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The hallmark of my research is a biophysical and biological chemistry approach to dissecting mechanisms of neoplastic transformation and aging. The actions of biomacromolecular assemblies essential for the life of a human cell are in the center of my interest. Among these assemblies, a giant protease called proteasome is a major subject of my studies. The proteasome is an attractive drug target. A proteasomal inhibitor has already been approved for cancer treatment, and we are exploring the possibility of its specific targeting, as well as other proteases, which we found supplement the intracellular tasks of the proteasome.

To better understand the role of giant proteases on the cellular level, we are also dissecting the molecular mechanisms of regulation of activity of the proteasome. For this purpose, we developed a model of allosteric regulation of its enzymatic activity. In a small-scale rational drug design fashion, we created a series of small-molecule compounds affecting the proteasomal activities. Our goal is that the compounds or their derivatives will become specific and precise drugs against cancer, autoimmune diseases, stroke, heart diseases and other pathological conditions.

The unique features of research expertise:

- a) mass spectrometry: peptide mapping, identification of protein modifications;
  - b) chemistry of peptides: design and synthesis of peptides, peptide derivatives and peptidomimetics, their purification and characterization, computer modeling of their structure and interaction with intended targets;
  - c) atomic force microscopy (AFM), an exceptional technique to study dynamics of biomacromolecules and their interactions with ligands under native conditions;
  - d) spectrofluorometry, currently used to complement the AFM studies of the dynamic structure of the proteasome;
  - e) expertise in numerous other spectroscopic methods (EPR, ENDOR);
  - f) enzymology, including advanced enzyme mechanism and molecular modeling of enzyme-ligand interactions;
  - g) development of protein purification techniques designed for giant biomacromolecules;
- In addition to the above specialized methods and approaches, we are using standard molecular biology methods, yeast genetics and mammalian tissue culture techniques.