Reaction of urea hydrolysis catalyzed by enzyme — urease is causing production of large quantities of ammonia and, in consequence, significant increase of pH. This effect is crucial for survival of *Helicobacter pylori* bacteria in human gastrointestinal tract and is directly related with development of stomach and duodenal ulcers. This chemical reaction causes also negative consequences in the case of urinary tracts infections caused by ureolytic bacteria (e.g. *Proteus mirabilis*). It has been already proven that urease inhibitors could be useful in therapies of above-mentioned diseases. Design of urease inhibitors is not a trivial goal due to a small size of the active cleft and the loop of variable conformation, that is placed at the entrance of the active site. However, many urease inhibitors are known, significant majority of them shows moderate activity. The goal of this project is the development of new strategy of design of urease inhibitors based on compounds reacting with cysteine residue, that is placed at the entrance of the active site. Developed hypotheses will be tested with the use of four structurally diverse groups of compounds, that react with cysteine residue in various ways. Importantly, preliminary studies of compounds from each of proposed class showed significant inhibitory activity against urease (also in nanomolar range). Chosen lead structures will be optimized with the use of structure-based computer-aided methods. Results of enzymatic tests against bacterial ureases will be correlated with chemical reactivity of studied compounds (analyzed towards model compound - glutathione). Significant efforts will be devoted to obtain crystal structures of selected compounds complexed with studied enzyme. Studied classes of compounds can be further used for discovery of candidates drug against infections caused by *Helicobacter pylori* and/or *Proteus* spp. However, developed general methods of design of inhibitors binding cysteine residue can be also useful in the case of several other enzymes.