



INVESTIGATION OF CASPASE 1 INHIBITION VIA AU(I) PHOSPHINES Amelia St Clair (Amy M. Barrios) Department of Medicinal Chemistry

Rheumatoid arthritis is one of the major types of autoimmune diseases, affecting millions of people worldwide. Despite this, there remains no cure for this disease, and there are a very limited variety of treatments available.

Caspase 1 is a cysteine protease that is involved in the production of a key cytokine that is targeted for the treatment of rheumatoid arthritis and many other similar autoimmune diseases. In addition, Au(I) phosphine complexes have been shown to act as inhibitors of cysteine proteases, including several enzymes that are involved in inflammation response.

In this research, a library of Au(I) phosphine complexes were synthesized and tested as inhibitors of caspase 1. A fluorogenic substrate was used so that once cleaved by caspase 1 it would become fluorescent, which allowed for a way to measure the activity of the phosphines as inhibitors (Figure 1). It has already been confirmed that this substrate is turned over very well by caspase 1.



Figure 1. Scheme for detecting the enzymatic activity of caspase 1.

If it can be proven that caspase 1 can be inhibited by Au(I) phosphines, then this would yield a novel target for the treatment of rheumatoid arthritis and potentially many other autoimmune disorders.

