Synthesis of Deuterated, Protected Amino Acids Tyrosine and Serine

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Collaborative Summary

In the United States, 1 in every 8 women will be diagnosed with breast cancer at some point in their lives. This makes breast cancer the most common form of non-skin cancer as well as second leading cause of cancer-related fatalities in women. Although adjuvant therapies have improved therapy success after lumpectomy or mastectomy, therapeutic choices are made without adequate information to predict efficiency or effectiveness of the treatment.

Due to weak or inappropriate therapy choice, additional pressure and strain is placed on cells. This in turn causes proliferation of mutant clones that are resistant or unresponsive to treatment. Also, inappropriately targeted therapy often cause cells to compensate for loss of downstream signaling, activating other oncogenic pathways that are unaffected by treatment.

The goal of this collaborative project is to establish the first steps towards a standardized multiplex quantification of kinase activity in a breast cancer model through surface enhanced Raman spectroscopy (SERS) paired with peptide-functionalized nanoparticle based biosensors. By establishing this multiplex quantification, adjuvant therapies will become more effective and personalized for individuals with breast cancer.

Objective

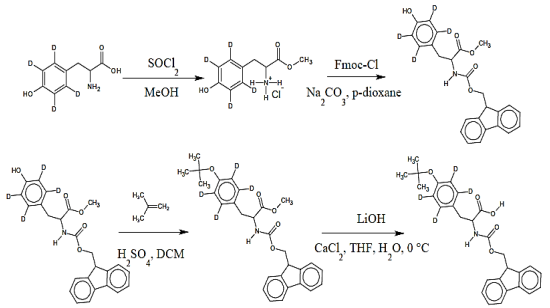
Our objective is to synthesize deuterated, protected amino acids, specifically tyrosine and serine. These deuterated isotopes will be used to create distinct chemical signatures on the peptide substrates that participate during kinase activities.

Due to high cost, the tyrosine and serine synthesis pathways were extensively tested with non-deuterated conformations.

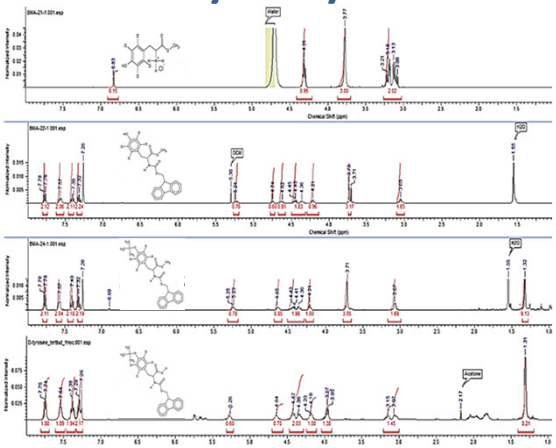
Potential Outcomes

By developing this technology, therapists can transform personal medicine through single cell monitoring of therapeutic response. It is also tunable to different kinase activities, which allows for simultaneous monitoring of multiple kinase activities (multiplexing). The technology is also non-destructive, allowing almost real-time detection of signal transduction in live cells without harm or need for a fluorescent genetic construct. The proposed technology will potentially transform cancer research and drug discovery.

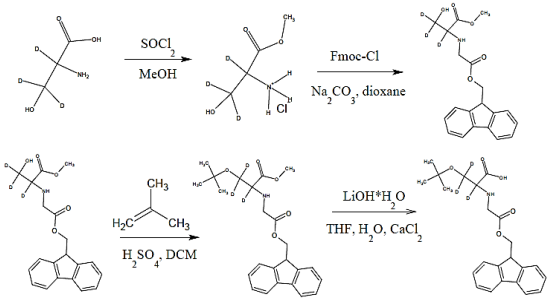
Tyrosine Synthesis



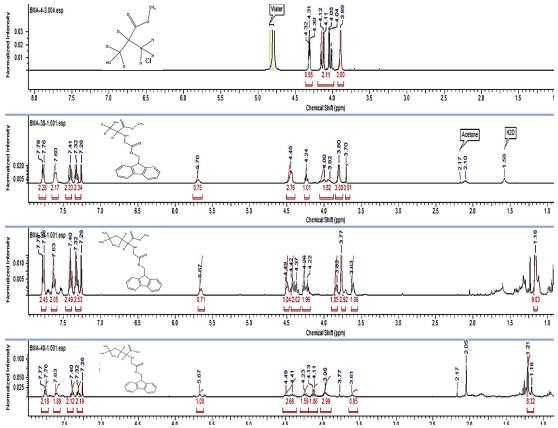
NMR Analysis: Tyrosine



Serine Synthesis



NMR Analysis: Serine

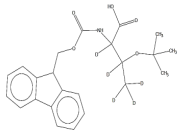


NMR graphs represent non-deuterated serine synthesis results.

Yields

Reaction Step #	Tyrosine Yields	Serine Yields
1	98%	97%
2	74%	87%
3	71%	88%
4	54%	43%

Future Studies



Synthesis of deuterated protected threonine compound.

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