

## CHEMISTRY Departmental Seminar

Spring 2022  
CHEM 285/191 Schedule  
*Extra Seminar*  
*Thursday at 4:30-5:45PM*

February 3<sup>rd</sup>, 2022

**Dr. Ryan Muir**  
Stanford University

### ***Development of Selective Covalent Inhibitors of the P. falciparum Proteasome***

The *Plasmodium* proteasome is an emerging antimalarial target due to its essential role in all the major life cycle stages of the parasite, and its contribution to artemisinin resistance. However due to high homology with the host proteasome, efforts to develop proteasome inhibitors as antimalarials must be primarily focused on achieving selectivity. Several parasite-specific proteasome inhibitors have recently been reported, however their selectivity and pharmacological properties must be improved to enable clinical development. We achieve this by screening diverse libraries of non-natural, synthetic fluorogenic peptide substrates to identify key specificities at multiple positions on the substrate that enhance selectivity. Combining this information resulted in linear peptides with high potency and selectivity towards the *Plasmodium* proteasome, and are highly synergistic with ART. Subsequent work to improve pharmacological properties by introducing cyclization strategies and bioisostere replacements have generated lead compounds to be used in *in vivo* antimalarial models.

Zoom link: <https://sjsu.zoom.us/j/84626719622>

Please RSVP at <https://forms.gle/QuLDzNBjckNJXjwK6> if you're not enrolled in Chem 285 or Chem 191

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