DATE: 21 May, 2018

SUMMARY of
2017 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		Investigation of stability mutants of β2-microglobulin affecting amyloid fibrillation propensity
Applicant	**Name**	KARDOS, József
	Affiliation	Department of Biochemistry, Institute of Biology, Eötvös Loránd University, Hungary
	Present Title	Associate professor
Research Collaborator (Host PI)		GOTO, Yuji

Summary

Background: Amyloid deposition accompanies over 20 degenerative diseases in human, including Alzheimer's, Parkinson's and prion diseases. Dialysis-related amyloidosis (DRA) is a serious complication, associated with the aggregation of β2-microglobulin (b2m). A comprehensive understanding of the mechanism and thermodynamics of the aggregation of b2m will help the development of efficient therapies for the prevention or treatment of DRA.

Aims: In the joint research plan, we aimed to study various mutant forms of b2m which have altered conformational stability. We study the stability, unfolding mechanism, amyloid fibrillation and the mechanism of aggregation inhibition of these variants in order to investigate their potential use as amyloid inhibitors. To realize our research plan we use a complex repertoire of spectroscopical and calorimetric methods.

Achievements and perspective: To perform the collaboration, Kardos visited IPR from June 23 to July 6, 2017. Because the mutant b2m proteins were not obtained by his visit, we performed a series of experiments with a wild-type b2m. Previously, we reported degradation of b2m amyloid fibrils to monomeric unfolded state at high temperatures at pH 2. Now, we carefully examined the temperature-dependent formation and degradation of amyloid fibrils at various concentrations of NaCl. We obtained an aggregation phase diagram of b2m dependent on temperature and NaCl concentration, giving insights into the comprehensive mechanism of protein aggregation.

Kardos gave two lectures, first in a class to graduate students and second in a seminar, both entitled "New perspectives in CD spectroscopy for the study of protein structure", in which he introduced a new methodology for CD analysis on the basis of their paper: "Accurate secondary structure prediction and fold recognition for circular dichroism spectroscopy", Micsonai, A., et al. and Kardos, J. Proc. Natl. Acad. Sci. USA. (2015) 112(24), E3095-2103.

With other international collaborators, we planned and applied for the JSPS Core-to-Core Program, a program designed to create top world-class research centers, and the proposal has been accepted. The program: "An international cutting-edge network for the study of protein aggregation" will continue for 5 years (2017-2022) and we will advance our collaboration on b2m amyloid fibrils taking advantage of this program.