

# Aza-peptide Aldehydes and Ketones: A New Class of Inhibitors for Proteases

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## Technology description

### The Need

Proteases play an important role in cell processes such as apoptosis, immune response, protein turnover, digestion, blood coagulation and wound healing, fertilization, cell differentiation and growth, and cell signaling among other processes. Due to their large involvement in such processes, uncontrolled proteolysis can lead to many disease states such as cancer, neurological disorders, viral infections, inflammation, and arthritis. Uncontrolled proteolysis can be stopped by inhibition, thus research in design and synthesis of novel inhibitors is of interest. While many inhibitors have been synthesized, most are nonselective and react with other proteases, thus they cannot be considered as therapeutic agents. The challenge in protease inhibition is to come up with a design, where the electrophilic warhead is reactive enough to result in inhibition, and inert enough to be specific for the targeted protease family or clan.

### The Technology

Researchers at The Ohio State University, led by Dr. Ozlem Dogan Ekici, have rationally designed a novel class of aza-peptide inhibitors capable of reversible chemical protease inhibition. It was demonstrated that a new class of aza-peptide inhibitors, aza-peptide aldehydes and ketones, are effective inhibitors of protease enzymes. The inhibitors were tuned to be selective for the threonine protease, the constitutive- and immuno-proteasomes, as well as the caspases, members of the clan CD cysteine proteases, by variation of the peptide backbone sequence and aza-P<sub>1</sub> residue to suit the preferences for the specific enzymes. The proteasome inhibitors displayed  $\mu\text{M}$   $K_i$  inhibitory constants in vitro and ex-vivo, and showed essentially no in vitro cross-reactivity with cathepsin B, a clan CA protease, and  $\alpha$ -chymotrypsin (a trypsin-like serine protease) proving their selectivity. These compounds can be used to target diseases associated with protease activity, such as cancer (multiple myeloma), cardiovascular, inflammatory, neurodegenerative (Alzheimer's & Parkinson's diseases), bacterial infections, viral infections, and parasitic diseases.

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## Application area

Pharmaceuticals

Cancer therapies

Anti-Viral

## Advantages

More drug-like and selective activity

Reversible inhibitors

Reduction in side effects

Novel aza-peptide reversible protease inhibitors, which permit more drug-like and selective activity than current irreversible aza-peptide containing inhibitors.

## Institution

[Ventech Solutions](#)

## Inventors

[Ozlem Dogan Ekici](#)

## 联系我们



叶先生

电话：021-65679356

手机：13414935137

邮箱：yeyingsheng@zf-ym.com