DEPARTMENT OF
Chemistry
UNIVERSITY OF WISCONSIN–MADISON

# *Ph.D. Dissertation Defense*

## Kacie Rich

Zanni Research Group

**Friday, March 22nd - 3 pm in room 9341 Chemistry**

## *"Cytotoxic intermediates of human islet amyloid polypeptide studied using two-dimensional infrared spectroscopy"*

There are many diseases caused by proteins that aggregate into amyloid plaque. Determination of the structures these proteins adopt along their aggregation pathway in forming these plaques is vital in locating toxic forms, leading to disease onset. My graduate research has focused on studying the aggregation of human islet amyloid polypeptide (hIAPP), or amylin, the amyloidogenic peptide associated with type II diabetes. Using rapid-scan two-dimensional infrared (2D IR) spectroscopy and $^{13}C^{18}O$ isotope labeling, I have determined intermediate structures along the *in vitro* aggregation pathway of hIAPP in the presence of membranes as well as solution aggregation. From this research and previously published research I have also successfully trapped intermediate species by mutating the sequence and evaluating the retention of the intermediate structures and cytotoxic effects. These projects have established a scheme that is applicable to many amyloid proteins to help determine potential intermediate structures and their relevance to disease.