

DATE: 21 May, 2018

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

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| Research Title | | New approaches to characterize the mechano-enzymatic mechanism underlying TTR amyloidogenesis |
| Applicant | Name | BELLOTTI, Vittorio |
| | Affiliation | University College London, London, UK |
| | Present Title | Professor of Medical Biochemistry Metabolism & Experimental Therapeutics |
| Research Collaborator (Host PI) | | GOTO, Yuji |
| <p>Summary</p> <p>Molecular mechanism of systemic amyloidosis caused by human transthyretin (TTR) is still obscure. Vittorio Bellotti and his team have shown that exposure of TTR to low level of trypsin under physiological conditions triggers formation of TTR (Proc Natl Acad Sci USA 2014; 111: 1539-1544). This discovery may shed light on the real pathogenic mechanism of TTR amyloidosis in vivo and explain the finding of the presence of truncated TTR in natural amyloid deposits. The collaboration with Goto (IPR) will allow to test the kinetics of fibril formation by TTR using a combination of a water bath type ultrasonicator and microplate reader.</p> <p>To perform the collaboration, Bellotti, Vittorio visited IPR from December 3 to 7, 2017 and Verona, Guglielmo (PhD Candidate) visited IPR from December 2 to 6, 2017. We discussed the mechanism of amyloid fibril formation with a focus on their structural transitions of transthyretin (TTR) and β2-microglobulin (b2m) induced by proteolysis or ultrasonication. On the basis of a series of discussion, Goto and coworkers at IPR started the expression of TTR with E. coli system. The expressed TTR formed amyloid fibrils. Goto in collaboration with Bellotti will study the role of proteolytic cleavage with various approaches available at IPR.</p> <p>Bellotti and Verona participated in the Second Joint Symposium between the Institute for Protein Research (Osaka University) and the Research School of Chemistry (Australian National University) held December 3rd -5th, 2017 at IPR.</p> <p>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 fibril formation of TTR and b2m taking advantage of this program.</p> | | |