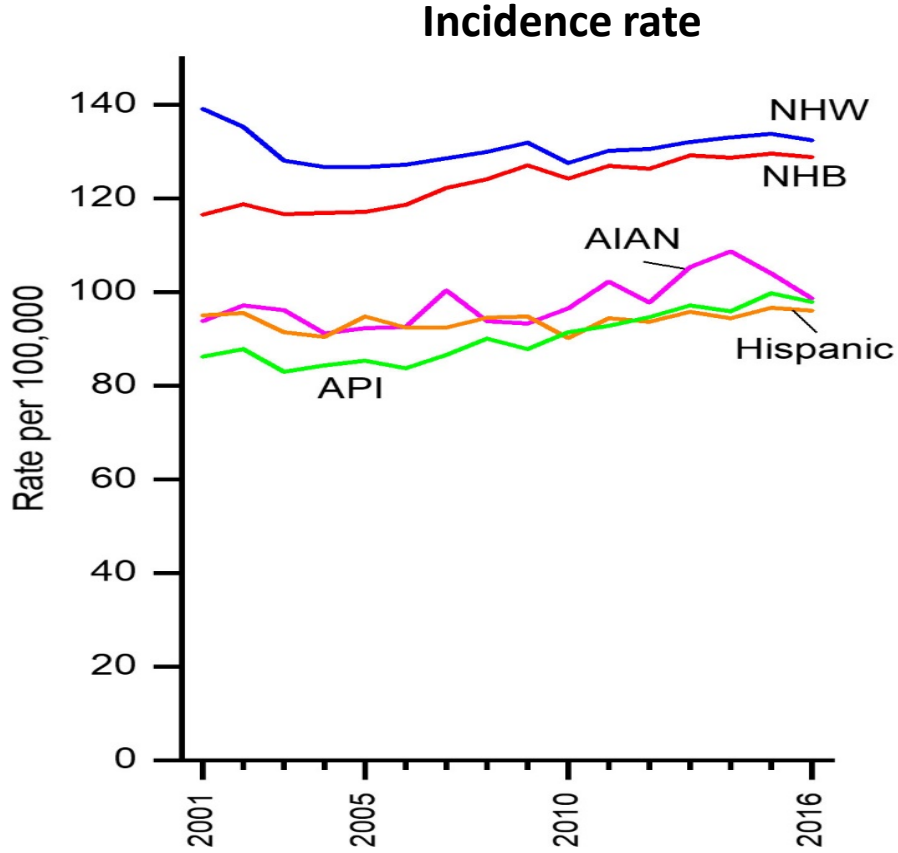
Bioengineered serum-derived exosomes-nanosystem for triple negative breast cancer therapy

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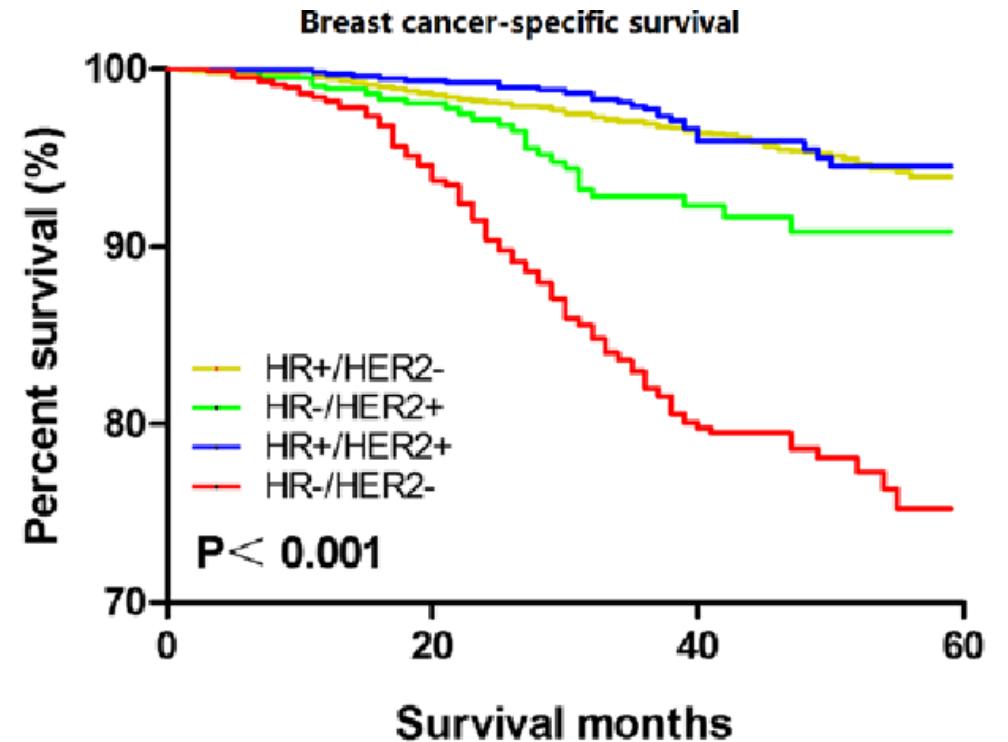
Trends in Female Breast Cancer by Race/Ethnicity



AIAN indicates American Indian/Alaska Native; API, Asian/Pacific Islander; NHB, non-Hispanic black; NHW, non-Hispanic white. 2001 to 2016, United States

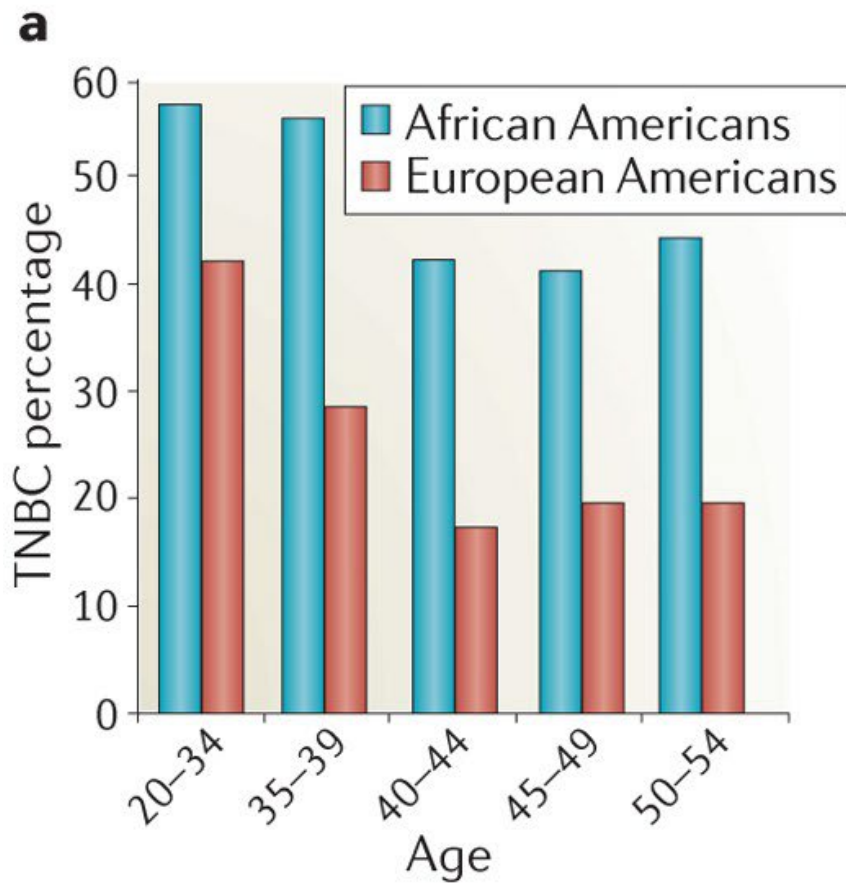
Triple Negative Breast Cancer (TNBC)

- ❑ Triple negative breast cancer (TNBC) definition:
 - Lack of expression of estrogen receptor (-ER) and progesterone receptor (-PR)
 - HER2 not overexpressed/amplified (-HER2)
- ❑ Triple negative breast cancer is the most lethal form of breast cancer
- ❑ 15-20 % of all breast cancers
- ❑ The prevalence of TNBC is higher in women of African American ethnicity
- ❑ TNBC is heterogeneous and harbors several molecular alterations

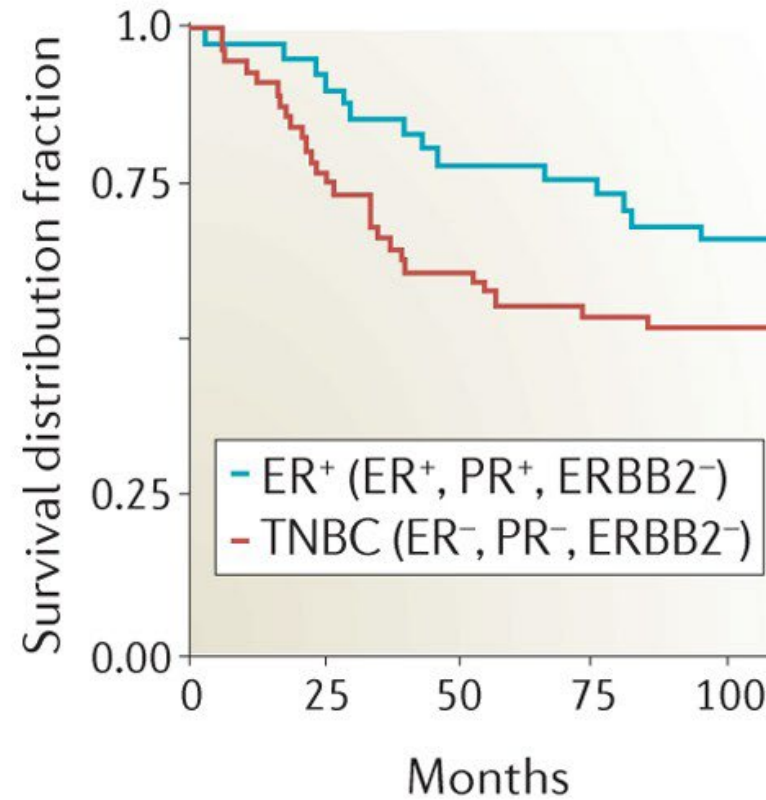


Overall survival in patients with triple-negative breast cancer (TNBC) and non-TNBC

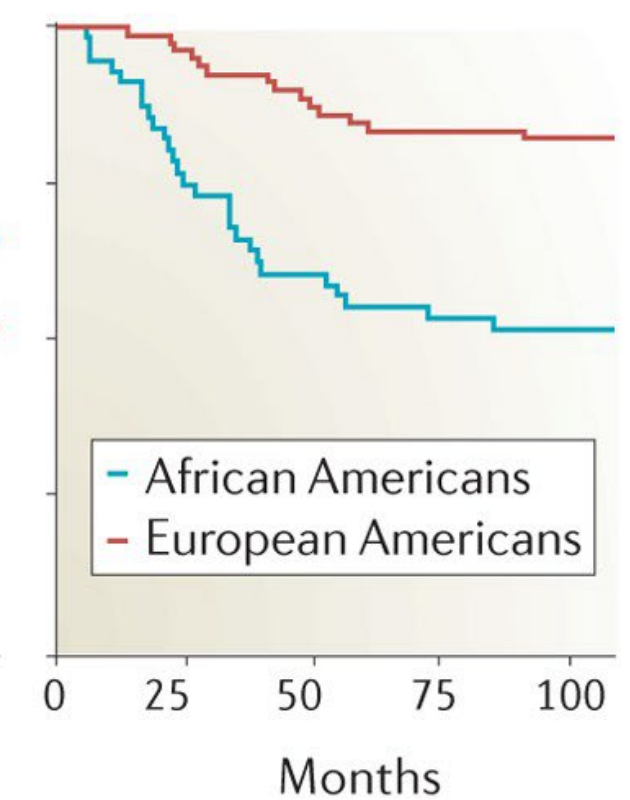
Racial Distribution of TNBC



b African-American women



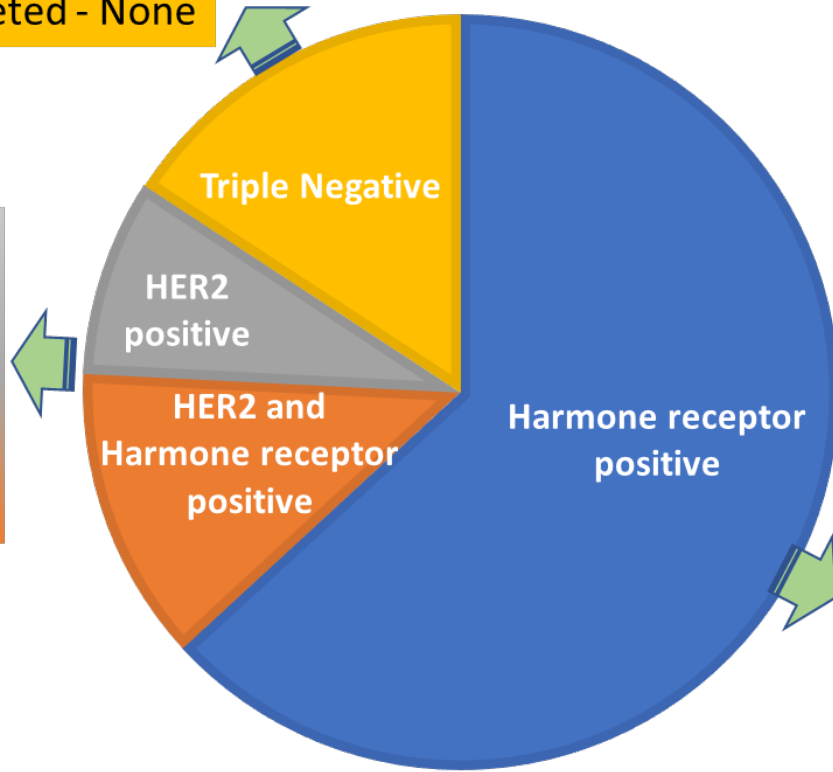
c TNBC: ER-, PR-, ERBB2-



Current Treatment Option for Breast Cancer

TNBC

- Surgery
- Chemotherapy
- Radiotherapy
- Targeted - None

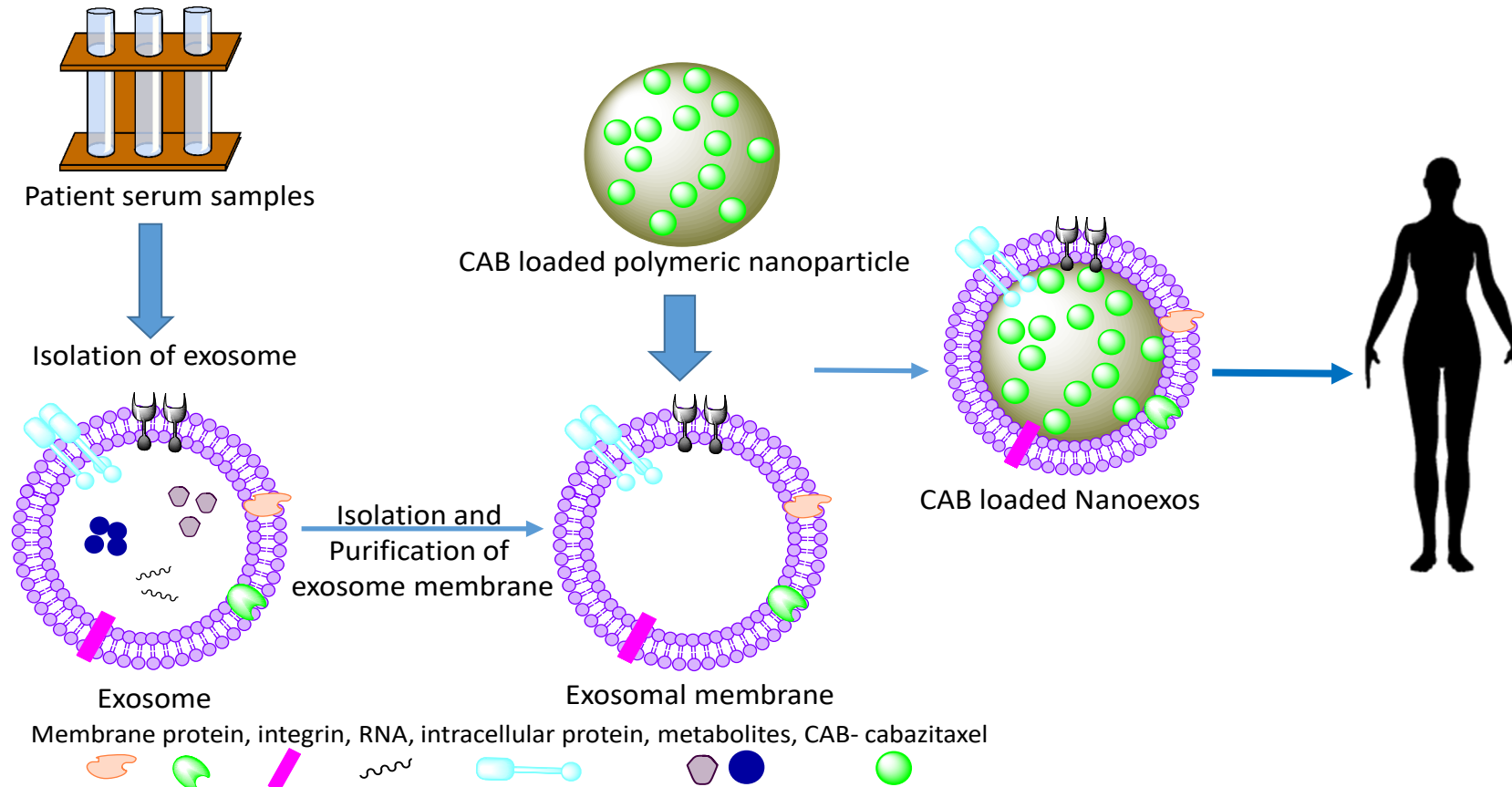


- Surgery
- Chemotherapy
- Radiotherapy
- Targeted – Herceptin or other anti HER2 therapy

- Surgery
- Chemotherapy
- Radiotherapy
- Targeted – Tamoxifen and other anti-endocrine therapy

- ❑ Conventional chemotherapy is only known standard treatment along with surgery and radiation therapy.
- ❑ Chemotherapy typically includes single agent or combination of Taxanes, Anthracyclines and Oxazophorines.
- ❑ There is no specific targeted therapy on TNBC. Development of new targeted therapies may be able to treat TNBC.

Bioengineered Serum-derived Exosomes-nanosystem

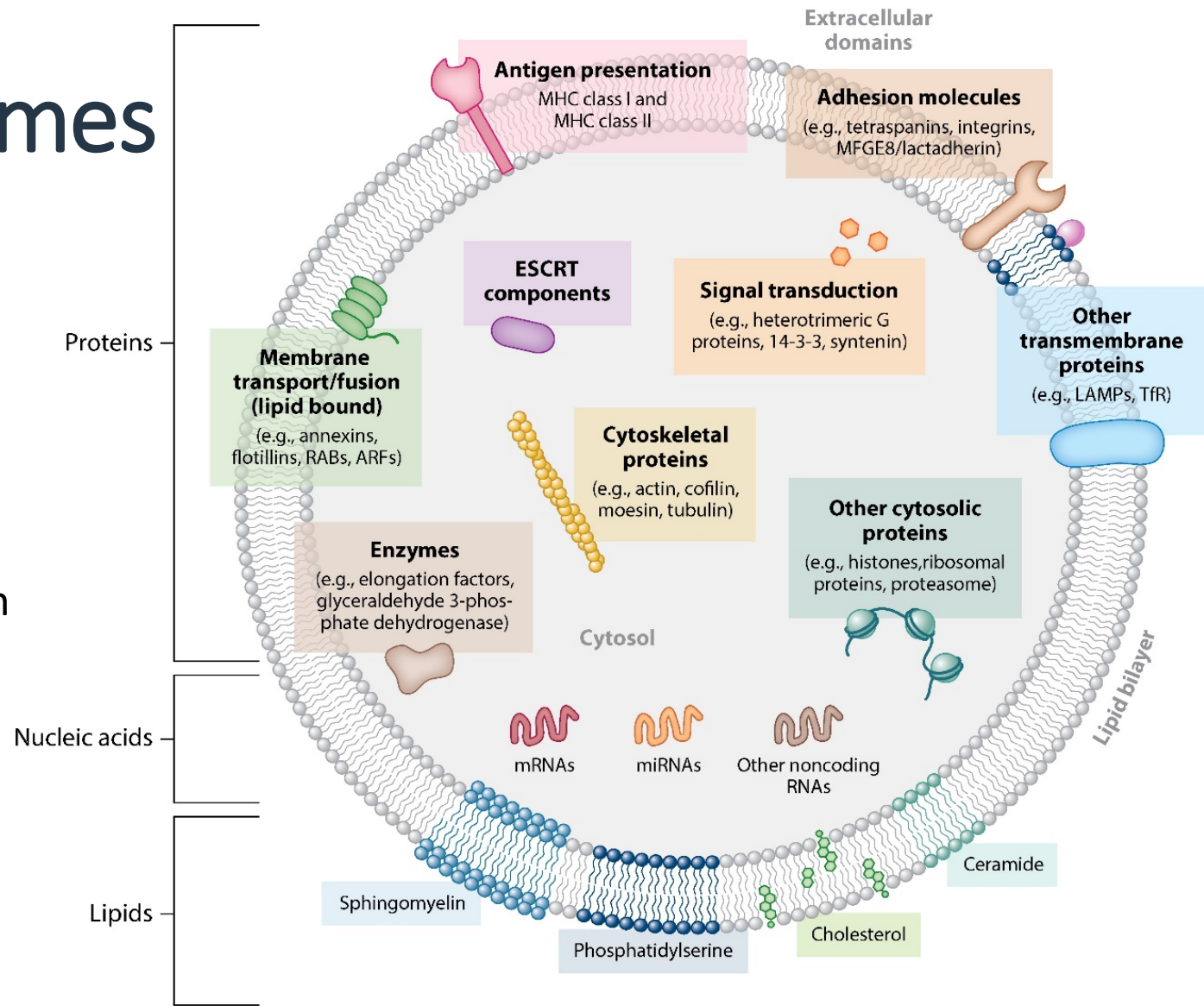


We will exploit the unique properties and advantages offered by exosomes and drug loaded polymeric nanoparticles and create a novel bioengineered serum-derived exosomes-nanosystem

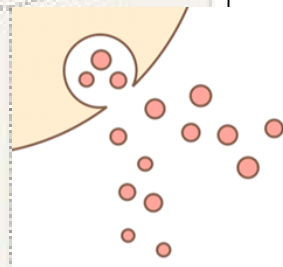
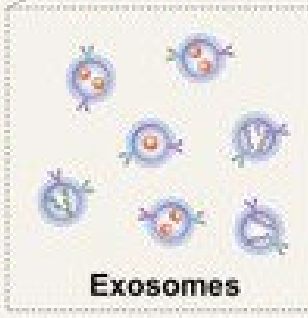
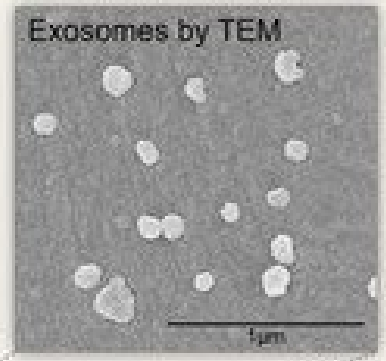
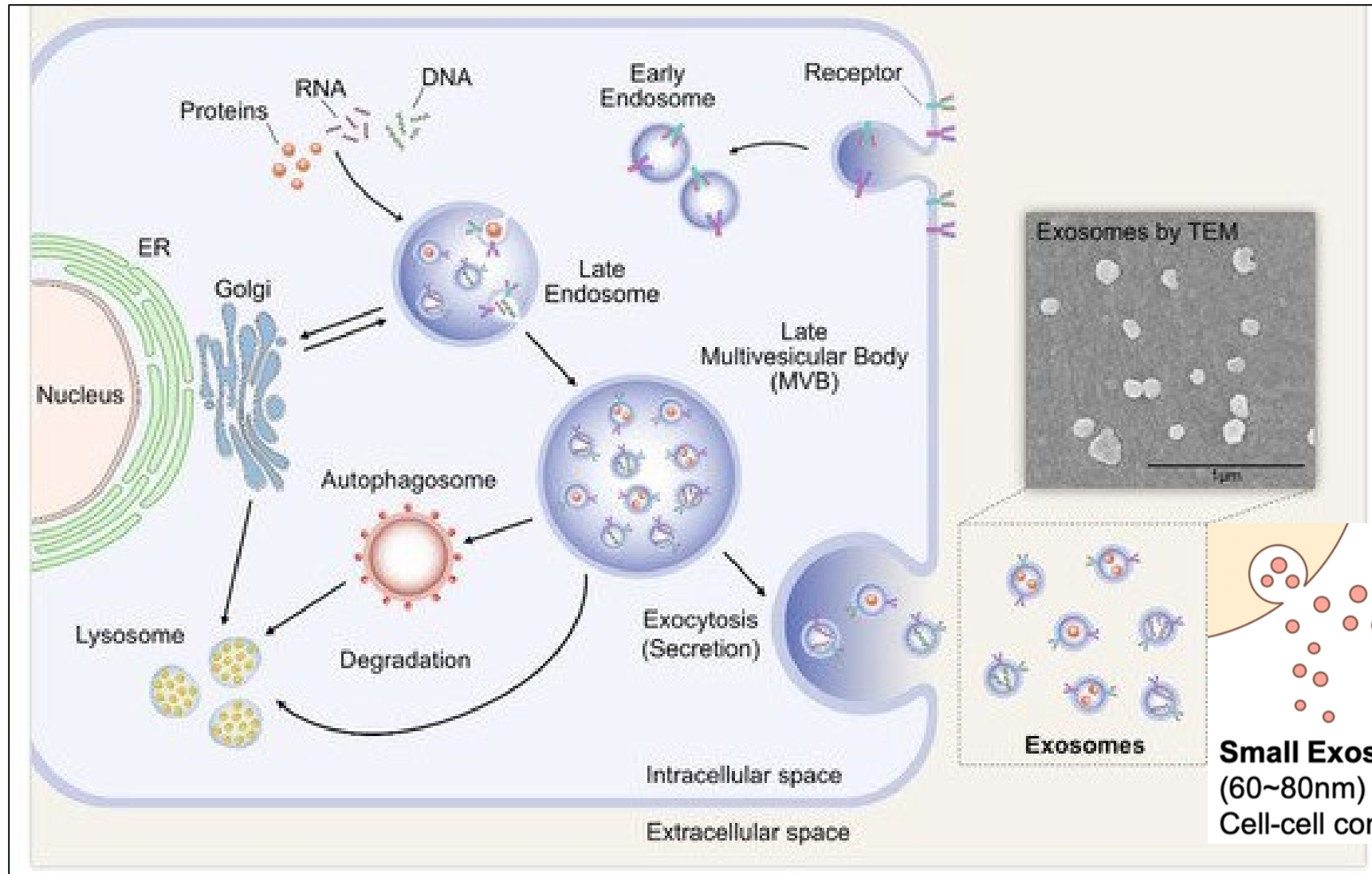
CAB: Cabazitaxel

Properties

- Long body circulations
- Biocompatibility and safe
- Cargo protection and encapsulation
- Biodegradable
- Enhanced biodistribution
- Targeted delivery



Exosome Biogenesis



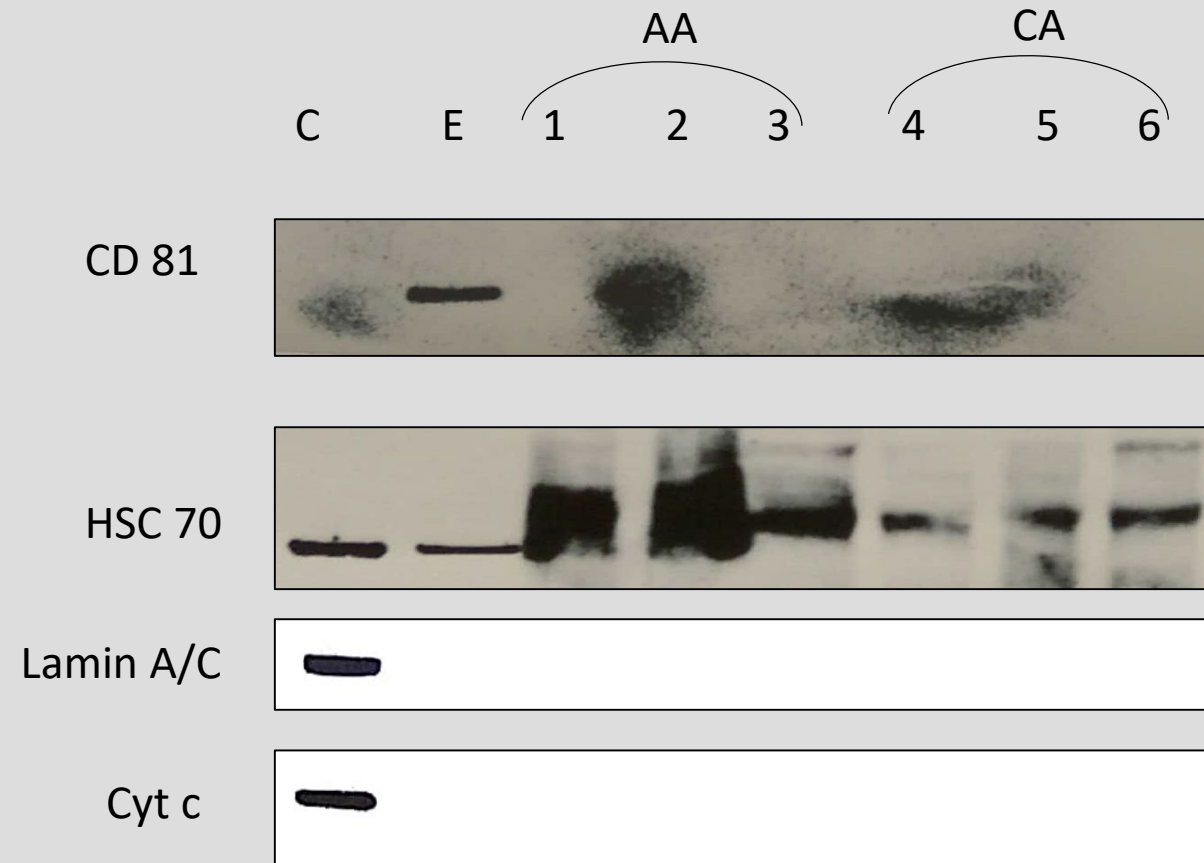
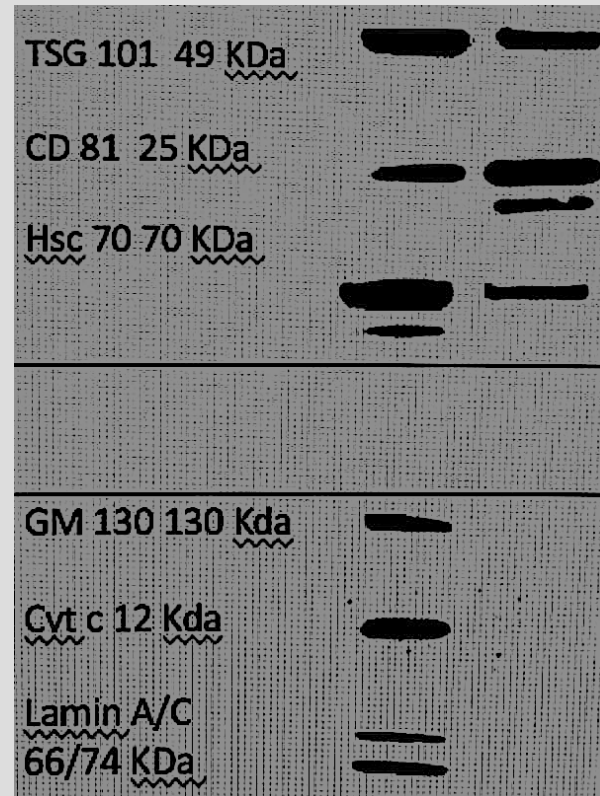
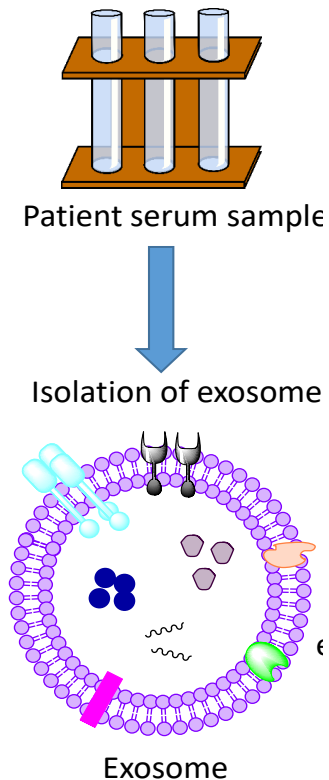
Large Exosomes
(90~120nm)
Cell-cell communication

Small Exosomes
(60~80nm)
Cell-cell communication

Isolation and Characterization of Exosomes from Serum

Control: TNBC cells – MDAMB 231

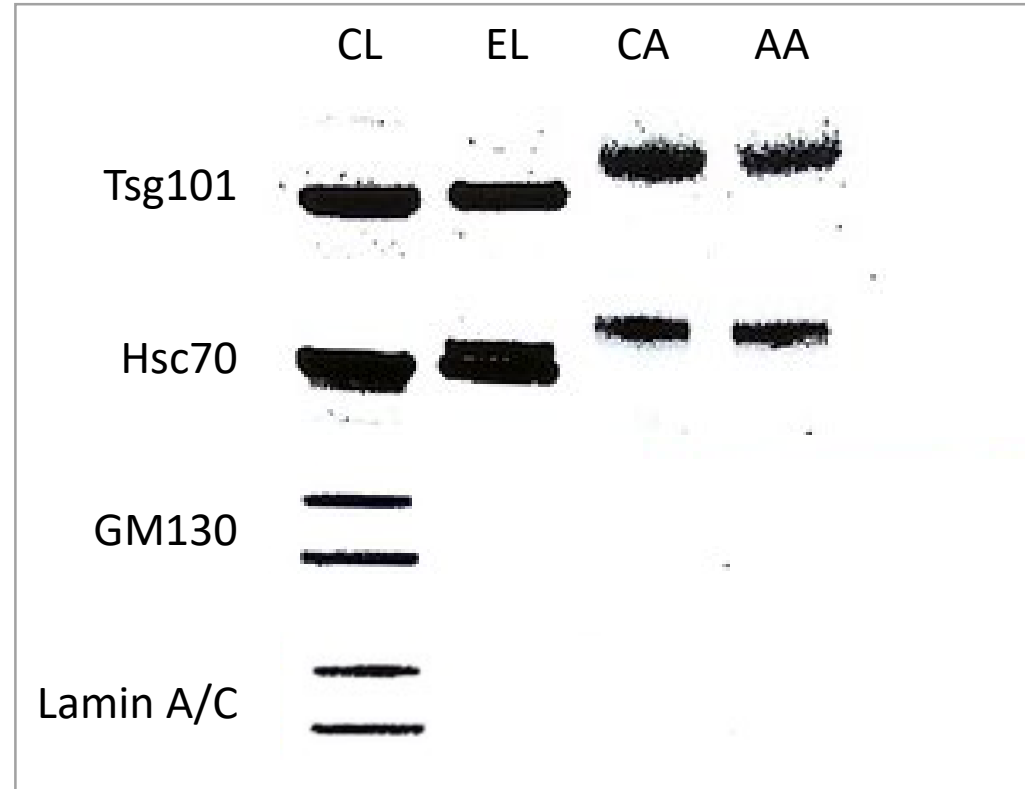
TNBC-Serum samples



Exosomal surface markers: positive markers: TSG 101, CD 81, Hsc70; Negative markers: GM 130, Cyt c, Lamin A/C

Isolation and Characterization of Exosomes from Pooled Human Serum

TNBC Pool of five different serum samples

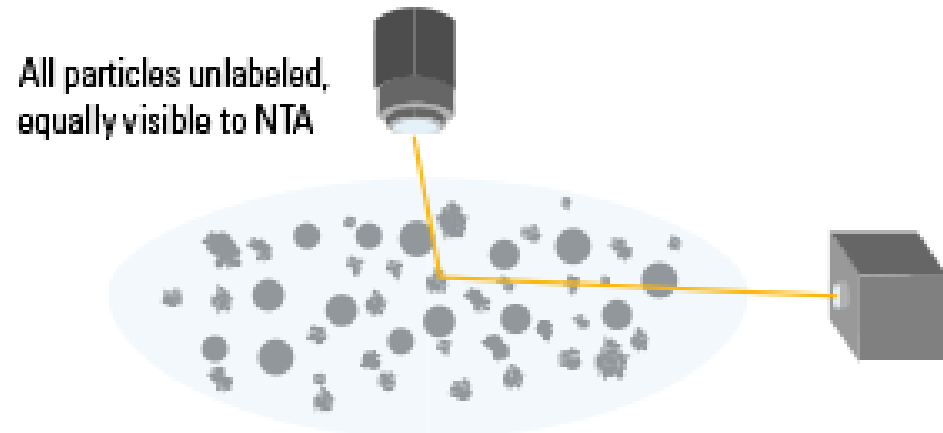


CL: Cell lysate
EL: Exosomal lysate
CA: Caucasian American
AA: African American

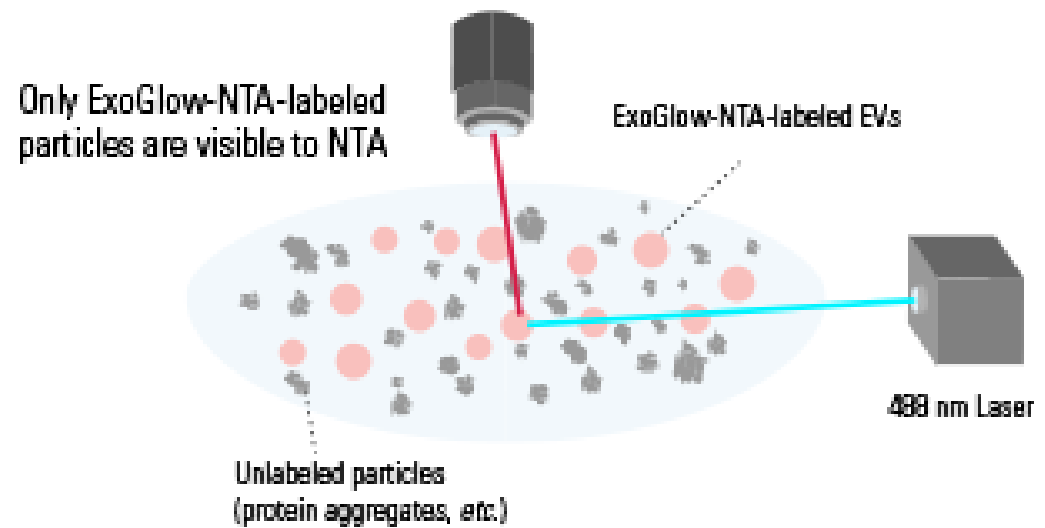
Exosomal surface markers: positive markers: TSG 101, CD 81, Hsc70; Negative markers: GM 130, Cyt c, Lamin A/C

NTA Measurement

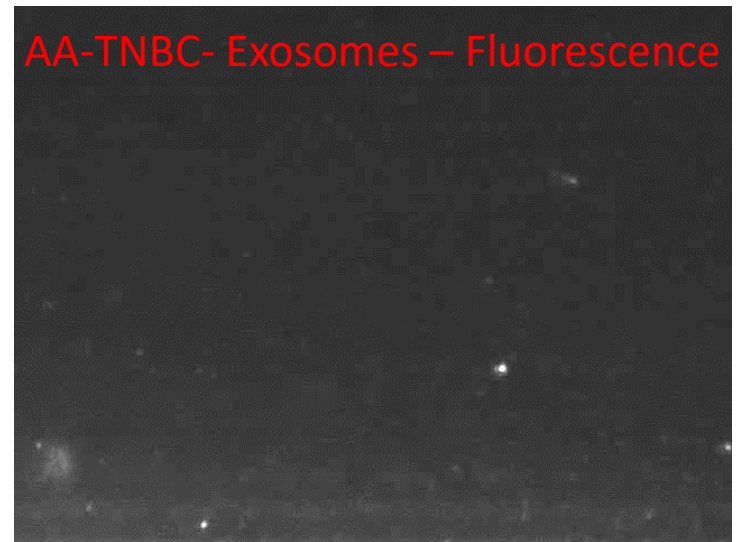
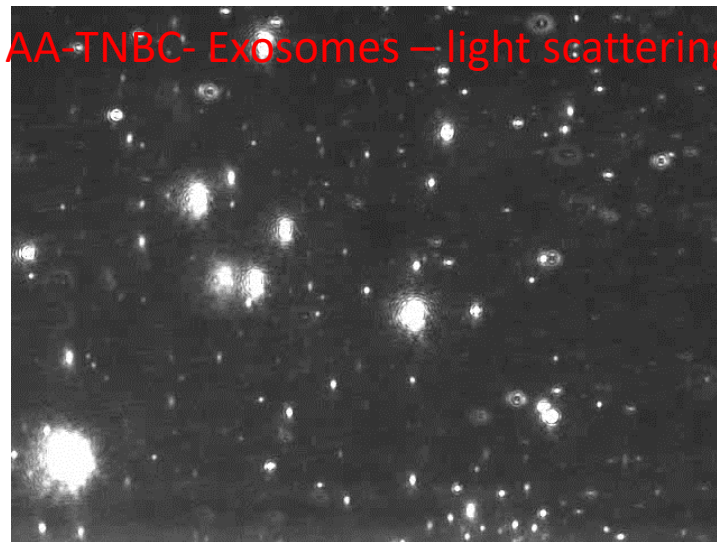
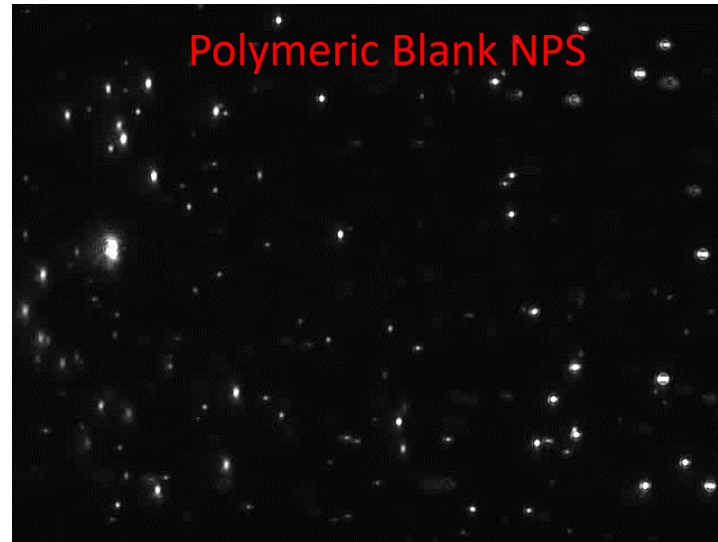
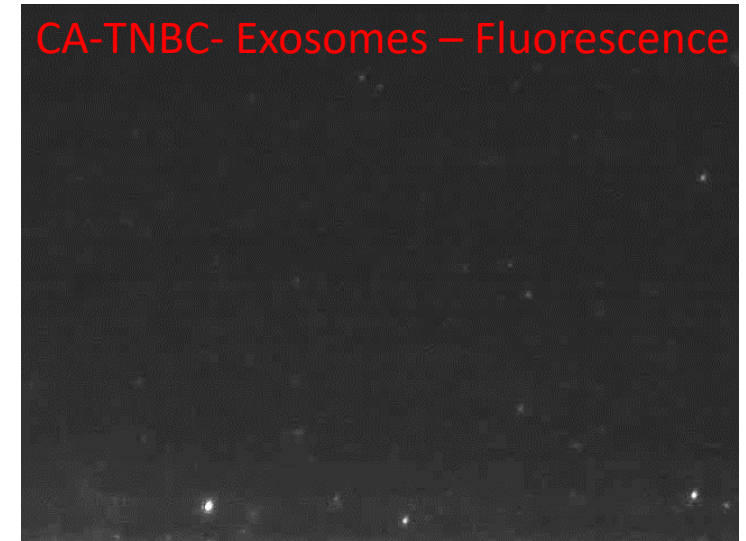
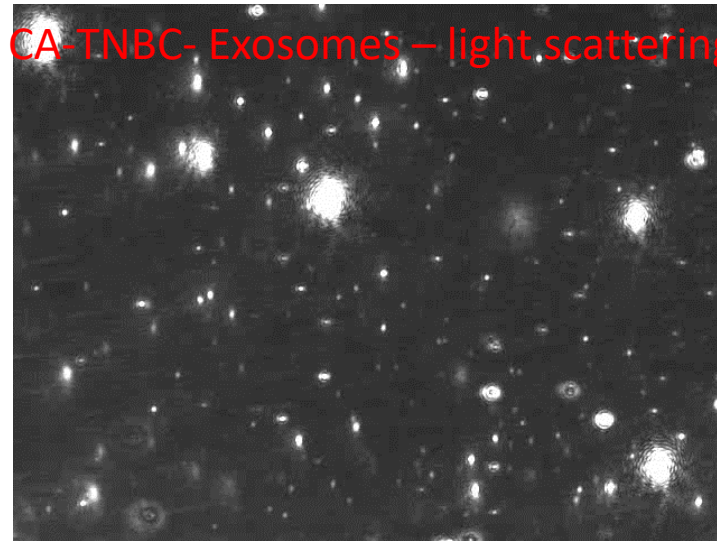
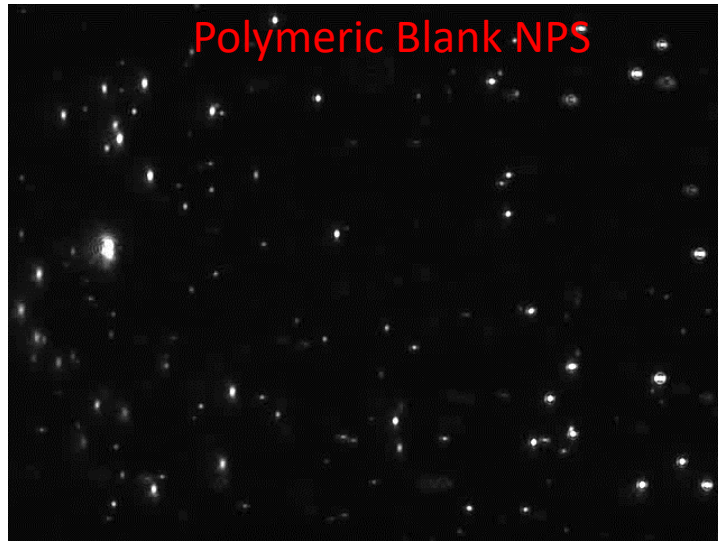
A. Conventional NTA



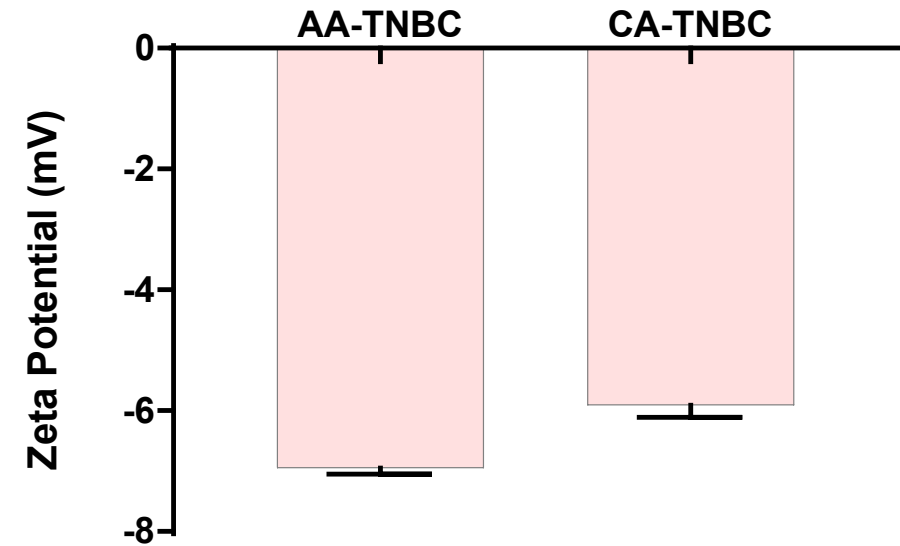
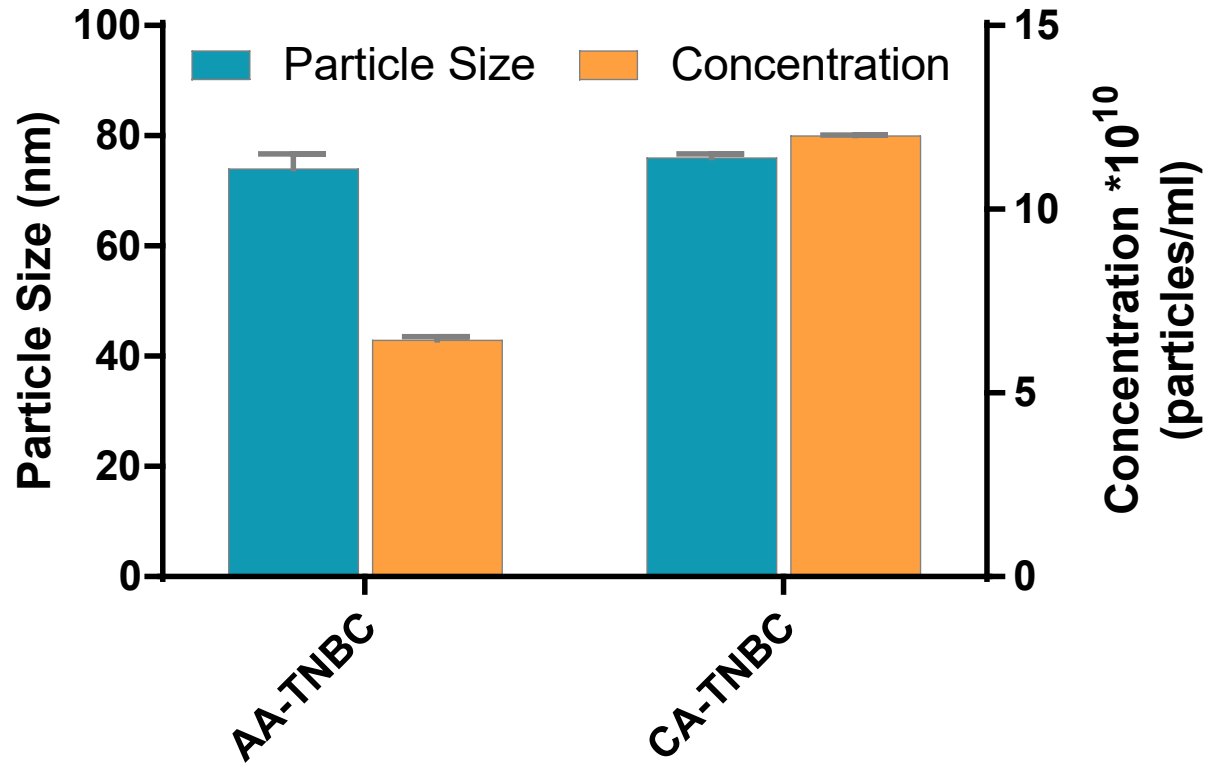
B. Fluorescent NTA



NTA Measurement of Serum Exosomes

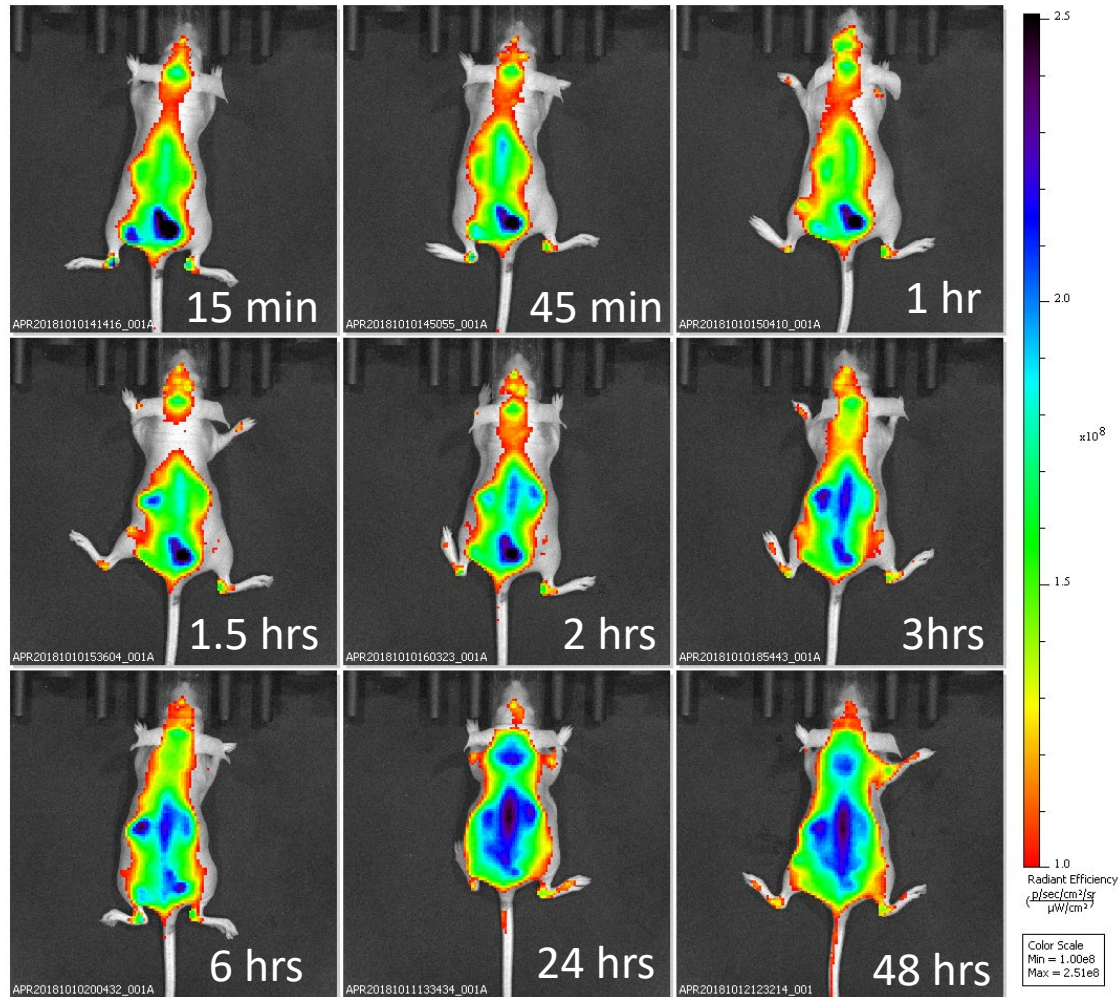


Particle Size and Zeta Potential

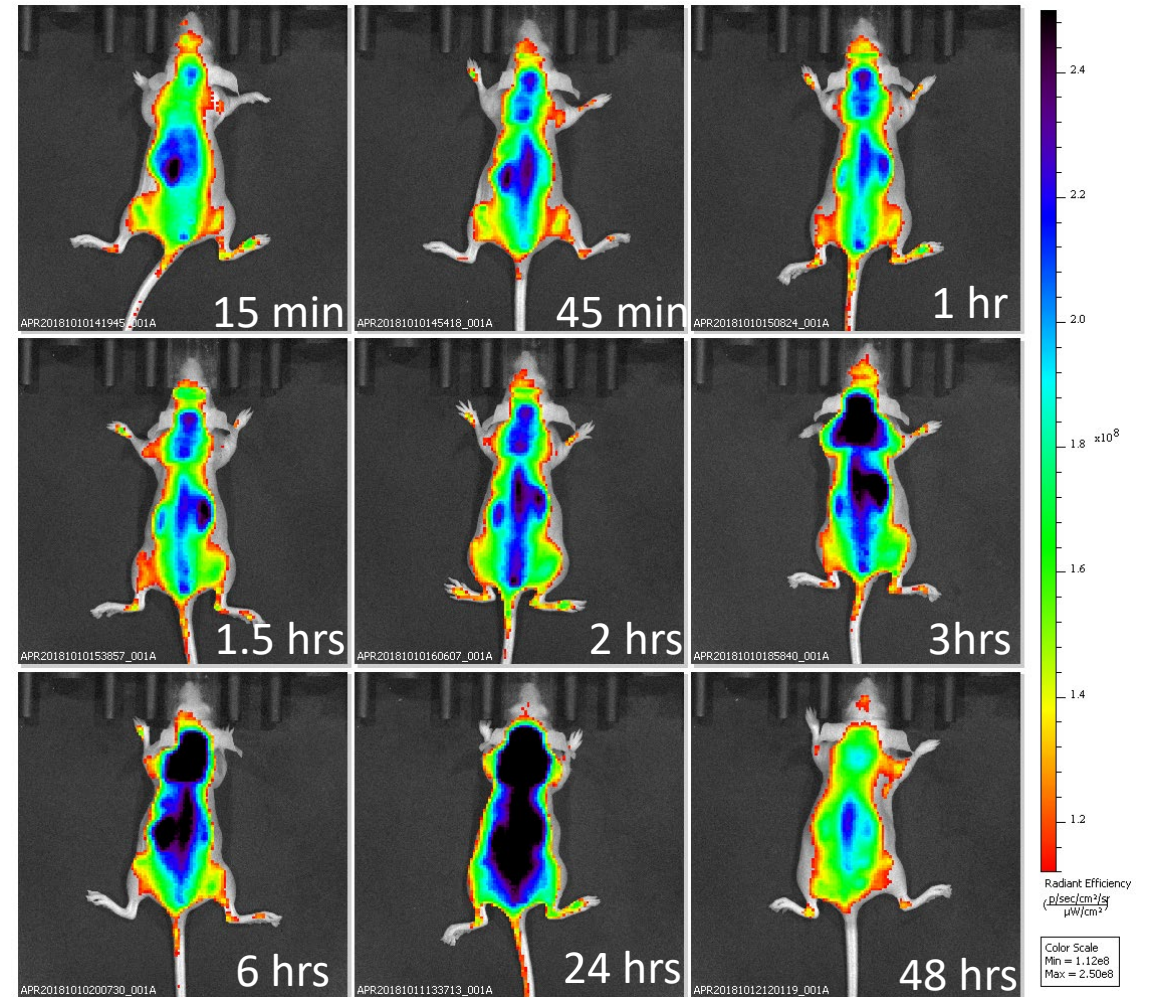


In vivo Biodistribution of Exosomes in Nude Mice

AA TNBC patient serum exosomes



CA TNBC patient serum exosomes

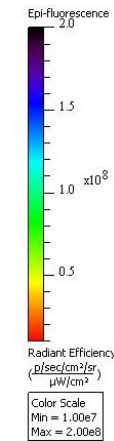
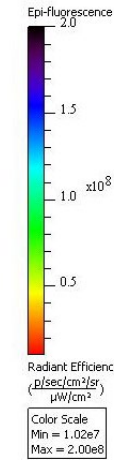
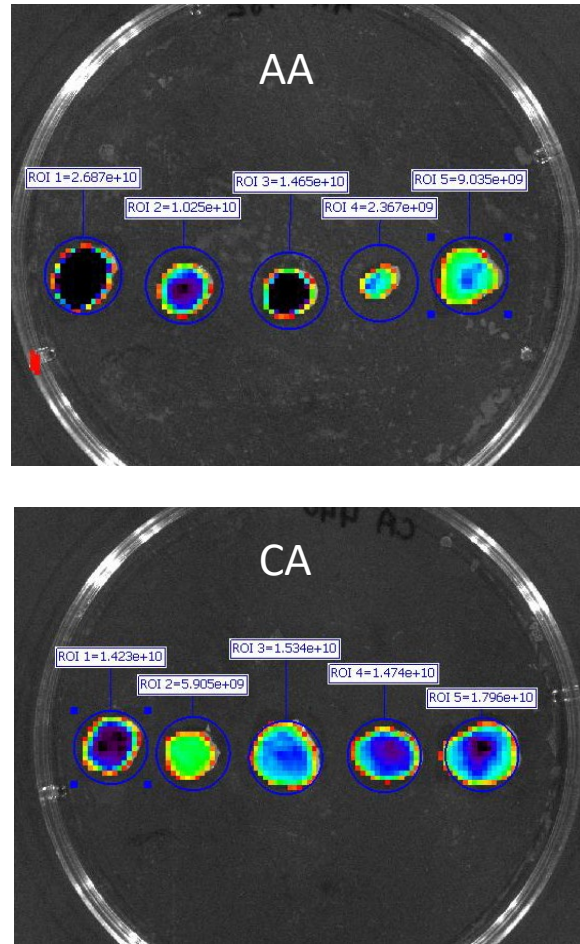
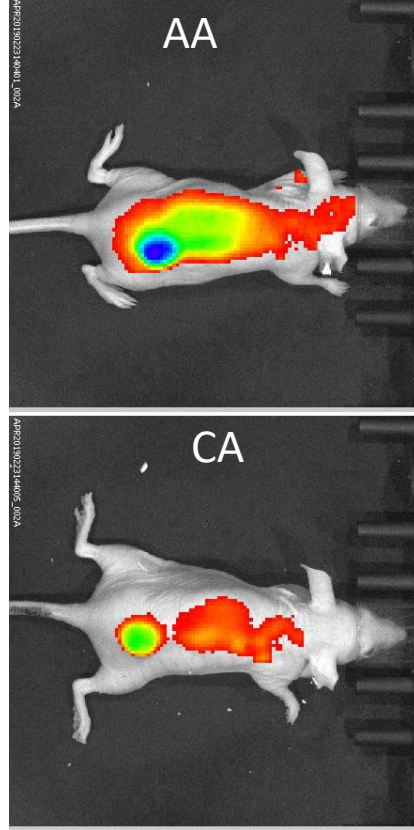
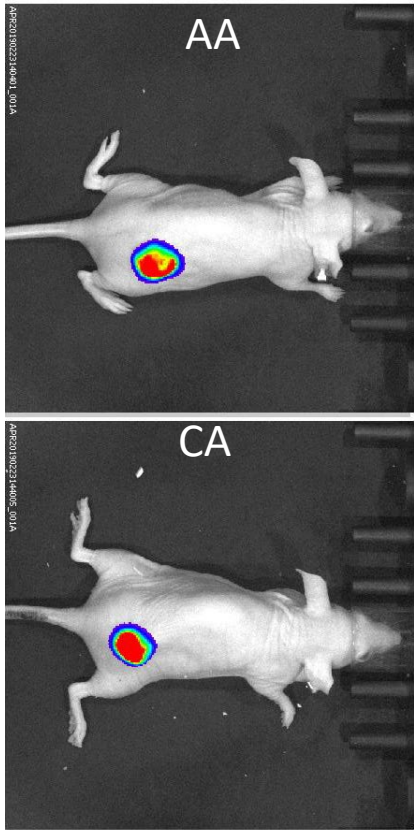


Biodistribution of serum exosomes in tumor bearing athymic nude mice

A

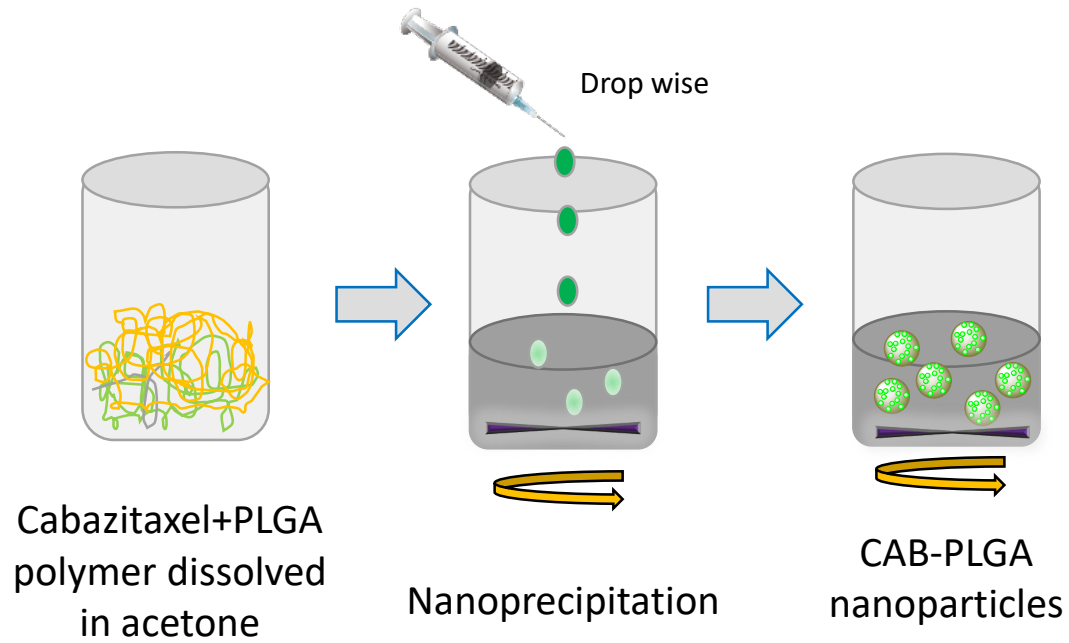
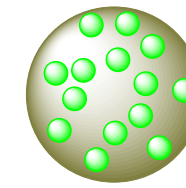
B

C



- A. Representative bio illuminance image of tumor
- B. Representative fluorescence image of IR dye tagged exosomes from serum samples,
- C. Serum exosome distribution in tumor of different mice.

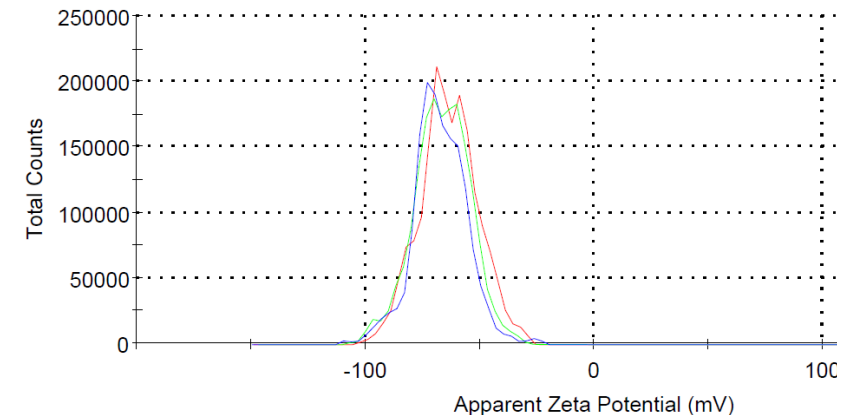
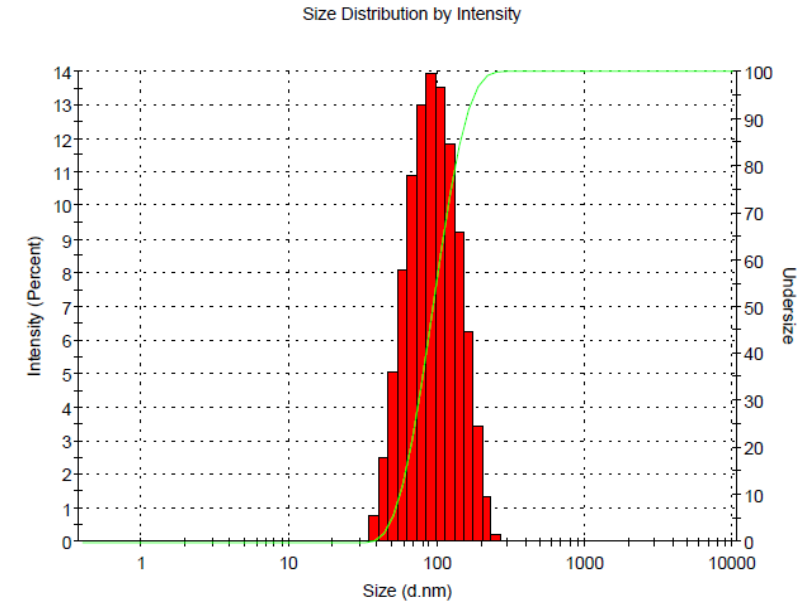
Formulation of Cabazitaxel Loaded PLGA Nanoparticles



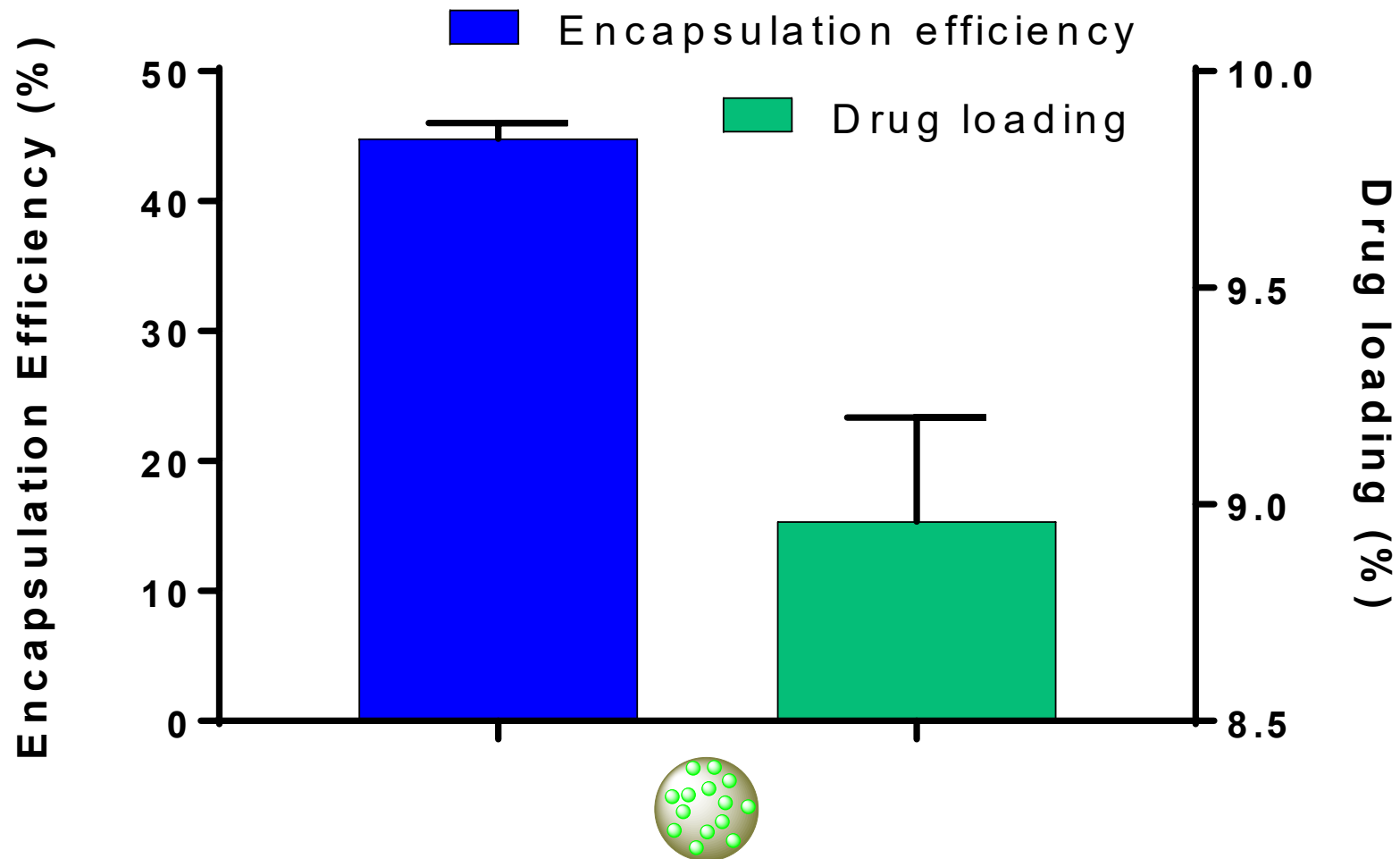
Particle size (nm): 87.83 ± 1.5

PDI: 0.113 ± 0.014

Zeta potential (mV): -45.5 ± 2.60



Drug Loading and Encapsulation Efficiency

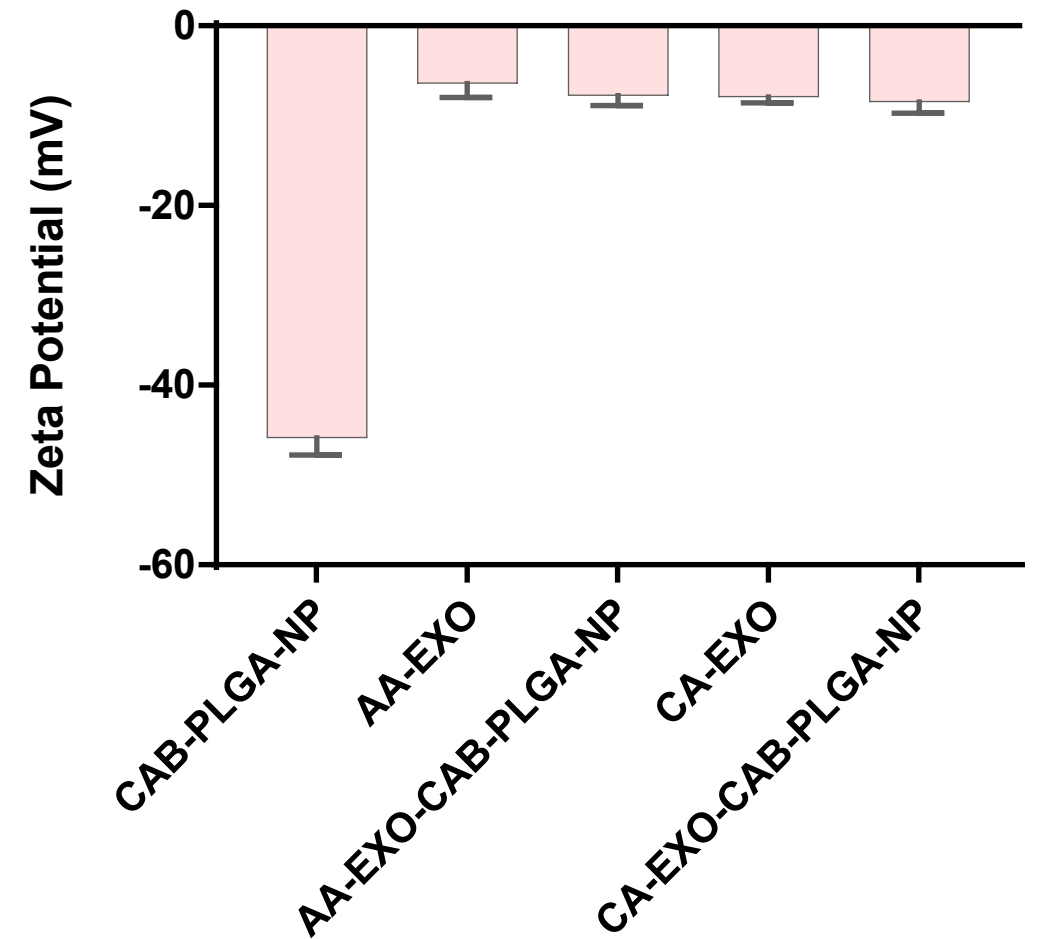
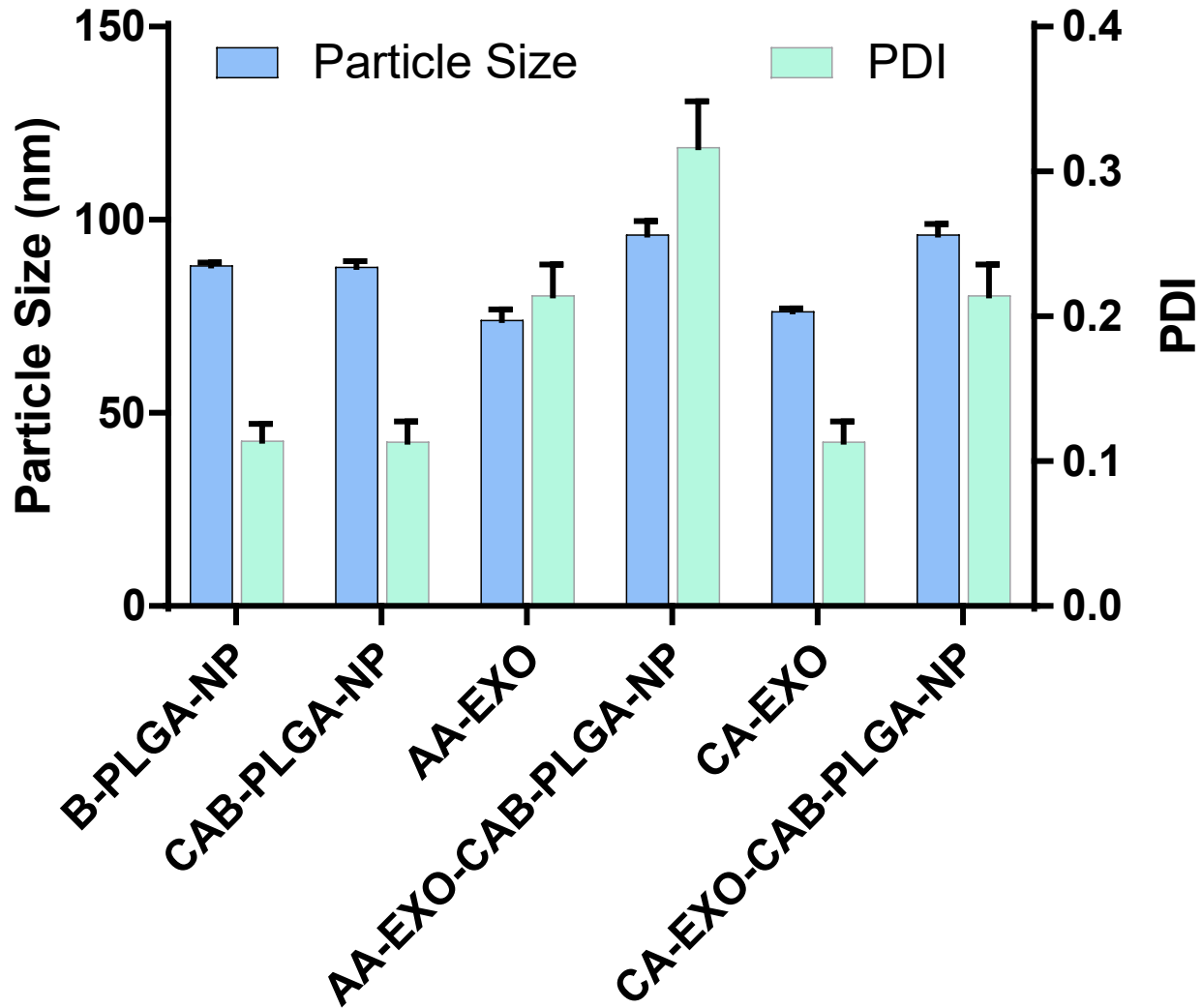


Bioengineered serum-derived exosome coated PLGA nanoparticles



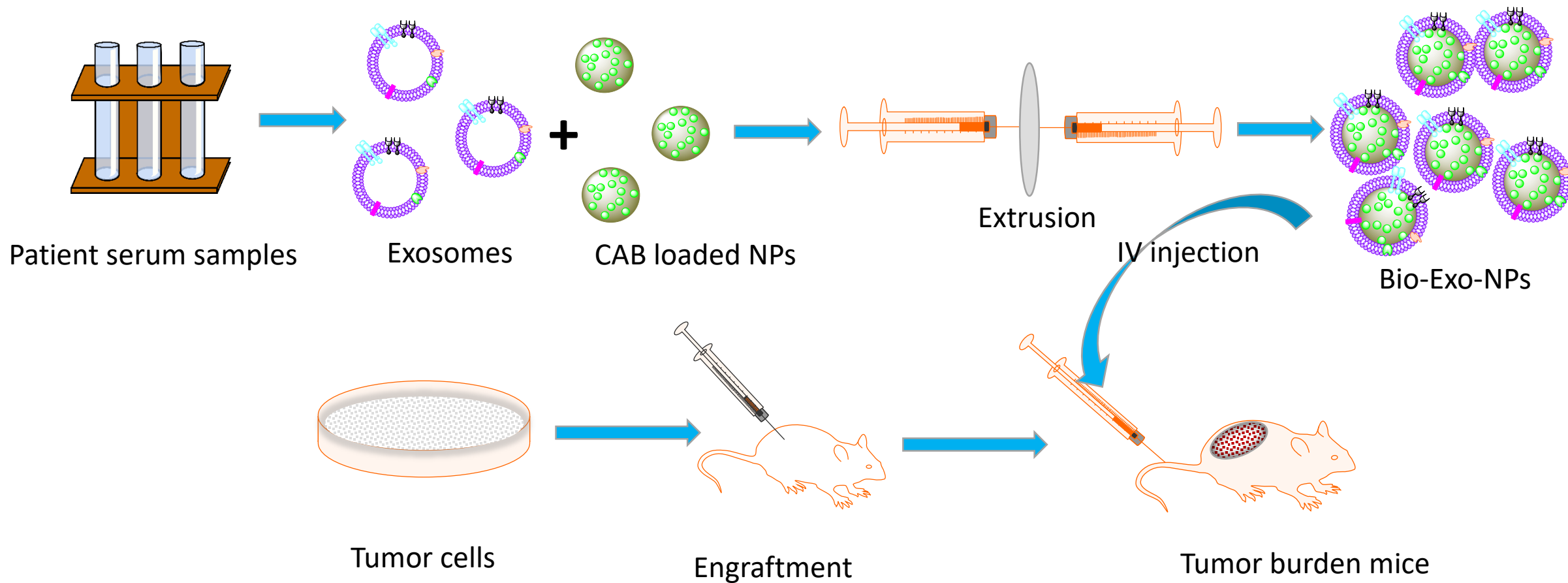
Schematic of exosome coated PLGA NP preparation by Co-extrusion methods

Physiochemical Characterization of Bio-Exo-NPs



In vivo Tumor Efficacy of Bio-Exo-NP in the Tumor Mouse Model

In progress



Conclusions/Take Home Messages

- ❑ **Triple negative breast cancer (TNBC)** is a molecularly heterogeneous disease whose incidence is disproportionately higher in African American (AA) women compared to European American (EA) women.
- ❑ TNBC is an aggressive **subtype of breast cancer**, with nearly **no targeted therapies available** today.
- ❑ **Exosomes** are membrane bound extracellular vesicles generally have a natural high targeting potential make them attractive for use in **targeted drug delivery**.
- ❑ Exosome from distinct racial distinct patient serum samples shows disparate localization in mouse model
- ❑ Further, these exosome shows specific tumor targeted localization due to diverse signature molecules on surface.
- ❑ We have successfully bioengineered the **exosome cloaked PLGA nanoparticles** loaded with cabazitaxel for investigating the **targeted chemotherapy of TNBC**.

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Thank you.

Question !

