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

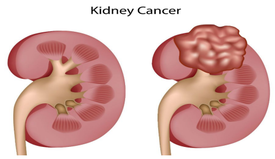


***Figure 1**: Image showing a kidney without vs. with tumour*

About 7 out of 10 people with RCC have clear cell renal cell carcinoma. ccRCC is a malignant tumor. The cells appear to look very pale or clear.

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.

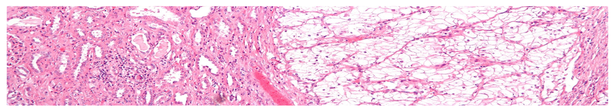


***Figure 2**: Image of clear cell renal cell carcinoma (ccRCC).*

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).

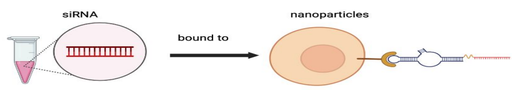


***Figure 3**: siRNA being bound to nanoparticles in order to deliver siRNA therapy to cancerous cells in the kidney. Photo Credit: Alisella Hernandez*

Results

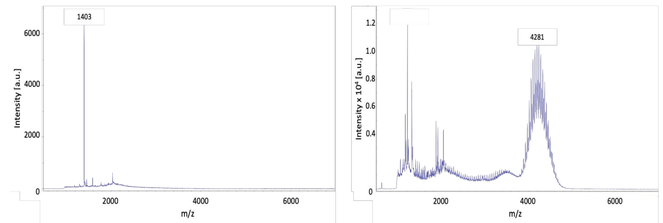


***Figure 4**: Mass spectrometry data confirming proper synthesis of CD70-targeting peptide (left, expected MW: 1403) and peptide amphiphile (right, expected MW: 4343). Photo courtesy of Noah Trac.*

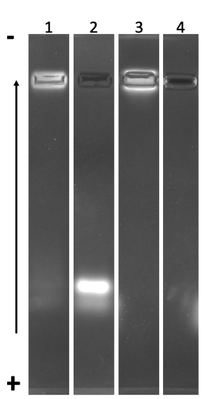


***Figure 5**: Gel electrophoresis experiment showing incorporation of siRNA into nanoparticles. An electric current was run from the negative to positive electrode, and samples containing negatively charged siRNA migrated down the ge, based on size. siRNA incorporated into nanoparticles were larger and did not migrate as far down the gel as siRNA that was not in nanoparticles Lanes: 1) HIF2a siRNA nanoparticle, 2) HIF2a siRNA, 3)HIF2a siRNA nanoparticle + RNAse, 4) HIF2a siRNA + RNAse. Photo courtesy of Noah Trac.*

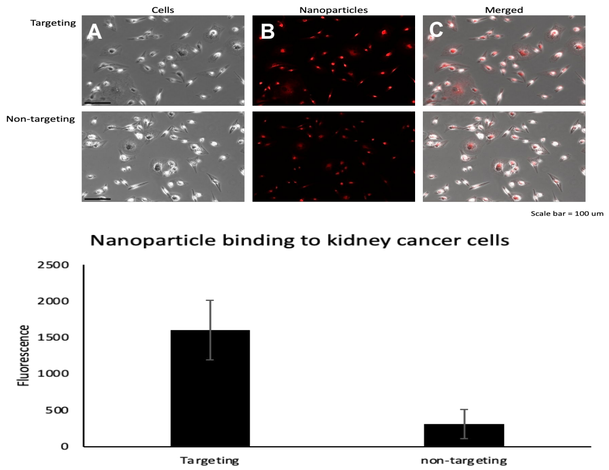
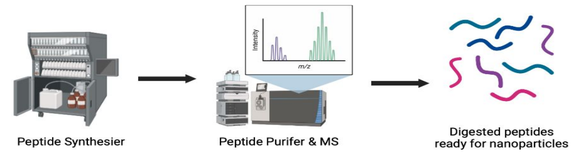


***Figure 3:** Nanoparticle binding to kidney cancer cells. Patient-derived ccRCC cells were incubated with fluorescently labeled targeting (A) or non-targeting (B) nanoparticles and images. Fluorescence measurements for each group were quantified in (C). Scale bar = 100 um. Photo courtesy of Noah Trac.*

Skills and Techniques Learned

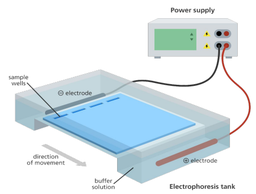
Nanoparticles Synthesis

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



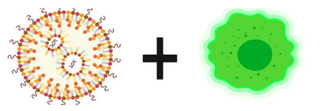
Electrophoresis Gel

- Used to confirm siRNA incorporation into nanoparticle
- Cast agarose gel
- Load samples



In-vitro cell culture and nanoparticle binding

- Changed media for cells (food)
- Incubated fluorescent nano-particles with cells
- Used microscope to image cells
- Used spectrophotometer to quantify nanoparticle binding



How this relates to my STEM Coursework

Courses I've taken that relate to SHINE are:

- 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 helps us to understand and improve the healthcare system

In SHINE, you get hands on experiences that you might not receive in a classroom setting. I obtained information better and quicker compared to a lecture at school due to a mentor by my side.

Next Steps for You OR Advice for Future SHINE Students

In the future for myself, I definitely see myself furthering my interest for STEM, especially in research. USC is also a college I'll look into more as the research and campus was alluring.

Advice for Future SHINE Students:

- Do not be intimidated! If you got accepted for SHINE, that shows you are already capable enough.
- Be hard-driven! Show off your skills and also be open to learning new ones.

Acknowledgements

I'd like to thank Professor Chung for inviting me to work in her lab and being so welcoming. To my PhD mentor Noah Trac for being so informative and understanding. I'd like to thank my middle school teacher, Ms. Kim, for introducing my love for STEM. Thank you to my center mentor Mary for checking in our on us. Lastly, a huge thank you to Dr. Katie Millis for founding this amazing once in a lifetime program and AMI USC for helping fund my SHINE Scholarship. I appreciate it so much!

References

1. "Biorender." *BioRender*, https://biorender.com/.
2. "Clear Cell Renal Cell Carcinoma." *National Cancer Institute*,https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-kidney-tumors/clear-cell-renal-cell-carcino
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