DATE: Day 12 Month 4 Year 2021

SUMMARY of
2020 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		**Computational modelling of EML4-ALK signaling pathway**
Applicant	**Name**	Iosifina Sampson
	Affiliation	Faculty of Biological Sciences, School of Molecular and Cellular Biology, University of Leeds
	Present Title	Postdoctoral Researcher
Research Collaborator (Host PI)		**Mariko Okada**

Summary

A fusion between EML4 (echinoderm microtubule associated protein-like 4) and ALK (anaplastic lymphoma kinase), EML4-ALK, was discovered in non-small cell lung cancer (NSCLC) in 2007, and there are at least 15 different variants that differ in the breakpoint in the EML4 gene. EML4 is a member of EML protein family with functions in microtubule regulation and mitotic spindle organisation. ALK is a tyrosine kinase receptor and studies have shown that point mutations, gene amplification or gene fusions lead to oncogenic activity of ALK. The EML4-ALK fusion leads to abnormal cell signaling of PI3K/AKT, RAS/RAF, JAK/STAT and MEK/ERK and consequently increased cell proliferation and cell survival. Patients identified with EML4-ALK mutation are treated with selective ALK inhibitor such as crizotinib, ceritinib, alectinib or lorlatinib, however the type of variant influences the response of patients to ALK therapy and secondary mutations that confer resistant to these inhibitors arise in some patients within a year. The most frequently occurring variants, variant 1 and 3a/b are expressed in 33% and 29%, respectively, of positive EML4-ALK patients.

We plan to build a computational model that will predict the changes of downstream signalling molecules such as JAK/STAT3, ERK/MAPK and PI3K/AKT pathways upon ALK inhibition in variant 1 and 3a/b EML4-ALK positive cell lines. We jointly have established a successful beginning for this project to developed a modelling platform, called BioMASS, to estimate the parameters of our model describing the biological processes of the EML4-ALK signaling.

However, due to the influence of COVID-19, Iosifina Sampson was not able to visit IPR and we were not able to carry out our international collaborative research for the year 2020.

***Deadline: April 30, 2021**
***Please submit it to E-mail: tanpakuken-kyoten@office.osaka-u.ac.jp.**
***Please describe this summary within 1 sheet. Please DON'T add some sheets.**
***This summary will be published on the web.**