Global Link Online 2021 : Abstract for Science Project

Submission Deadline : 6th August, 2021

Study Area *Please mark a circle on your subject

Physics Chemistry Medical Science・Biology Earth Science・Geoscience
Mathematics・Informatics・Computer Science Others( )

Division *Please mark a circle on your division

Advanced General

Presenter(s)

【School Name】Yokohama Science Frontier High School

【Project Member(s)】

Chiharu Kameda

Abstract of Presentation

【 Title 】

Development of new method using metabolite information in pancreatic cancer patient's blood for estimating important proteins in pancreatic cancer

【 Introduction/Background/Motivation 】

To detect cancer earlier is required for complete cure. To find cancer, there are two kinds of clinical test called biopsy and laboratory test. As first step, patients are examined with X-ray examination or electrocardiograph as biopsy. Then they are picked a part of their body sample like urine and organ tissue, blood as laboratory test. In addition to biopsy information, Laboratory tests provide cancer characteristics to us. For instance, high level of neuron specific enolase in blood indicates the possibility of small-cell lung cancer. High level of CA19-9 in blood indicates the possibility of colorectal cancer. These biomarkers used in laboratory tests target proteins and glycans. Using these data, Diagnosis is determined. After that, medicines are also determined. However, **there are possibilities of ineffective of medicines for cure of cancer due to mismatch between medicine target molecule and activating signaling pathway in cancer.** The mismatch causes damage progression of cancer, loss time for cure to patients.

In the case of pancreatic cancer, detecting pancreatic cancer at early stage is difficult and the cancer are detected at late stage. There is not much time to find matched medicine for the cancer.

To deal with the problem, more detailed information of cancer characteristics is needed. To get information of cancer, picking a part of cancer tissue for providing proteomics using mass spectrometry is one of the choices. However, picking tissue cause damages to patient and risk of metastasis. Therefor blood analysis is preferred in term of less invasive test. Compositions of blood are proteins and metabolites. In analyzing them, dealing with metabolites for providing mass spectrometry is easier than protein. In addition to this, cancer have unique character called Warburg effect. It is observed at almost cancer. Metabolic change in blood of pancreatic patient is observed.

【 Research Purpose/Problem Statement 】

In this study, **I focused on significant changed metabolite** in pancreatic cancer patient's blood and combining protein-protein interaction database and protein-metabolite database. **I developed a new method for estimating important proteins in pancreatic cancer using significant changed metabolite in pancreatic cancer.**

【 Study Plan/Approach 】

Extraction of metabolites changed significantly in pancreatic cancer patient's blood

I extracted metabolites changed significantly in pancreatic cancer patient's blood of three different reports (Mayele J et al [3], Shiro et al[4], Guoxiang Xie et al[5]).

Making new database combining protein-protein interaction database with protein-metabolite database

I created new database integrating protein-protein interaction database, called iRefindex[1] with protein-metabolite interaction database, called human metabolome database (HMDB) [2].

Making network derived new database and metabolites from each report

I picked up interactions between metabolites and proteins and re-picked up interaction between first-extracted proteins and proteins or metabolites. I created three networks in every report with extracted interactions.

Evaluation of network's composition factor in term of relationship with cancer

I provided all composition proteins to Gene Ontology (GO) analysis to check relationship between

protein characteristic and cancer, and also provided their proteins pathway analysis to check whether their proteins are annotated into cancer signaling pathway.

Estimation of important proteins in each pancreatic cancer

I analyzed these networks in term of bridging centrality in CentiScape 2.2, a network analysis software. I determined high score proteins in bridging centrality [6] as estimated important proteins.

Evaluation of important proteins in each pancreatic cancer

I drew a Venn diagram with the statistical software R and the top 30 proteins with high score of bridging centrality. I also made another Venn diagram with 30 proteins with high score after 30 top proteins. In addition to this, I checked top 60 proteins in term of reports of pancreatic cancer and the others types of cancer in each three reports. (Fig. 1)

【 Results and Discussion 】

Size of network created

I created three network. In Mayele J's sample, the network had 3557 kinds of protein. In Shiro's sample, the network had 1910 kinds of protein. In Guoxiang Xie's sample, the network had 1938 kinds of protein.

Evaluation of network's composition factor in term of relationship with cancer.

I analyzed protein with GO analysis and pathway analysis. In Mayele J's sample, phosphatidic acid biosynthetic process and 'pathway in cancer' were extracted. In Shiro's sample, phosphatidylcholine acyl-chain remodeing and 'pathway in cancer' were extracted. In Guoxiang Xie's sample, phosphatidylcholine acyl-chain remodeing and 'pathway in cancer' were extracted. **These GO terms and pathways have relation with cancer. Therefore, I could create cancer related network.**

In addition to this, In metabolites derived from Mayele J and Guoxiang Xie's sample, their proteins were annotated into protooncogene Ras and mTOR. However, in metabolites derived from Shiro report, their proteins were not annotated. **This indicated pancreatic cancer have diversities and unique signaling pathway and my method might have potential to detect difference of signaling pathway.**

Estimation of important proteins in each pancreatic cancer

I analyzed bridging centrality against each network. In metabolites derived from Mayele J report, NRSN2, GBAA_1901 and TRMT44 had high score. In Shiro's sample, PGK2, fadH and SLC27A5 had high score. In Guoxiang Xie's sample, FBXO46, HLA-DMB and ITGB8 had high score. **Estimated important proteins for pancreatic cancer was almost different in each report. These result also might indicate my method might have potential to detect difference of pancreatic cancer.** (Fig. 2)

Evaluation of important proteins in each pancreatic cancer

I checked top 60 proteins in term of reports of pancreatic cancer and the others types of cancer in each three reports. In all conditions, more than 67 % proteins have relation with pancreatic cancer and the others cancer. **Therefore, I could develop new method for estimating important protein in cancer.**

【 Future Study Plan 】

Molecular target drug exposure experiment might be needed to check the validation of my method. However, this method has the potential to estimate the characteristic of cancer more concretely. Therefore, this method surely will be helpful to determine molecular target and medicine. I hope that the practical application of this technology will open new possibilities for order-made medical care for each individual patient. (Fig. 3)

【 References 】

[1] Razick, Sabry, George Magklaras, and Ian M. Donaldson (2008). "*iRefIndex: a consolidated protein interaction database with provenance*." BMC bioinformatics.

[2] Wishart DS, Feunang YD, Marcu A, Guo AC, Liang K, et al (2018)." *HMDB 4.0 — The Human Metabolome Database for 2018*" Nucleic Acids Res.

[3]Mayerle J(2017). *"Metabolic biomarker signature to differentiate pancreatic ductal adenocarcinoma from chronic pancreatitis"* Gut

[4] Shiro Urayama(2010). *"Comprehensive mass spectrometry based metabolic profiling of blood plasma reveals potent discriminatory classifiers of pancreatic cancer"* Rapid communications in mass spectrometry

[5] Guoxiang Xie(2015). *"Plasma metabolite biomarkers for the detection of pancreatic cancer"* ACS publications

[6] Woochang Hwang(2006). *"Bridging Centrality: Identifying Bridging Nodes In Scale-free Networks"* KDD

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Appendix (Picture or Chart if any)

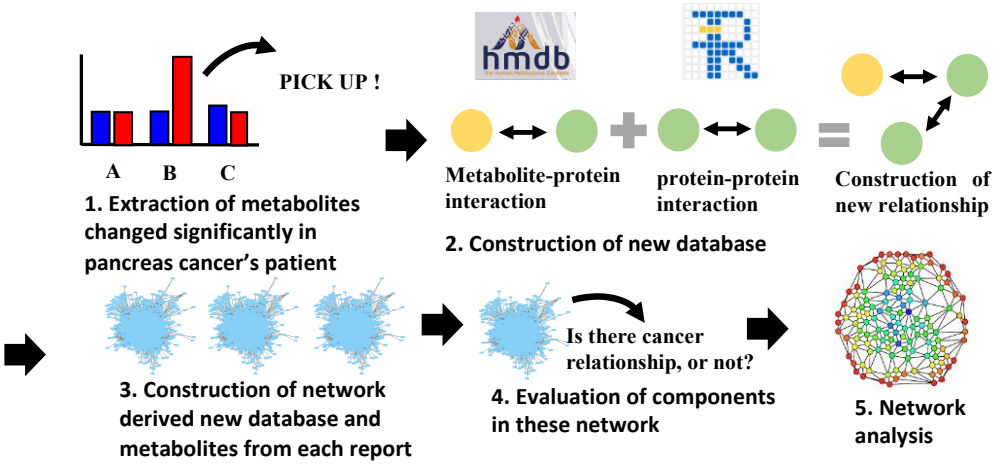

Fig. 1 Experiment procedure

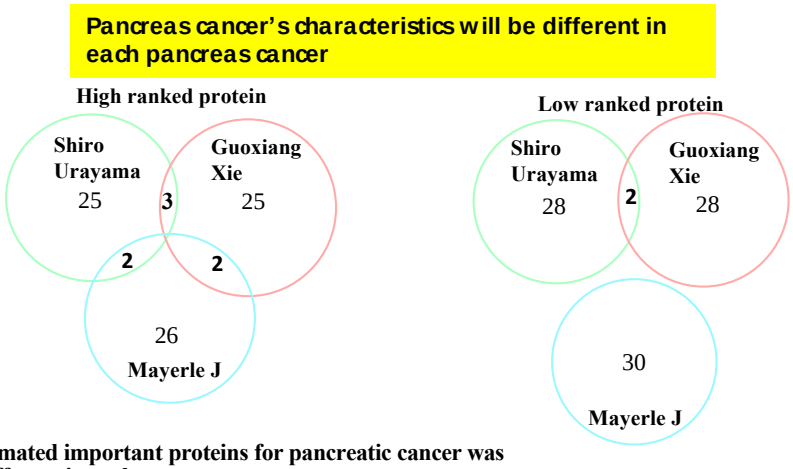

Fig.2 Estimated important proteins for pancreatic cancer was almost different in each report

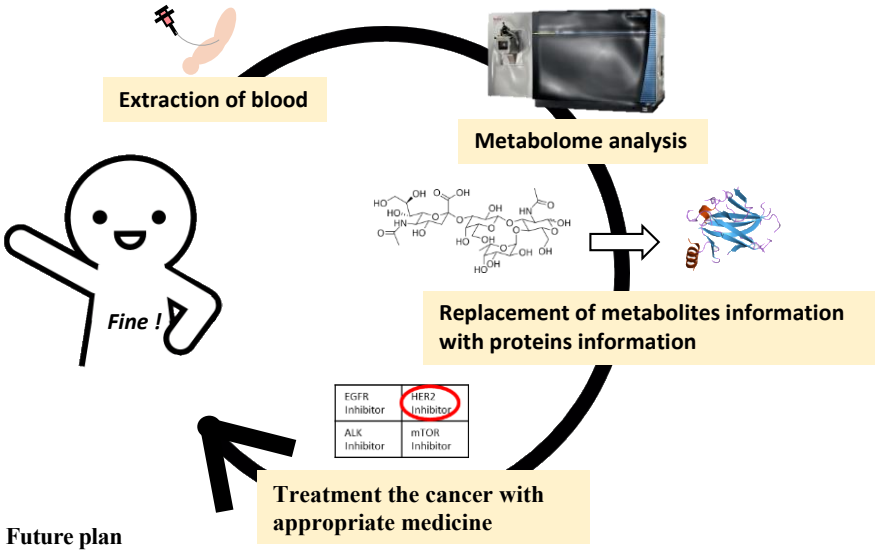

Fig. 3 Future plan

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<Instruction for Preparing the Abstract>

*** Font and Size : Times New Roman 10.5pt**

***The Number of Pages : Maximum 2 pages without Appendix**

Maximum 3 pages with Appendix (Abstract 2 pages + Appendix 1 page)

***School Name : Reconfirm the official name of your school in English before the submission**

***Project Member(s) : Indicate as "First/Given name + Middle name + Family Name"**

***Reference(s) : See below as minimum requirement for "References".**

ex) John Thomas (1995). *"World of wonder"* ABC Books

Author + (Year of Publishing) + *"Title"* + Publisher

***Appendix (Picture or Chart if any) : Picture and Chart are only allowed in the Appendix section.**

Do not insert them into other sections.