AFRICAN UNIVERSITY OF SCIENCE & TECHNOLOGY [AUST]

MATERIAL SCIENCE DEPARTMENT

FUNCTIONALIZATION OF GOLD NANOPARTICLES FOR CANCER THERAPY AND DIAGNOSIS

BY

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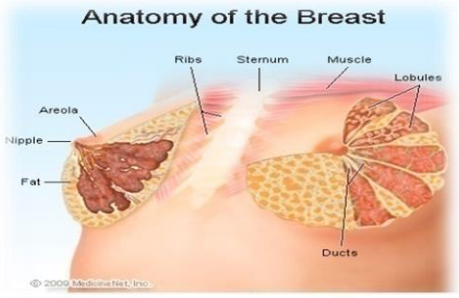
OUTLINE

- INTRODUCTION/BACKGROUND
- AIMS/OBJECTIVES
- EXPERIMENTALS
- SUMMARY/CONCLUSION



INTRODUCTION

Cancer is a world-wide problem!!!

12 million new cases and **7.6 million** deaths in 2008, to **26.4million** with **17 million deaths** by 2030

Most of these new cases of cancer are expected to occur in the developing world, particularly, India, China and Africa.

Cancer kills more people than HIV/AIDS, tuberculosis and malaria combined

(AMERICAN CANCER SOCIETY, 2010)

INTRODUCTION (contd.)

- **An estimated 1 million cases of breast cancer are diagnosed annually worldwide (Anders and, Carey, 2009)**
- **Of these, approximately 170,000 are of the triple-negative (ER–/PR–/HER2–) phenotype (Anders and, Carey, 2009)**
- **TNBC is the most prevalent type of breast cancer in Africa (Foulkes *et al*,. 2010)**
- **About 47% of women in Africa are diagnosed with Triple negative breast cancer (TNBC)**
- **The incidence is more than twice that found among white women of American origin, with a record of 22% cases (Kaplan *et al, 2006)***

BACKGROUND /MOTIVATION

- TNBC affects **mostly young women (between age 25 - 40,** as against age 40 - 60 or older, as obtainable with other types of breast cancer).

- A study by Stark *et al* in 2010, compared women with breast cancer in the United States (**Detroit)** and Africa (**Ghana**)

- 1008 **white Americans**, 581 **African-Americans** and 75 **Ghanaians**

- **Ghanaians** had the highest prevalence of triple-negative tumours (**82%),** followed by African-Americans **(33%)** and white Americans (**10%).**

Synthesis of AuNPs using *Nauclea latifolia*

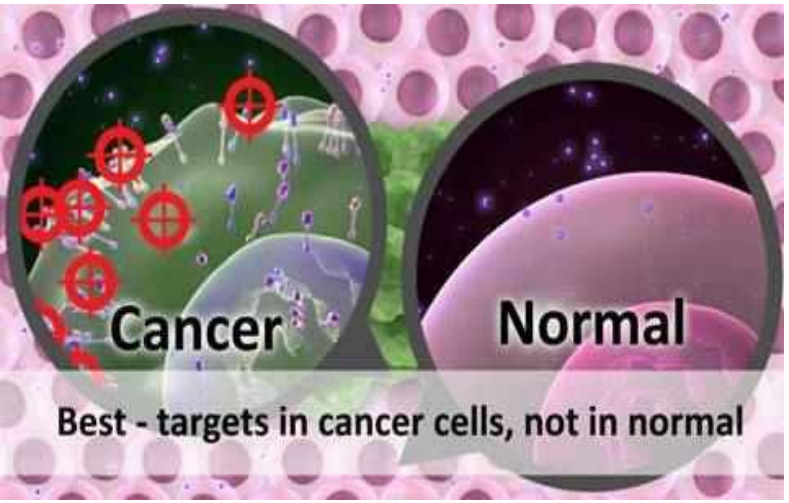
- $HAuCl_4 + 3e^- \longrightarrow Au^0 + 4Cl^- + H^+$
- $Au^{3+} + 3e^+ \longrightarrow Au^0$

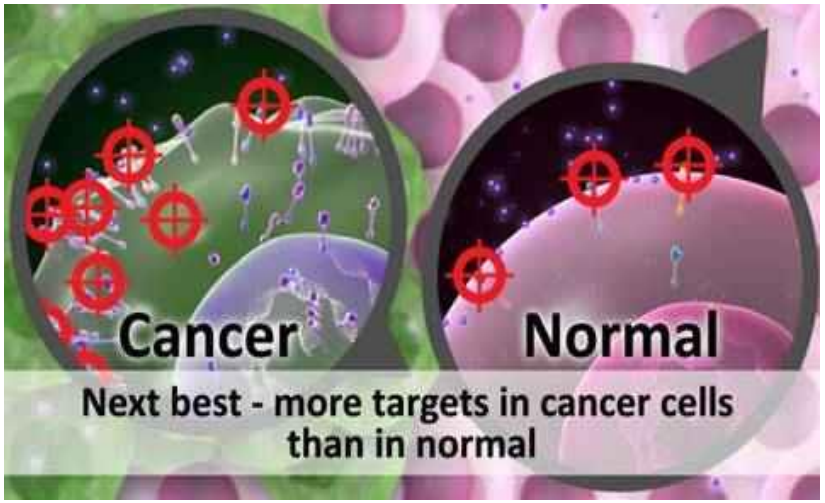
HOW TO CHOOSE A TARGET

- The best target for therapy is a molecule or pathway that is present ONLY in cancer cells and absent in normal cells

- However, it is often difficult to find targets that are present only in cancer cells, partly because cancer cells evolve from normal cells

- molecule that is present more frequently in cancer cells compared to normal cells





WHY FOLATE?

- **Folate, or vitamin B9, is an essential cofactor in the synthesis of purines and pyrimidines and other cellular methylation reactions including DNA, proteins and lipids (Elnakat & Ratnam 2004).**

- **Folate Receptor alpha is Frequently Expressed in Triple Negative Breast Cancers (**Hoang et al, 2015**)**

- **In a study by Tacha and Bremer at Biocare Medicals, Canada, in 2013, they found that triple negative breast cancers (TNBC) expressed FRα in 80% of cases.**

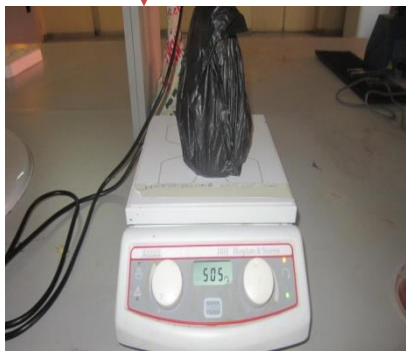
CONJUGATION OF AuNPs WITH FOLIC ACID

20ml DMSO

+ 0.5ml triethyamine

+ 1.0g folic acid + 0.94g DCC

+ 0.52g NHS



Stir in dark for 12hrs

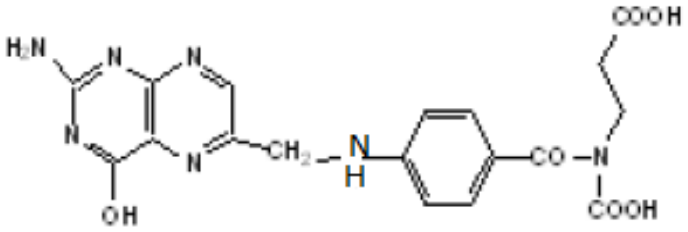
Filter off dicyclohexylurea

Precipitate with anhydrous ether containing 30% acetone

23mg NHS –FOLATE
+ AuNPs

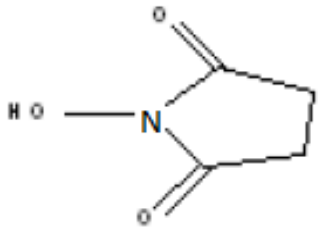
AuNPs-Folate

REACTIONS FOR THE ESTERIFICATION OF FOLIC ACID



FOLIC ACID

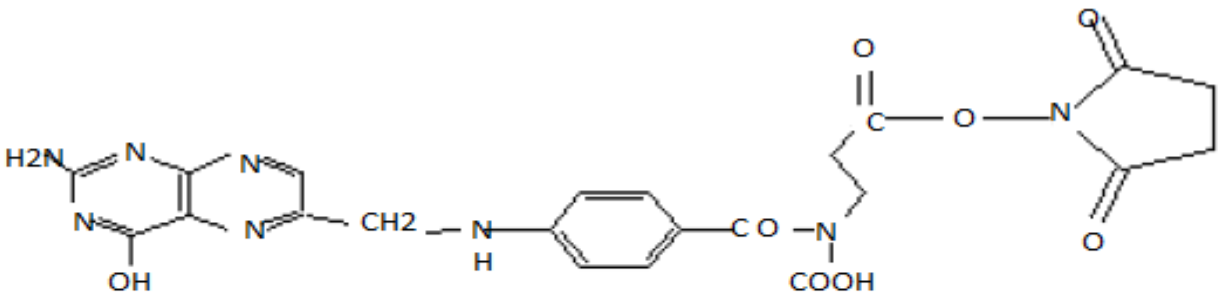
+



N-HYDROXYSUCCINAMIDE

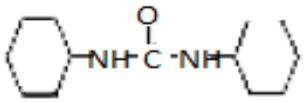
DICYCLOHEXYL CARBODIIMIDE

DMSO, TEA

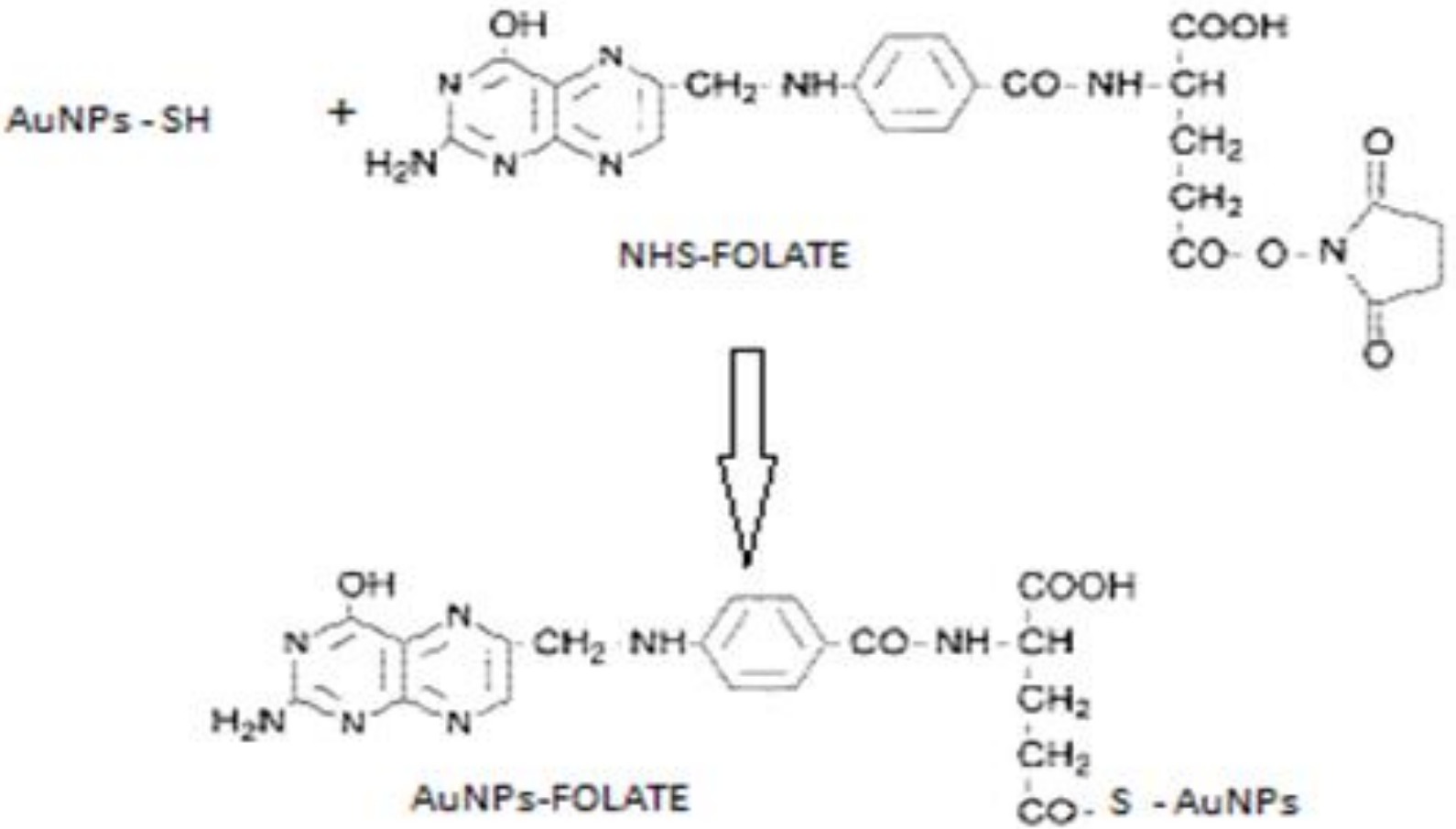


NHS-FOLATE ESTER

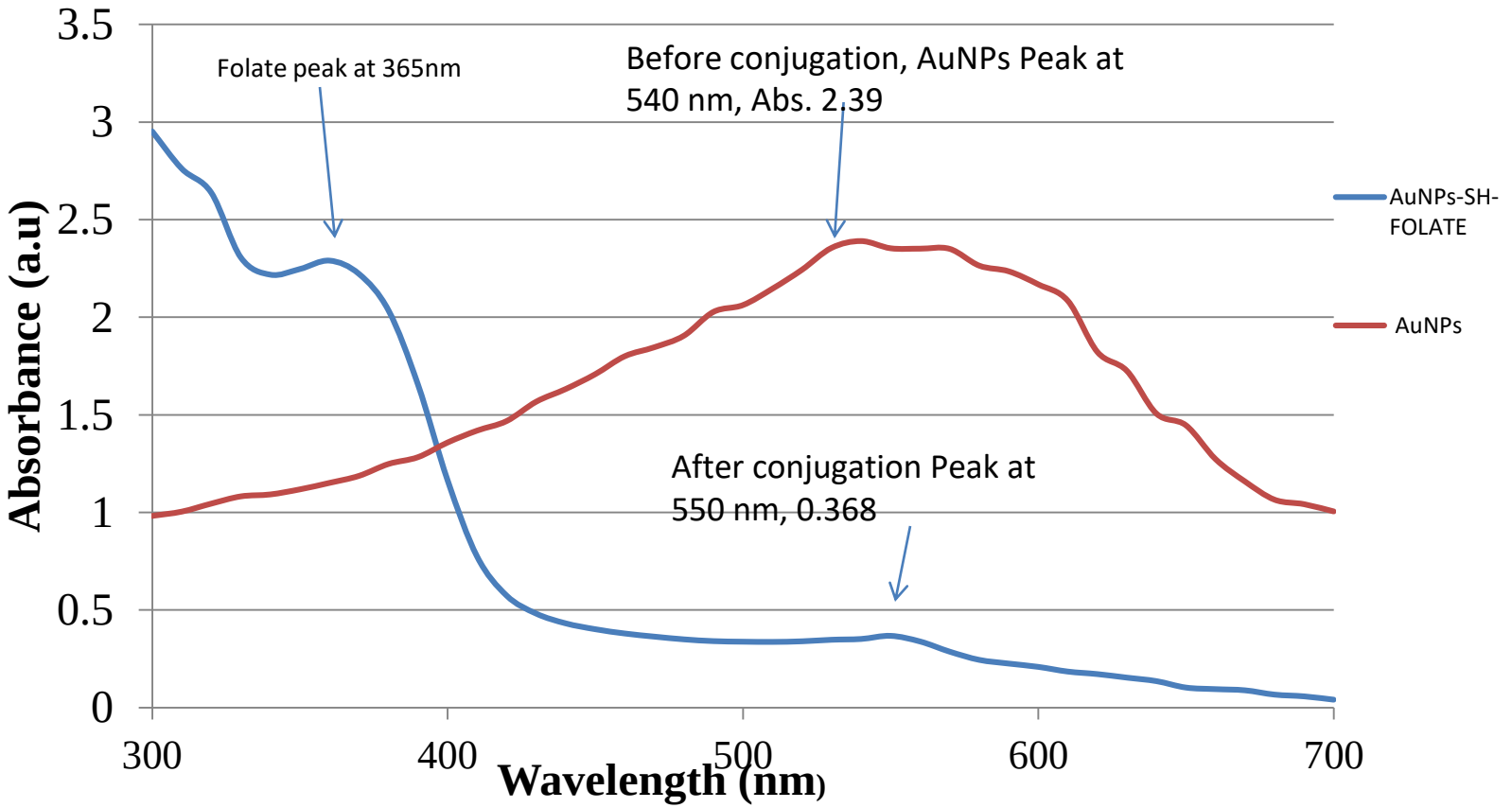
+



DI-CYCLOHEXYL UREA

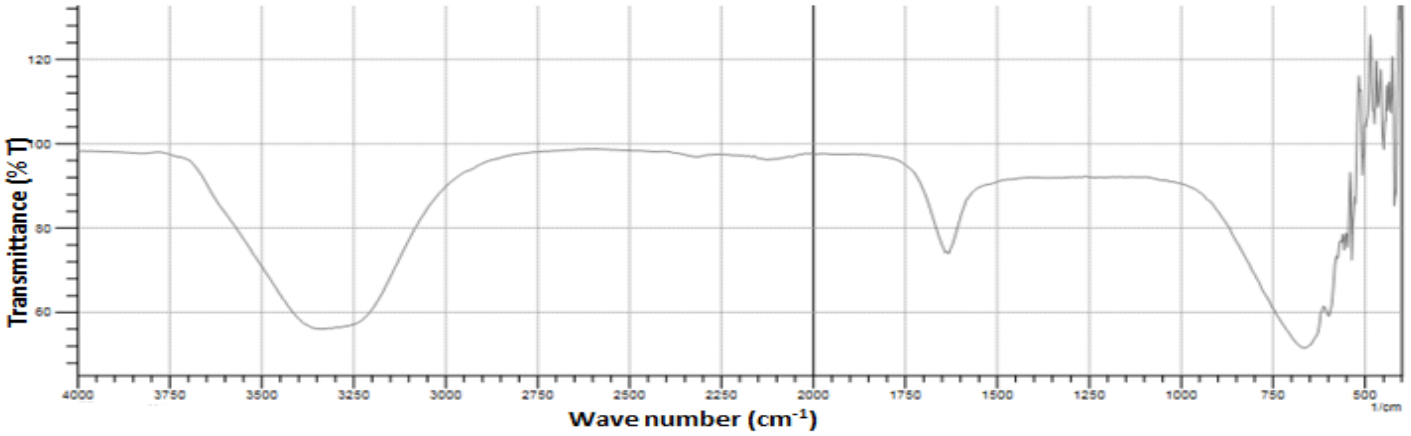

AuNPs - SH
+
NHS-FOLATE
AuNPs-FOLATE
AuNPs

UV-Vis spectra of AuNPs and Folate conjugated AuNPs



FTIR ANALYSIS

(a) AuNPs before conjugation



(b) AuNPs after conjugation

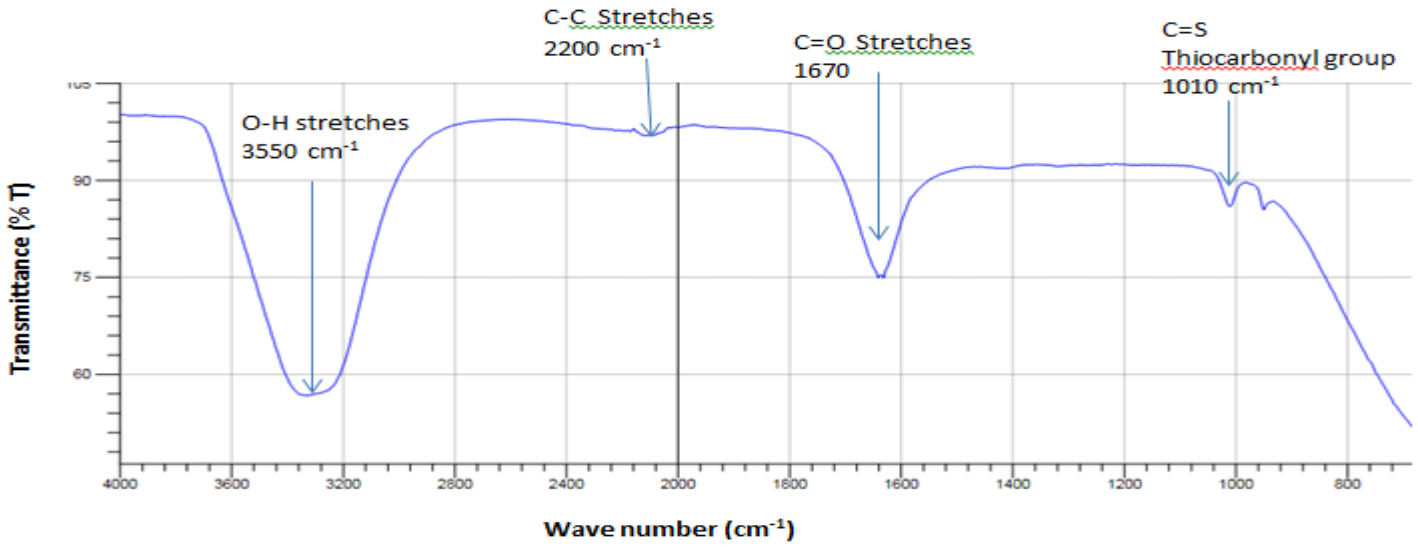


Fig. 3: Showing FTIR results obtained for AuNPs (a) before and (b) after conjugation with folate

HEM ANALYSIS

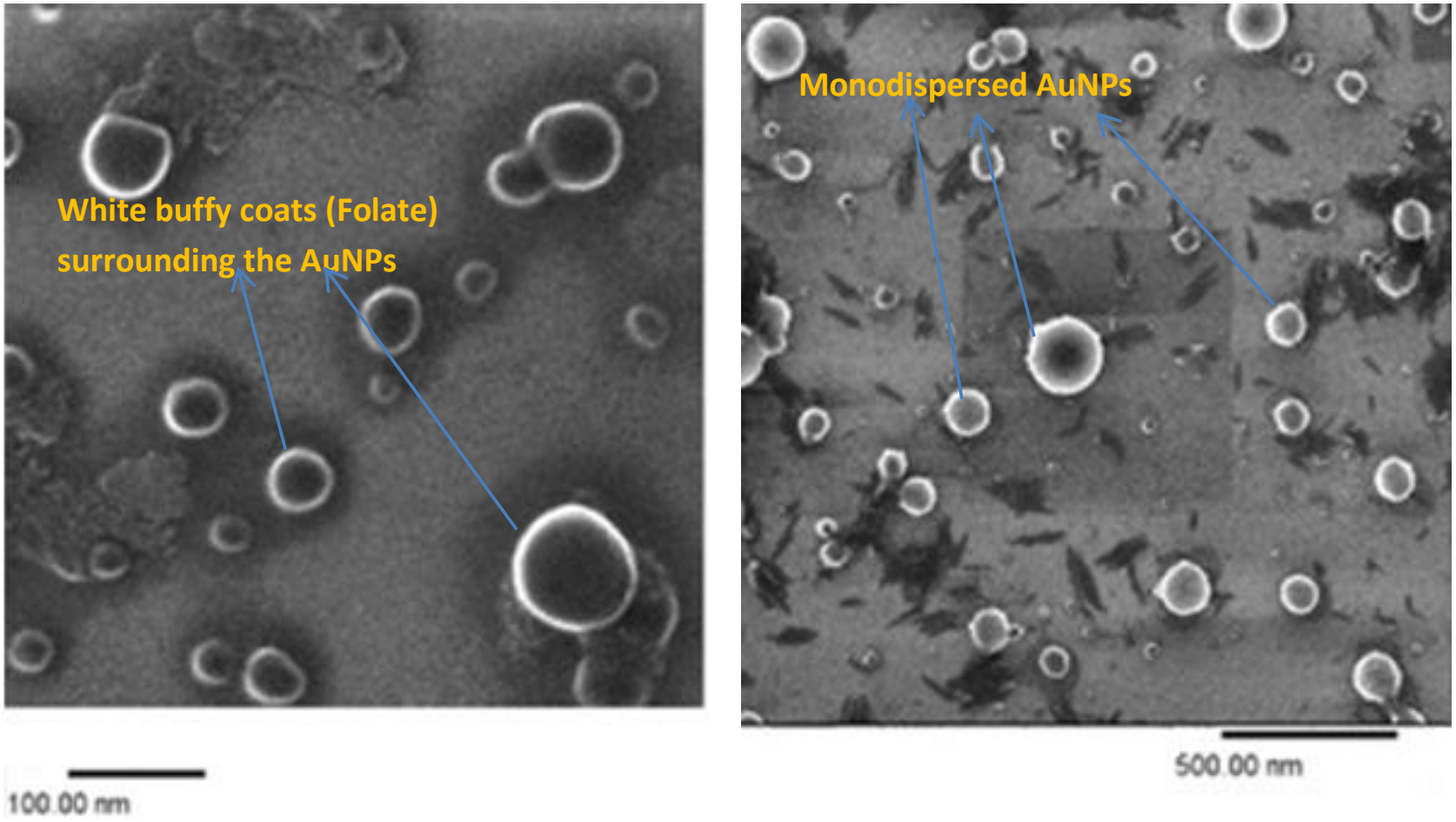
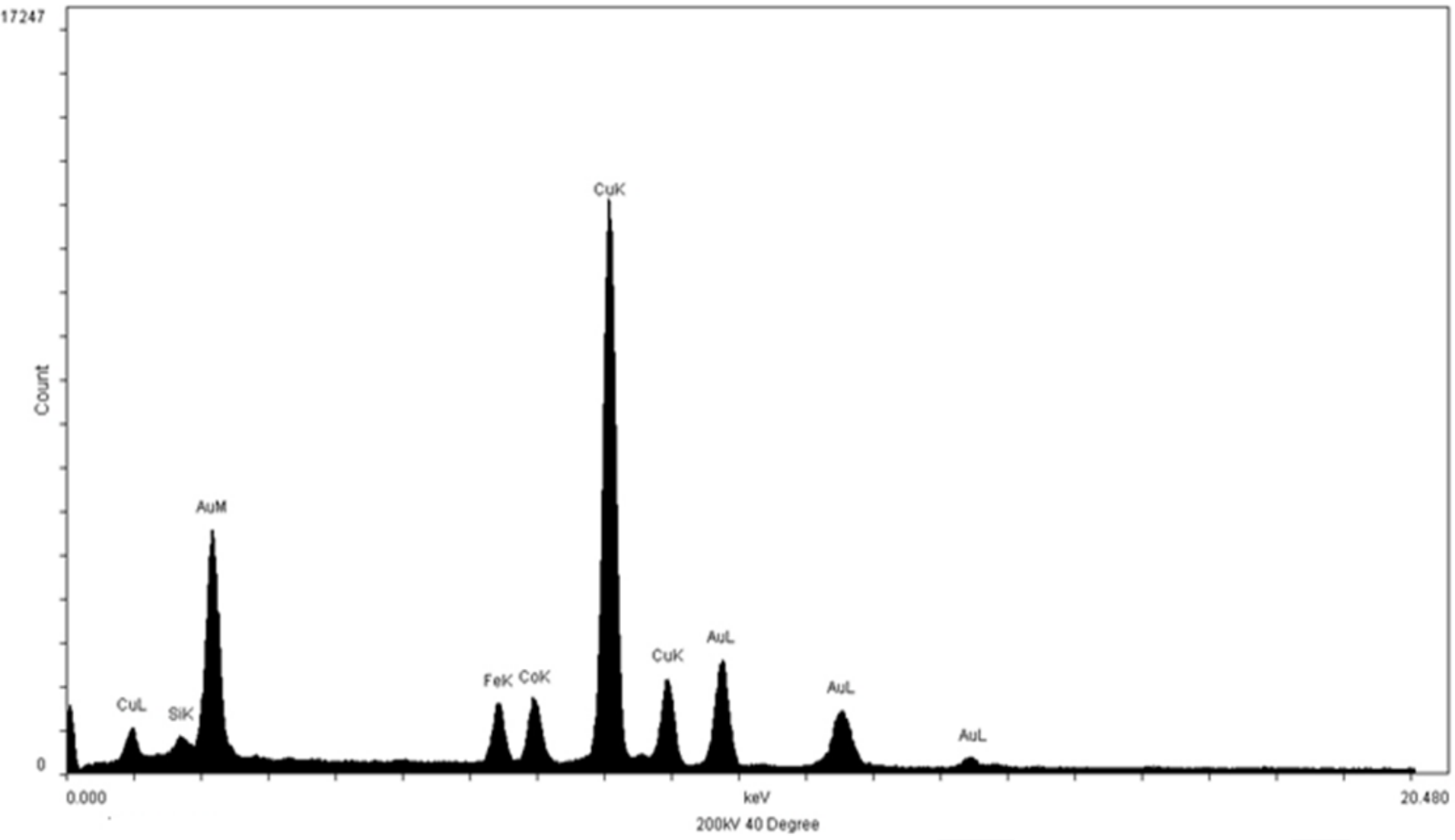
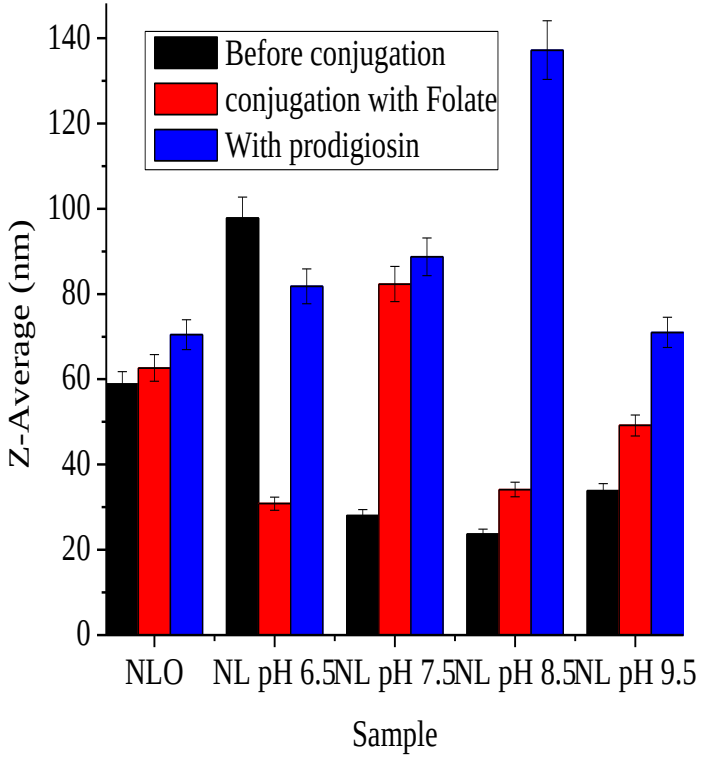


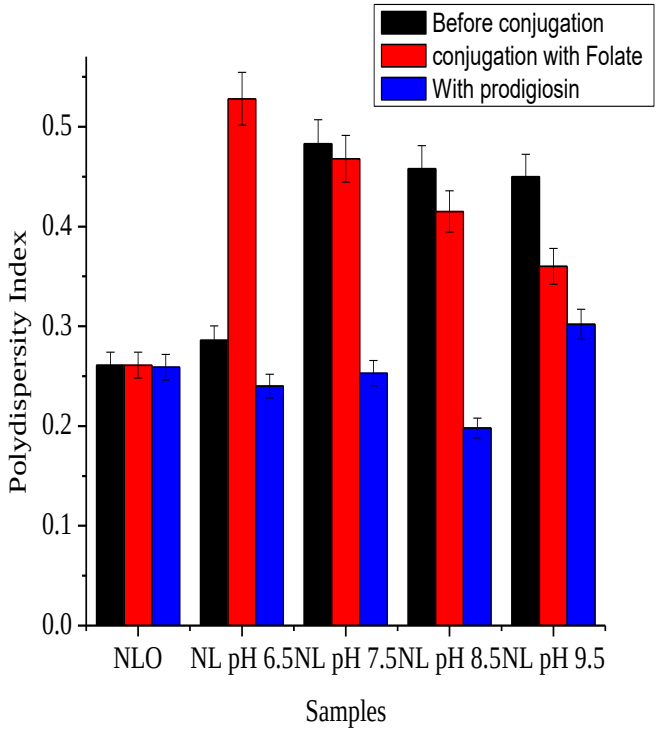
Fig. 7: Helium ion microscopy images of gold nanoparticles conjugated with folate (a) at 1 µm field of view, (b) at 4 µm field of view

EDX ANALYSIS



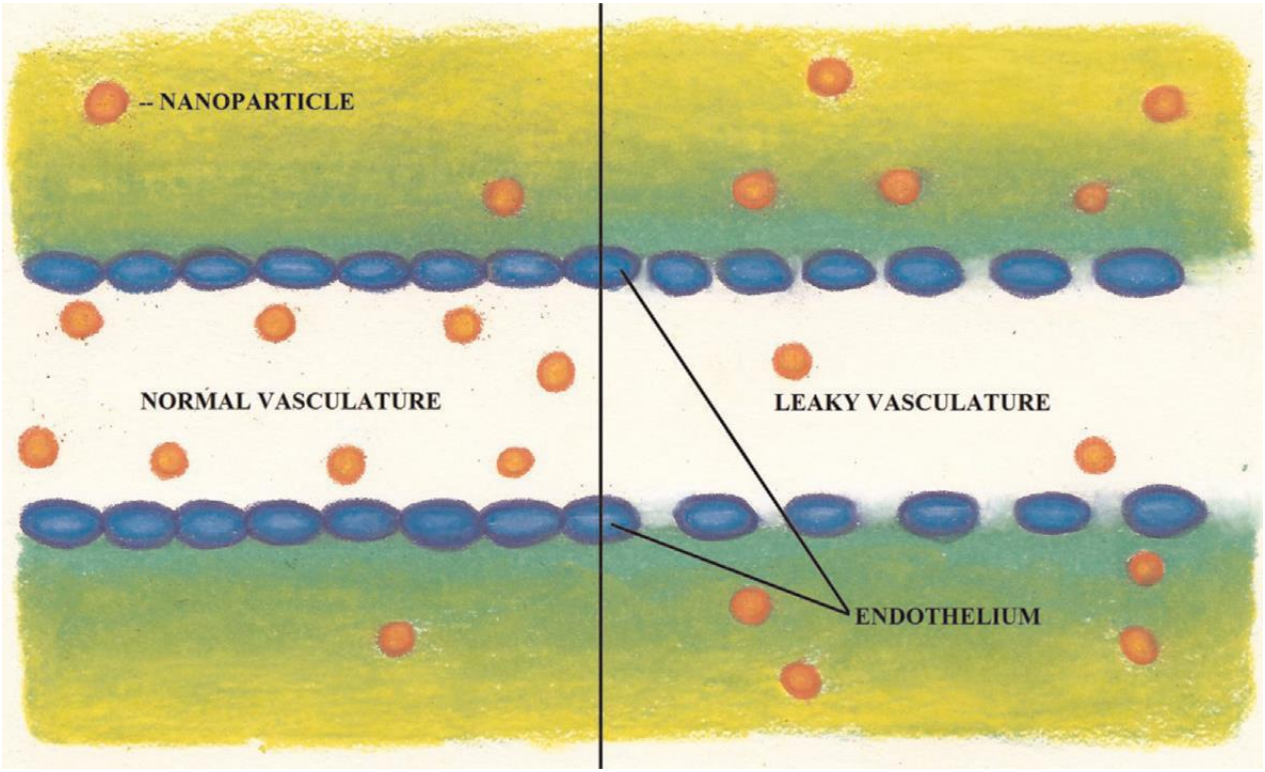
DLS ANALYSIS





MODE OF TARGETING

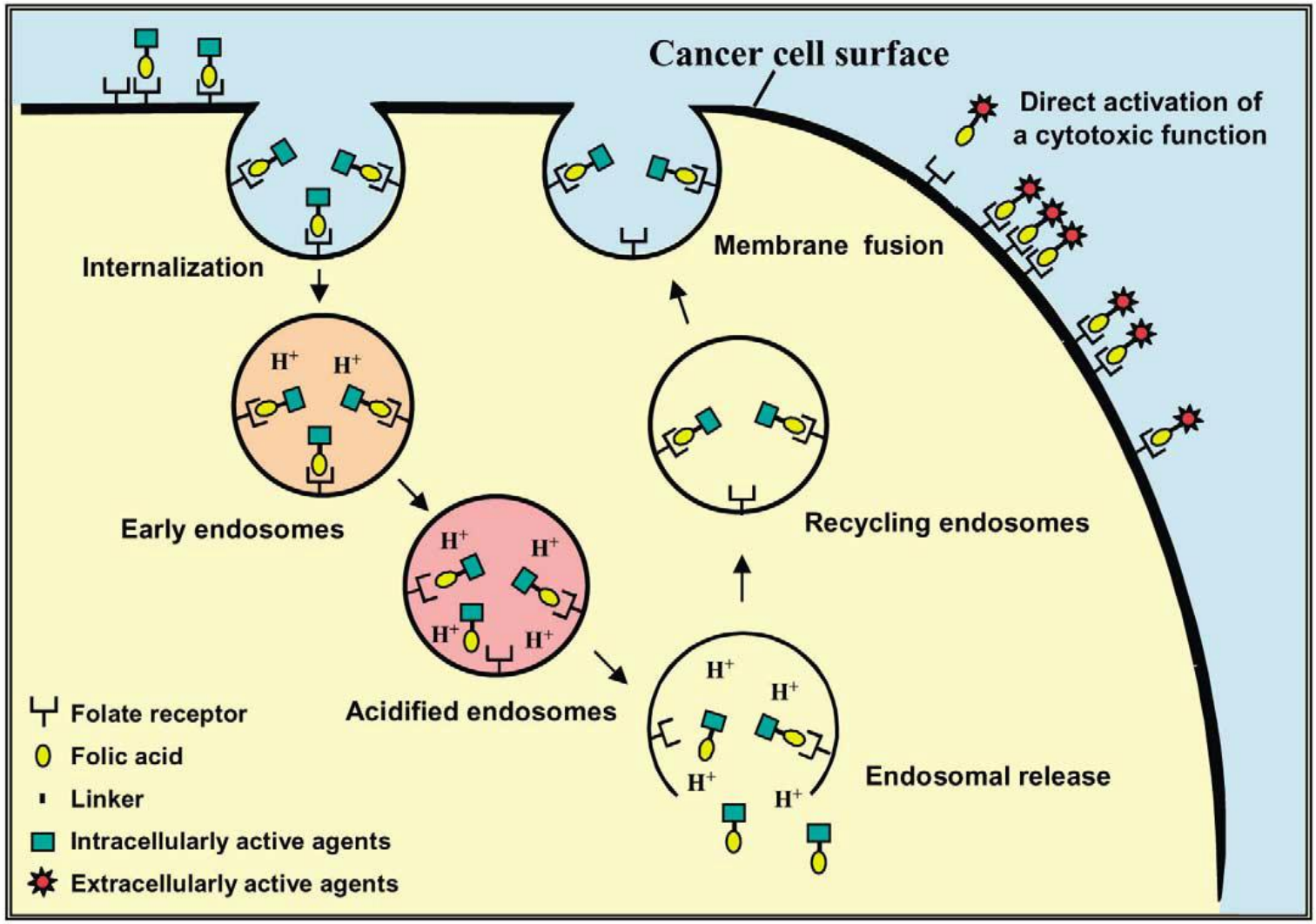
Passive Targeting



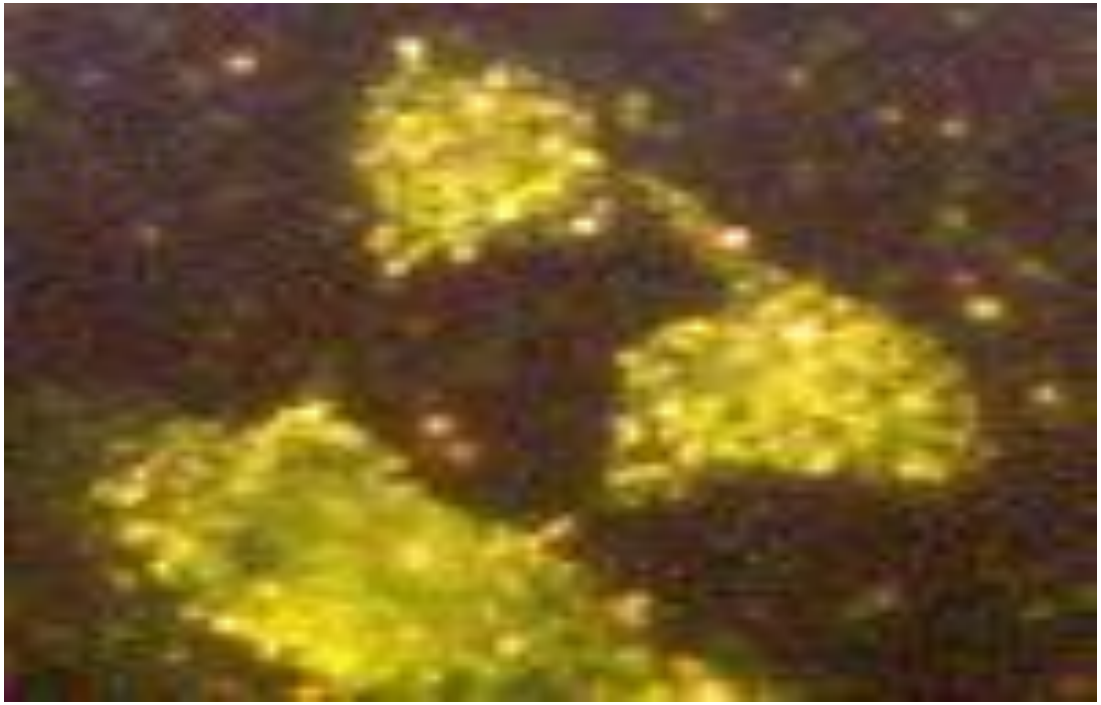
The vasculature of cancerous tissues can be more leaky than that of healthy tissues. This difference in leakiness can be exploited in anticancer drug delivery. Vasculature of the tissue on the left is normal while the tissue on the right is leaky.

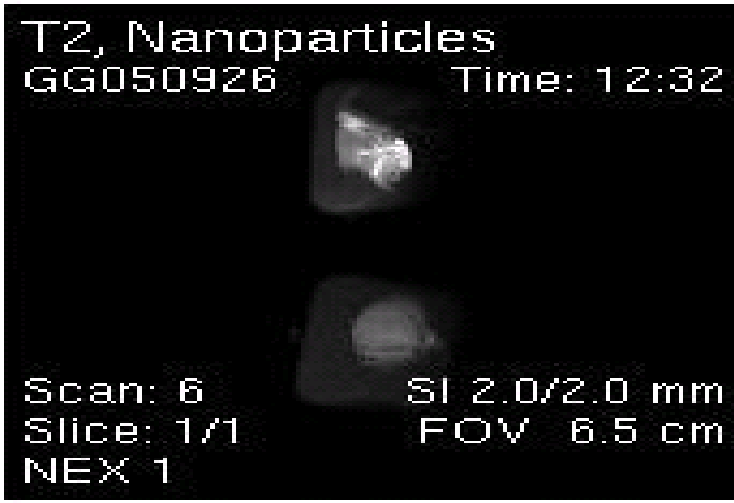
The nanoparticles passively enter through the leaky vasculature into the tumor tissue due to the enhanced permeability and retention(EPR) effect.
(Illustrated by Samantha L. Lindberg).

Active Targeting



USE IN EARLY DETECTION





Light scattering images of malignant cells after incubation with anti-EGFR antibody conjugated gold nanoparticles.

SUMMARY AND CONCLUSION

- **Biosynthesis of gold nanoparticles is very efficient and biocompatible**
- **Folate and prodigiosin were successfully conjugated to the AuNPs**
- **Folate conjugated AuNPs as a hope for treatment of Triple negative Breast cancer**
- **With functionalized AuNPs early detection will be greatly improved.**

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