Implantable Nanosensor Detection of an Ovarian Cancer Biomarker In Vivo

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Ovarian cancer accounts for 238,000 new diagnoses and 151,000 deaths per year worldwide. Late-stage diagnoses occur in over 60% of patients, higher than any other form of cancer. However, five-year survival is 92% in patients diagnosed at early stages of disease. Unfortunately, current screening methods have a high false-positive rate and poor sensitivity, none of which reduce mortality.

Single-walled carbon nanotubes (SWCNT) exhibit optical properties well-suited for biosensing applications. Nanotubes exhibit tissue-penetrant near-infrared (NIR) photoluminescence and unique photostability, allowing for repeated, long-term measurement. SWCNT are also sensitive to their local environment and photoluminescent emission can undergo modulation of the optical bandgap, causing a shift in wavelength. Prior work has also shown nanotube fluorescence in live mice and can detect analytes in complex biological environments. These characteristics allow nanotubes to optically transduce analyte concentrations over time in vivo.

We engineered an ovarian cancer biomarker sensor by non-covalently attaching an antibody to the polymer wrapping of SWCNT. Nanosensor selectivity and specificity were characterized in vitro via NIR spectroscopy. We then measured the biomarker ex vivo in patient serum and ascites samples by NIR hyperspectral microscopy. We developed an implantable device by encapsulating the sensor in a semipermeable, biocompatible membrane. This implantable sensor was initially surgically immobilized in the peritoneal cavity of healthy mice, where we injected control protein or the specific biomarker. Probe-based NIR spectroscopy and whole-animal hyperspectral imaging was used to obtain the sensor response. Finally, mice bearing four orthotopic models of ovarian cancer were implanted with the sensor device and the response of the sensor was measured.

The sensor exhibited exquisite specificity and low-nanomolar selectivity for the ovarian cancer biomarker. It also differentiates the serum and ascites of patients with ovarian cancer versus benign conditions. In vivo, we quantitatively measured exogenous biomarker injected into healthy mice. Finally, we differentiated between two mouse models that produce the specific biomarker versus two that do not.

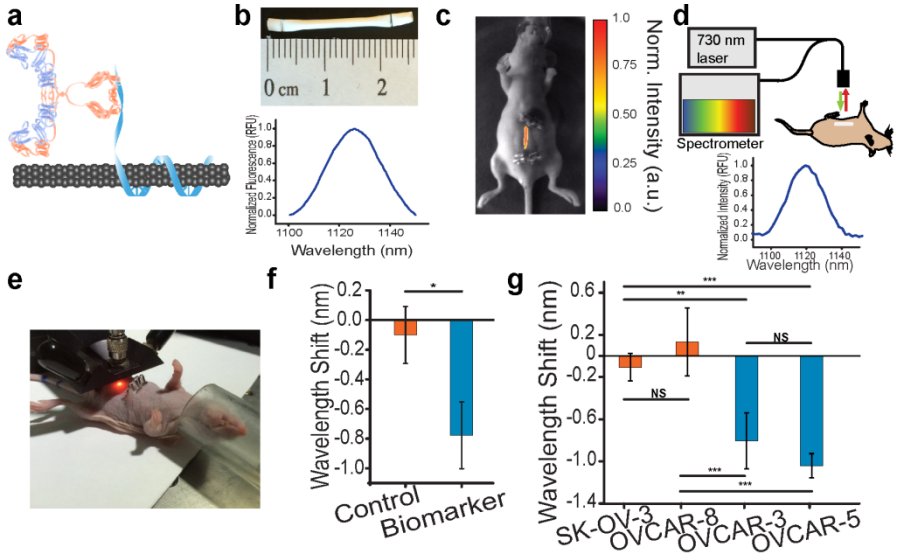

Figure 1. In vivo biomarker detection by SWCNT. a) Nanosensor schematic. b) Implantable sensor device with encapsulated nanosensor. c) Whole-animal NIR imaging of implanted sensor. d) NIR probe spectroscopy system. e) Mouse undergoing NIR probe spectroscopy. f) Exogenous biomarker detection in vivo. g) Biomarker detection in orthotopic mouse models of ovarian cancer, where SK-OV-3 and OVCAR-8 do not produce the biomarker while OVCAR-3 and OVCAR-5 do.

We developed an implantable sensor for an ovarian cancer biomarker that quantitatively measures protein injected into mice. Further, this device can detect the biomarker produced by orthotopic ovarian cancer. We expect to further test the in vivo lifetime and range of this sensor device towards clinical translation. We hope to increase early detection rates, enhancing patient prognosis by translation of this device to detect ovarian cancer at the site of early disease.