Designing Nanoparticles for siRNA Therapy targeted to Kidney Cancer
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Introduction

- Renal cell carcinoma (RCC), also known as renal cell cancer or renal cell adenocarcinoma, is the most common type of kidney cancer.
- The lifetime risk for developing kidney cancer in men is about 1 in 46 (2.02%). The lifetime risk for women is about 1 in 80 (1.03%).
- Side Effects include: blood in the urine, pain, weight loss, feeling tired, fever, a lump in the side

Objective & Impact of Professor’s Research

Due to chemotherapy not being very effective against advanced kidney cancer, drug delivery and combinations of targeted therapies are more practical and functional for patients. Kidney cancers that cannot be removed by surgery or have spread outside the kidney are situations in which patients need to have a viable option and targeted drug delivery does just that.

Data

- ccRCC is known to be aggressive, grow faster than other kidney cancers, and has a high mortality rate. This is why my mentor and I worked throughout the summer to develop nanoparticles that could bind to the CD70 protein expressed in ccRCC cells to deliver siRNA therapy targeted to HIF2a (which promotes cancer progression).

Results

- Figure 1: Image showing a kidney without versus with tumour
- Figure 2: Image of clear cell renal cell carcinoma (ccRCC).
- Figure 3: Nanoparticle binding to kidney cancer cells. Patient-derived ccRCC cells were incubated with fluorescently labeled targeting (A) or non-targeting (B) nanoparticles and images. Fluorescence measurements for each group were quantified in (C). Scale bar = 100 um. Photo courtesy of Noah Trac.
- Figure 4: Mass spectrometry data confirming proper synthesis of CD70-targeting peptide (left, expected MW: 1403) and peptide amphiphile (right, expected MW: 4343). Photo courtesy of Noah Trac.
- Figure 5: Gel electrophoresis experiment showing incorporation of siRNA into nanoparticles. An electric current was run from the negative to positive electrode, and samples containing negatively charged siRNA migrated down the gel, based on size. siRNA incorporated into nanoparticles were larger and did not migrate as far down the gel as siRNA that was not in nanoparticles. Lanes: 1) HIF2a siRNA nanoparticle, 2) HIF2a siRNA nanoparticle + RNAse, 3) HIF2a siRNA nanoparticle + RNAse, 4) HIF2a siRNA + RNAse. Photo courtesy of Noah Trac.

Skills and Techniques Learned

- Nanoparticles Synthesis
  - Peptide Synthesis using automated peptide synthesizer
  - Peptide purification using HPLC and Mass Spectrometry
  - Peptide conjugation to nanoparticles

- Electrophoresis Gel
  - Used to confirm siRNA incorporation into nanoparticle
  - Used to determine the migration of siRNA

- How this relates to my STEM Coursework

  - Medical Detectives: analyze genetic testing results to diagnose disease and study DNA evidence
  - Biotechnology: create pharmaceutical and diagnostic products to benefit society
  - Biology: problem-solving techniques of engineering to biology and medicine
  - Chemistry: can help us to understand and improve the healthcare system


References