UNIWERSYTET GDAŃSKI

IN MARI VIA TUA

CHEMIA UG

dr hab. prof. UG
Sylwia Rodziewicz-Motowidło
Head of the Department of Biomedical Chemistry

Gdańsk, 12.01.2017 r.

LETTER OF INTENT

Dear prof. Michał Dadlez
Institute of Biochemistry and Biophysics
Polish Academy of Sciences
Warsaw, Poland

This letter is to confirm that the Department of Biomedical Chemistry is highly interested in using the HDXMS spectrometry for the purpose of analyzing protein-protein or protein-ligand interactions. Currently, substantial research in Department of Biomedical Chemistry is directed toward:

1) Amyloidosis AA
   Amyloidosis AA is a life-threatening condition developing as a consequence of inflammation accompanying tissue injuries and chronic diseases such as cancer, rheumatoid arthritis and tuberculosis. The precursor protein of AA amyloidosis is serum amyloid A protein (SAA), belonging to a small and highly conserved family of apolipoproteins. Despite intensive studies still very little is known about the mechanism of SAA aggregation and possible ways of inhibition of this pathological process.

   Hydrogen-deuterium exchange coupled with mass spectrometry can be very useful for structural characterization of the oligomerization process of human SAA. By probing differences in H/D exchange patterns between the monomer and oligomers it will be possible to determine regions interacting with each other in the course of oligomerization. We will utilize this information for design of inhibitors of hSAA (human SAA) aggregation. By application of HDX-MS we will be also able to determine the binding place for inhibitors, which will allow for further optimization of their structure to gain higher affinity and greater inhibitory capacity.
2) Amyloidosis of hCC protein

   Second amyloidogenic protein of our interests in human cystatin C. This protein is moderately amyloidogenic by itself (especially in the native form) but possesses highly aggregation-prone endemic variant (hCC L68Q), which is a cause of hereditary amyloid angiopathy among Icelandic families. Moreover cystatin C is associated with other amyloidogenic disease, that is Alzheimer disease. Our work is focused on on design of potential therapeutic goals in combating the hereditary disease cerebral amyloid angiopathy connected with hCC protein. Our research goal is to find the new ligands (potential therapeutics), which could interact with HCC and inhibit amyloid fibril formation. In the scope of interest is developing a novel method of ligand's design, studies of the mode of their action (based on MS spectrometry) and rational chemical synthesis, investigating interactions of the cystatin C with antibodies or with peptides.

Faculty of Chemistry Department Biomedical Chemistry
Wita Stwosza 63, 80-308 Gdansk
tel. +48 523 50 37, email: s.rodziewicz-motowidlo@ug.edu.pl

3) Immunotherapy

Our studies are focused on identification of the binding sites between proteins such as: BTLA, HVEM, CD160 and their antibodies. Those proteins belong to the receptors presented on lymphocytes T and acts as negative regulators of T cell responses. It is known that antibodies could inhibit the interaction between proteins: BTLA-HVEM and CD160-HVEM, what is used in cancer immunotherapy. However, antibodies have many disadvantages and the other smaller molecules are searched. In our studies we would like to find the binding fragment of antibodies which could be used to blocking the protein interaction. Therefore epitope/paratope mapping will be performed by amide hydrogen/deuterium (H/D) exchange in solution coupled mass spectrometry (HDXMS). We will utilized this information for design of inhibitors of BTLA-HVEM and CD160-HVEM complexes.

Cystatin C is a subject of our studies concerning the application of immunotherapy to combat several diseases, including the neurodegenerative ones. Hydrogen-deuterium exchange coupled with mass spectrometry can be also very useful for characterization of interaction of hCC with anti-hCC antibodies. We will utilize this information for design of inhibitors of hCC aggregation.

This letter indicates our willingness to future cooperation and signing a partnership agreement, determining detailed rights and duties of contracting partners.

Sincerely,

Sylwia Rodziewicz-Motowidło

KIEROWNIK
Katedry Chemii Biomedycznej

dr hab. Sylwia Rodziewicz-Motowidło, prof. UG

Faculty of Chemistry Department Biomedical Chemistry
Wita Stwosza 63, 80-308 Gdansk
tel. +48 523 50 37, email: s.rodziewicz-motowidlo@ug.edu.pl