

平成 28年度 委託研究開発成果報告書

I. 基本情報

事業名：(日本語) 医療分野国際科学技術共同研究開発推進事業
戦略的国際科学技術協力推進事業 日本-フィンランド 研究交流
(英語) International Collaborative Research Program
Strategic International Research Cooperative Program(SICP)

研究開発課題名：(日本語) 心不全に対する再生医療におけるバイオインフォマティクスデータベースの構築
(英語) Bioinformatics Platform for predicting autologous cell therapy efficacy in patients with heart failure

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II. 成果の概要(総括研究報告)

本プロジェクトは心不全に対する再生医療で得られた知見を集約した、世界中からアクセス容易なバイオインフォマテクスデータ基盤整備を目的とした。心不全領域の再生医療という新しい分野について、国際的なデータベースはまだなく、また希少疾患や難病においては日本国内だけで知見を収集する事は容易ではない。本課題の遂行により、希少疾患や難病を国際的にデータベース化することで迅速かつ広範囲の情報の提供が可能となるシステム構築が開始された。日本とフィンランドが疾患患者由来のiPS細胞の構築、サンプルの収集、網羅的遺伝子発現解析、データの整理などを分担し相互的に取り組むことで、国際的な利用を視野に入れた他に類を見ないバイオインフォマテクスデータベースの構築を目指した。

初年度(平成26年度)はiPS細胞の樹立および輸出入に必要な体制構築を行った。日本側はiPS細胞樹立技術の習得および研究に係る書類整備、フィンランド側はInnovatics社と共同でLaboratory Information Management System(LIMS)およびCSC社と共同で高性能演算システムのためのクラウドの準備を行った。また、9月にキックオフミーティングを行い、両国間の役割分担と進め方についての認識を共有した。平成27~28年度は、日本側で循環器疾患患者由来末梢血を中心とした検体からiPS

細胞の樹立をし、品質評価を行った後低分子化合物を用いて心筋細胞への分化誘導を行った。分化誘導後の心筋細胞集団に対し、特定の細胞外マトリックスに接着させることで活性の高い心筋細胞集団を簡単に短時間で精製できる事を見いだした。更に心筋分化誘導前後の核酸の検体収集を行った。フィンランド側ではイノバティクス社と共同でLIMSとCloudとのインターフェースの開発およびRNA-seqパイプラインの策定を行った。

本プロジェクトの期間中に日本側からプロジェクトの中心メンバーや若手研究者らが年1回以上訪問し、再生医療やバイオインフォマティクスに関する議論を行った。若手医師が延べ3週間程度滞在し、施設訪問、臨床現場での実践を含めた見学、意見交換を行った。また最終年度（平成28年度）には、日本において共同シンポジウムを開催した。シンポジウムは臨床・基礎研究両方から多くの研究者が参加した。若手研究者を中心に英語で研究発表を行い、活発な討議がなされた。また、フィンランド側研究者は日本側のiPS研究を中心とする研究施設へ訪問を行い、交流、意見交換を行った。研究の成果は共著論文2報を含む計14報の原著論文、総説4報、連名の学会発表1件、国際学会発表31件を含む学会発表57件として発表した。また、研究成果で得られた知見については日本側から特許を出願し、JSTの支援を受けて国際出願を行った。

本プロジェクトが目指した国際的なデータベースの構築を通じて若手研究者を中心とした活発な人的交流が行われ研究者育成に寄与したと考える。また、本データベースが構築され稼働した場合は、これを活用する事で病態解明、創薬スクリーニング、ドラッグリポジショニングが加速され、ひいては新しい知の創造、科学技術の進展に資するものと考えられる。

The aim of this project is the development of bioinformatics infrastructure, which is internationally accessible data storage and analysis system based on cell therapy trials in heart failure. There is no international database of regenerative therapy for heart failure, because it is relatively new area. Furthermore, it is not easy to collect the knowledge from the patients of rare disease or orphan disease only in Japan. It has started to develop that the infrastructure that enables to quickly share the disease information worldwide through the international database construction. We: Japan and Finland achieved the bilateral cooperation such as iPS cell establishment from patient, collecting samples, comprehensive gene expression analysis, which contributes the bioinformatics infrastructure in worldwide setting.

The first year, 2014, environment to research of regenerative medicine using human iPS cell was prepared. In Japan, it was approved to export cultured human cell or nucleic acid, following security export control. We also learn how to establish iPS cells. In Finland, schema for Laboratory Information Management System (LIMS) was created with Innovatics Ltd. Cloud-instance acquired for high-performance computing was prepared with CSC Ltd. We also had kick-off meeting at Helsinki in September, and shared the perception of procedure and each assignment of the research. In 2015 to 2016, peripheral blood-derived iPS cell was established from the patient of cardiovascular disease. After evaluation of the quality, cardiomyogenic differentiation was induced using small molecule. We found that active iPS-derived cardiomyocyte can be purified easily in a short time by adhesion on a specific extra-cellular matrix. Furthermore, we collected nucleic acid from iPS cells of before/after differentiation. In Finland, LIMS-Cloud interface was developed with Innovatics Ltd. Furthermore, RNA-seq data-processing pipeline was developed with Institute for

Molecular Medicine Finland (FIMM).

During this project, core researchers or young researchers of Osaka University visited University of Helsinki constantly, discussed about regeneration therapy and bioinformatics. Young medical doctor stayed Helsinki for 3 weeks, visited laboratory and hospital including practice, and exchanged opinions. In the last year, 2016 symposium was took place in Osaka. Many researchers both from basic research and clinical research were participated. Young researchers made presentation and discussed actively in English. Finnish researchers also visited some laboratories including iPS research in Japan. The results of our Japan-Finland collaboration were disclosed as 14 original articles (including 2 co-authored), 4 review papers, 1 conference presentation of co-presenter, 57 conference presentations (including 31 international conference presentation). The knowledge derived from the research was applied for a patent from Japan. For international application, Japan Science and Technology Agency (JST) supported us.

We believe that this project contributed making active researchers interaction and fostering young researchers, through building international database infrastructure. Furthermore, if the database works, it would accelerate the resolution of rare or orphan disease, drug screening, drug repositioning, which may lead new knowledge and progress of science.

III. 成果の外部への発表

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(3) 「国民との科学・技術対話社会」に対する取り組み

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