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Developing a Technique Using Peptide and Dye Synthesis for Cancer Research

Developing
Scholars
Program

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ABSTRACT

Cancer occurs when a mutated single cell continues to divide uncontrollably, developing into one of the 200 different cancer types. Cancer is the second leading cause of death in the United States, with approximately 1.7 million new cases occurring this year [1]. Current cancer detection and treatment techniques are costly and not optimal, due to the lack of cancer specificity as well as early detection achieved in some cancer types. This project focuses on the synthesis development of peptides and fluorescent dyes that could be used for cancer research. The solid phase peptide synthesis procedure as well as cyanine 7 synthesis will be discussed here. Cyanine 7 is a blue fluorescent dye synthesized and used to label peptides, so they can be used to quantify protease levels as an aim for cancer detection technique. Establishing a well synthesized peptide will help us to advance for better cancer detection and treatment techniques.

BACKGROUND

Cancer

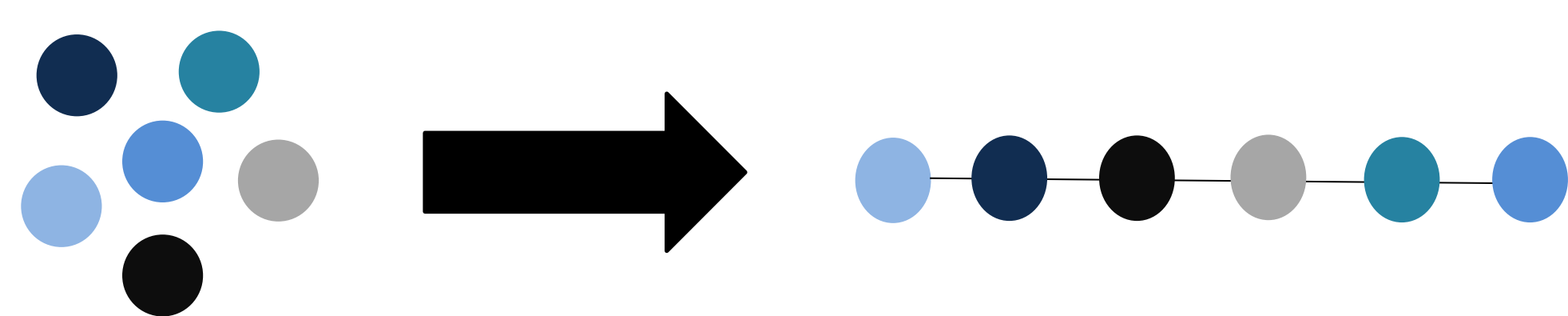
- ❖ As of 2019, about 606, 880 deaths will result from cancer in the United States [1].

Current Cancer Detection Techniques

- ❖ MRI: images due to magnetic and radio waves.
 - Drawbacks: causes nausea, pain at the needle site, headaches, low blood pressure, and expensive [2].
- ❖ CT scan: shows tumor's shape, size and location.
 - Side effects: causes rash, nausea, shortness of breath, itching or facial swelling. IV contrast dye could also affect the kidneys [3].

Peptides Synthesized for Cancer Research

- ❖ Capable to penetrate cells while carrying and delivering different payloads [4].
- ❖ Peptides with toxic properties can be synthesized to be used as both the nanocarrier and the anticancer drug.
- ❖ The Bossmann group have developed peptide-based nanobiosensors for early detection of pancreatic cancer [5].

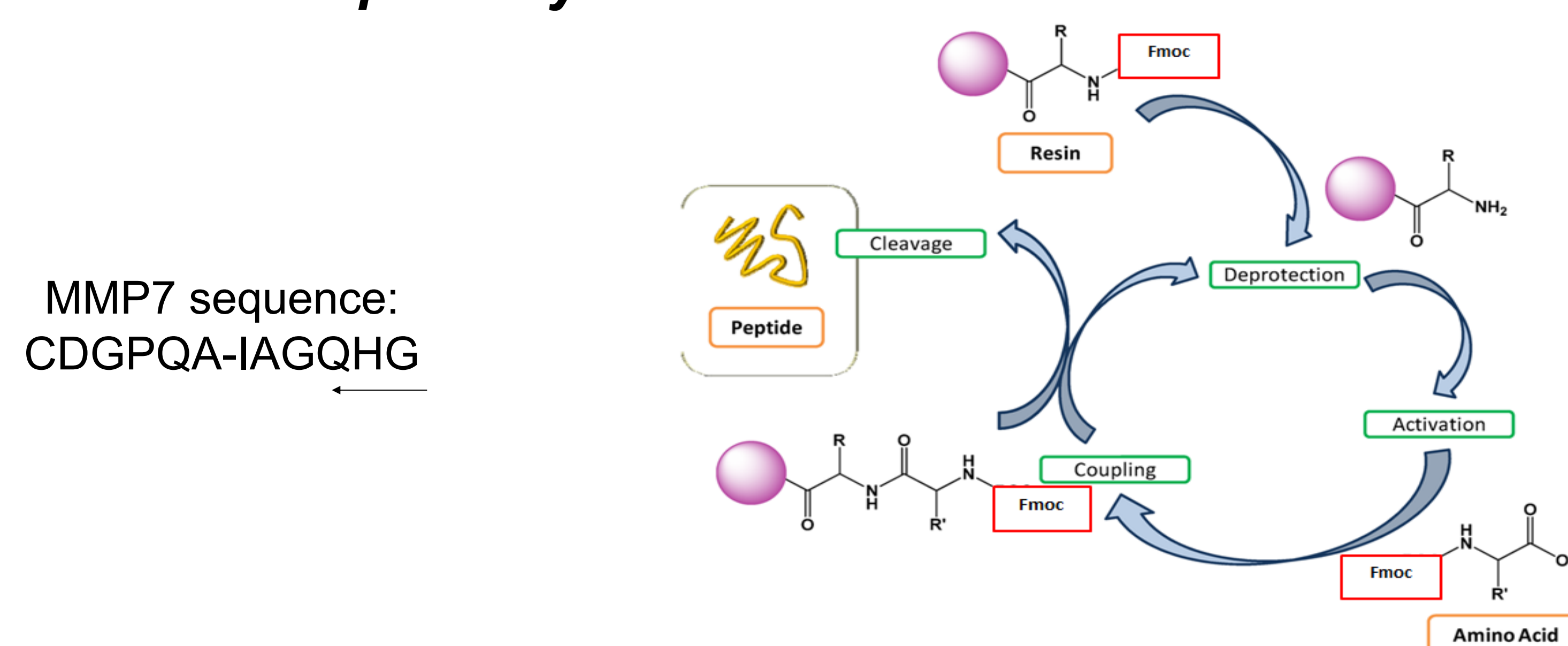


OBJECTIVE

The objective of this project is to synthesize a fluorescent dye, cyanine 7, as well as a protease peptide, to then link these two to generate a fluorescent label peptide to be used for cancer detection research.

METHODOLOGY

Solid Phase Peptide Synthesis Procedure

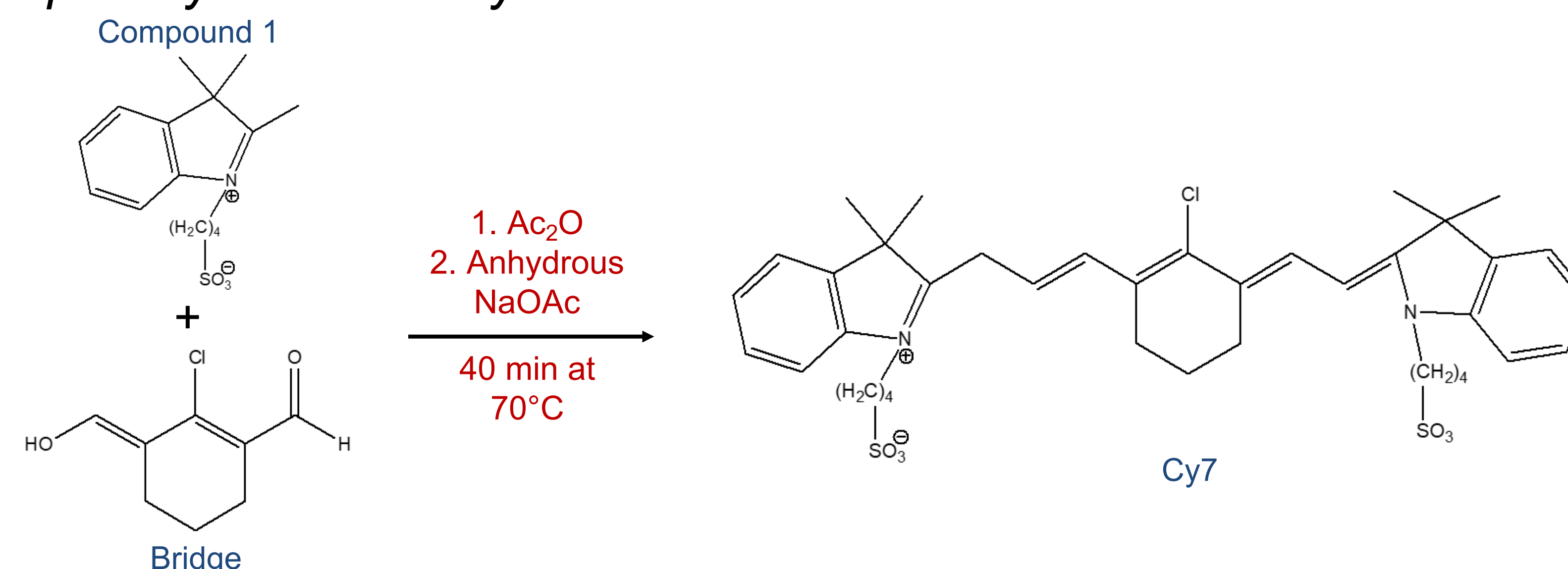


All amino acids and resins (containing the first amino acid already linked) are protected with an Fmoc group. The peptide synthesis cycle is as follows:

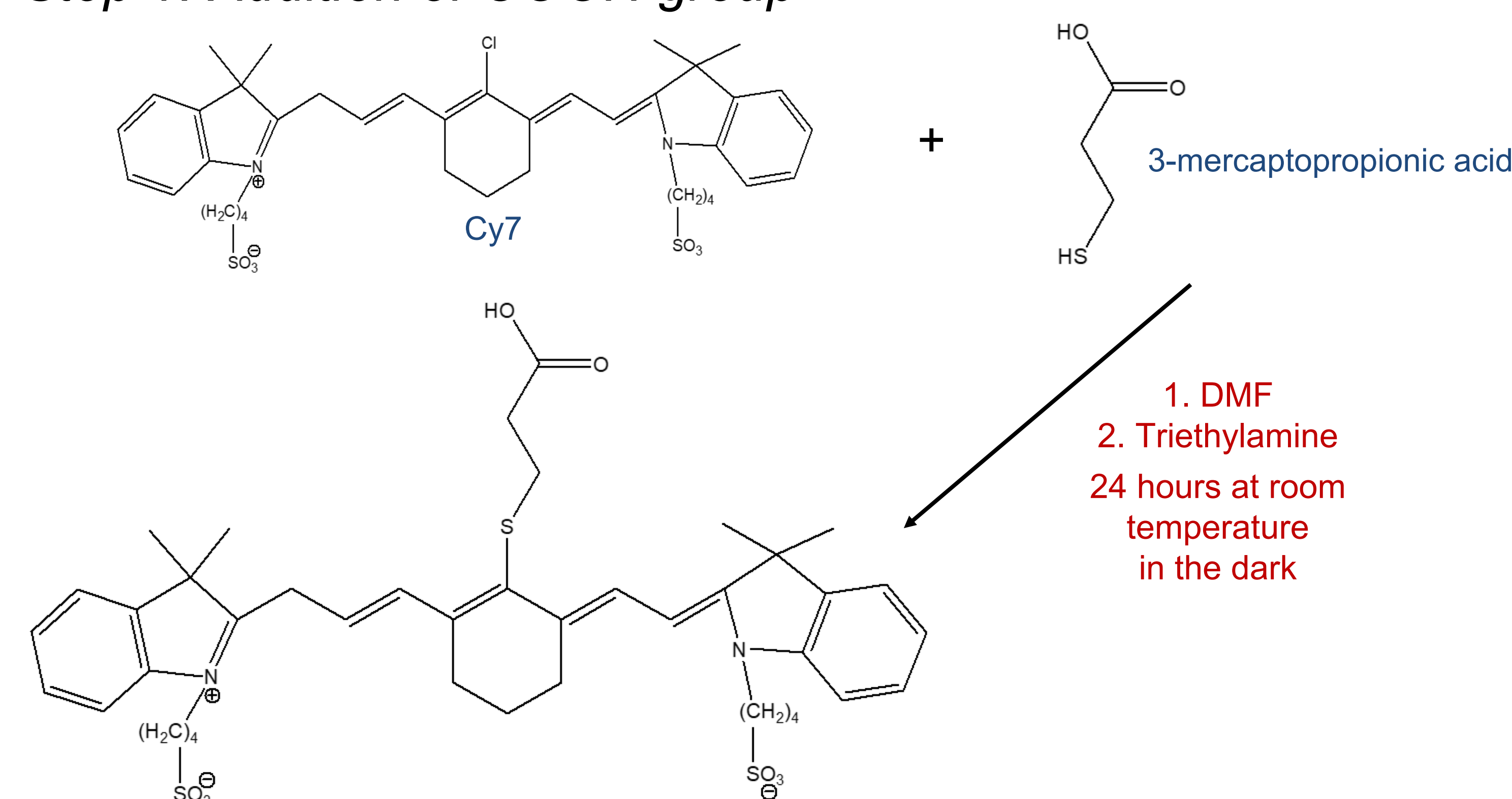
- Deprotection: cleavage of Fmoc using 20% dimethylamine.
- Washing: washings with DMF to remove excess cleaving solution.
- Coupling: carboxyl group of the next amino acid is activated and coupled to the peptide chain using HBTU.
- The cycle of deprotection, washing and coupling is repeated until entire sequence is completed.
- Last step: peptide can be labeled with a fluorescent dye, and then cleaved from the resin using trifluoroacetic acid.

SYNTHESIS OF CYANINE 7

Step 1: Synthesis of Cy7 scheme



Step 1: Addition of COOH group



RESULTS

- ❖ Cyanine 7 was characterized through NMR and FTIR, by identifying major component groups, like nitrogen, sulfur, and carboxyl groups.
- ❖ Synthesized blue fluorescent dye successfully.



CONCLUSION

- ❖ Successfully synthesized and characterized a blue fluorescent dye, cyanine 7.
- ❖ Successfully learned the solid phase peptide synthesis, and assisted on the synthesis of multiple protease and cell penetrating peptides sequences.

NEXT STEPS

- ❖ Continue exploring different mechanism pathways on how to successfully attach cyanine 7 to a protease peptide in order to be fluorescent.
- ❖ After peptide is successfully labeled, actual cleaving of protease peptide substrate will be determined using an active enzyme.
- ❖ Assemble a nanobiosensor composed of protease labeled with cyanine 7 to quantify protease activity as a mean to detect cancer.

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- ❖ The Bossmann research group members
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- ❖ Bridges to the Future Program

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