Nanoparticle Enhanced, Impedance-Based Biosensor Development for Colon Cancer Diagnostics

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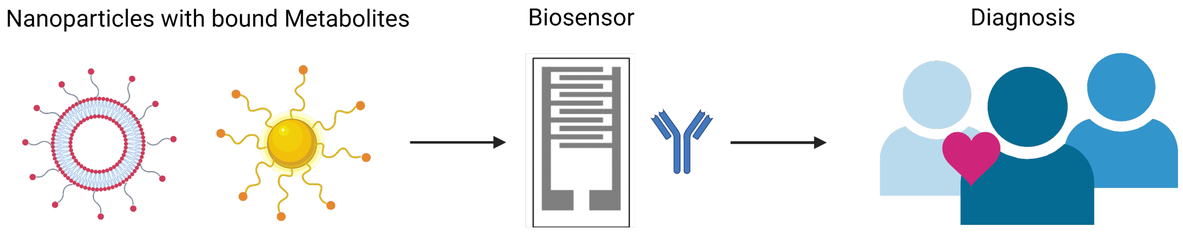
INTRODUCTION

BACKGROUND

As of 2020, colon cancer is the third most diagnosed cancer in Canada, according to the Canadian Cancer Society. Due to the prevalence of this disease, enhancing the accessibility and accuracy of diagnosis is essential to the well-being of patients. Our goal is to develop an impedance-based biosensor that utilizes nanotechnology to detect biomarkers for colon cancer in urine and by consequence a diagnostic test that is noninvasive and provides fast results.

As a control for the biosensor, gold nanoparticles and liposomes have been functionalized with 3 metabolites that are biomarkers for colon cancer: hippuric acid, diacetylspermine, and creatinine. These metabolites have been bound to the surface of nanobodies with the use of stabilizing ligands, linker molecules, and cross-linking chemistry to facilitate the formation of amide bonds. Throughout this process, considerations to determine which nanobody will function best in an electrical system are being examined.



METHODS

GOLD NANOPARTICLES

Gold nanoparticles are first incubated with large, heterobifunctional polyethylene glycol linkers that have a thiol group on one end and either a terminal carboxylic acid or primary amine on the other. The linker is bound to the surface of the nanoparticle and with the use of EDC/NHS catalysts and the metabolite with a carboxylic acid or a primary amine group is then bound to the linker.

Citrate Stabilized Gold Nanoparticles

- Inorganic
- High Conductivity
- High Density
- Inflexible
- High Refractive Index

METHODS

LIPOSOMES

To functionalize metabolite to the surface of liposomes, a phospholipid polyethylene glycol linker and the metabolite are bound first and form micelles in solution. Liposomes contain a phospholipid bilayer, and the linker-metabolite micelles and liposomes must be incubated together at 60 ° C. The linker and metabolite are then post-inserted into the bilayer of the liposome.

Liposomes

- Organic
- Low Conductivity
- Low Density
- Flexible
- Low Refractive Index

DATA ANALYSIS

ANALYSIS OF GOLD NANOPARTICLES

Gold nanoparticles exhibit a phenomenon called surface plasmon resonance. This where the electrons on the gold nanoparticle surface become excited from incident light and absorb wavelengths in the blue-green spectrum and reflect red light. This wavelength can be measured and used to correlate the particle's size and stability. We have observed a red shift in the spectra which indicates the nanoparticle has increased in size and the metabolite has been bound to its surface.

Sample	Absorbance Peak (nm)
Gold Nanoparticles (GNP)	518
GNP-Creatinine	522
GNP-AcSperm	522
GNP-Hippuric Acid	524

ANALYSIS OF LIPOSOMES

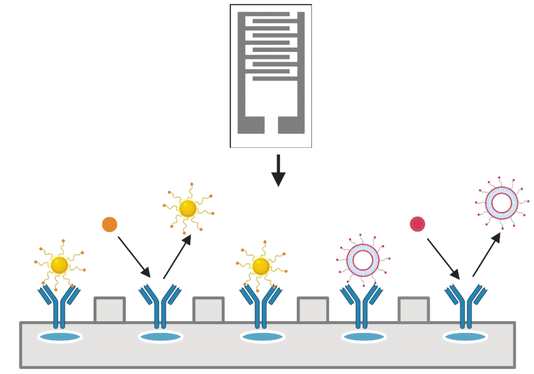
Dynamic Light Scattering is a technique used to measure liposomes and gold nanoparticles. Their relative size, homogeneity, and stability can be measured by irradiating the sample with a laser. The scattering of the laser due to Brownian motion of the sample can be measured and determine these characteristics.

Sample	Hydrodynamic Size (nm)
Bare Liposomes	93
Liposome-Creatinine	108
Liposome-AcSperm	99
Liposome- Hippuric Acid	100

BIOSENSOR

FUNCTION OF THE BIOSENSOR

The biosensor will be a competitive assay and will use a biological component which are antibodies. The antibodies will be bound to the surface of a silicon dioxide coated, interdigitated electrode. The antibodies will be prebound with the nanobody-metabolites on the electrode surface which will produce an impedance reading. Then, the urine sample of a patient will be tested, and free metabolites will unbind the nanoparticles as they have a greater affinity for the antibodies. This will cause a change in the impedance reading and will determine if a patient is at risk for colon cancer.



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