I. Title and Abstract:
“A photo-labile backbone amide linker for the Solid-Phase Synthesis of C-terminally Modified Peptides”
Cyclic peptides and other C-terminally modified peptides are of great importance for the development of peptide-based pharmaceuticals due to stability, hydrophobicity, and membrane permeability. One way of synthesizing these C-terminally modified peptides using solid-phase peptide synthesis (SPPS) is the utilization of a backbone amide linker (BAL). Most BAL requires acidic conditions for cleavage of the peptide product, which can be problematic when deprotecting an acid-labile sidechain protecting group. Thus, a photo-labile, acid-stable BAL, Hcna, was developed which adds an extra degree of orthogonality. This linker was used to synthesize dipeptides in solution as a proof of concept and then applied to SPPS. The linker was also optimized to avoid diketopiperazine (DKP), a by-product of Fmoc/t-Bu SPPS when adding a third amino acid. Additionally, cyclic peptides of various lengths and peptide thioesters were synthesized to show the versatility of the linker.

II. Title and Abstract:
“Discovery of New Lead Compounds to Target Class II-HMG CoA Reductase by Fragment-based Lead Discovery”
Antimicrobial resistance is an urgent global public threat affecting 2.8 million people in the US each year according to the CDC. Antibiotics available in the market or in the pipeline are variants of old classes or have the same molecular pathways as a result bacteria develop resistance to them very quickly. Class II HMG CoA reductase is an enzyme found in pathogenic Gram-positive bacteria and this enzyme is crucial for bacterial cell survival thus making it a potential new target to combat antimicrobial resistance. Fragments are small molecules with less than 300 Da molecular weight. Fragments from 3 libraries were screened by Lipinski’s rule of three and then tested against class II HMG CoA reductase for inhibition. 44 fragments were found to inhibit the enzyme at least by 15%. These fragments are currently being co-crystallized to check where they bind within the enzyme by our collaborators in the Stauffacher laboratory. New leads will be designed and synthesized once the X-ray crystal data are obtained.