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Comparison of venous and fingertip plasma using non-targeted proteomics and metabolomics

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ABSTRACT

Blood tests, which are used to evaluate health status, are relatively non-invasive and provide a great deal of health-related information. Blood is usually collected using a standard venous blood sampling protocol, but it is possible to collect blood from a subject's fingertip, and previous studies have investigated whether fingertip-derived blood can be used for various blood tests. In this study, the proteomes and metabolomes of venous and fingertip plasma were analyzed using non-targeted proteomics and metabolomics, respectively. In proteomics, the levels of 523 proteins were compared between venous and fingertip plasma. The correlation coefficient (r) for the relationship between protein levels of venous and fingertip plasma was 0.9999. Some proteins had high fingertip to venous plasma level ratios (finger:venous ratios), whereas others had low finger:venous ratios, and the mean ± standard deviation (SD) finger:venous ratio was 0.994 ± 0.304. In metabolomics, 40, 33, and 216 cationic metabolites, anionic metabolites, and lipids, respectively, were detected in venous plasma, and the equivalent figures for fingertip plasma were 40, 35, and 216, respectively. Regarding the correlations between metabolite levels in venous and fingertip plasma, the correlation coefficients (r) for cationic metabolites, anionic metabolites, and lipids were 0.9952, 0.9699, and 0.9980, respectively. The mean ± SD finger:venous ratio was 1.19 ± 0.584 for cationic metabolites, 1.23 ± 0.548 for anionic metabolites, and 1.00 ± 0.245 for lipids. Our study suggests that it might be possible to use fingertip plasma to measure plasma protein and metabolite levels, and will contribute to development of a fingertip blood sampling procedure for measuring blood biomarker levels.

1. Introduction

It is important for humans to maintain good health. In order to achieve this, it is useful to be able to assess people's health status. Health screening is one of the methods used to do this. In health screening, a variety of examinations, including physical (height, body weight, etc.), blood (glucose, triglycerides, cholesterol, etc.), urinary (glucose, protein, etc.), and imaging (X-ray, endoscopy, etc.) examinations, are carried out, and the subject's lifestyle habits (drinking, smoking, etc.) are also investigated. Among these examinations, blood tests are relatively non-invasive and can provide a great deal of health-related information. Blood is usually collected using a standard venous blood sampling protocol, followed by the separation of serum and plasma, except in tests of blood itself, for example the hematocyte test. However, some kits for collecting blood from subjects' fingertips have recently been developed, which can be used to measure the levels of certain molecules, such as glucose and triglycerides [1]. In addition, these kits make it possible for individuals to collect their own blood samples, which reduce the barriers to their usage.

In the medical field, studies involving searches for novel biomarkers that would facilitate the early detection of diseases or the monitoring of various conditions have been performed worldwide. In recent

Abbreviations: LC/MS, liquid chromatography/mass spectrometry; FDR, false discovery rate; LC/QqQMS, liquid chromatography/triple quadrupole mass spectrometry; LC/QTOFMS, liquid chromatography/quadrupole time-of-flight mass spectrometry; SD, standard deviation; LPC, lysophosphatidylcholine

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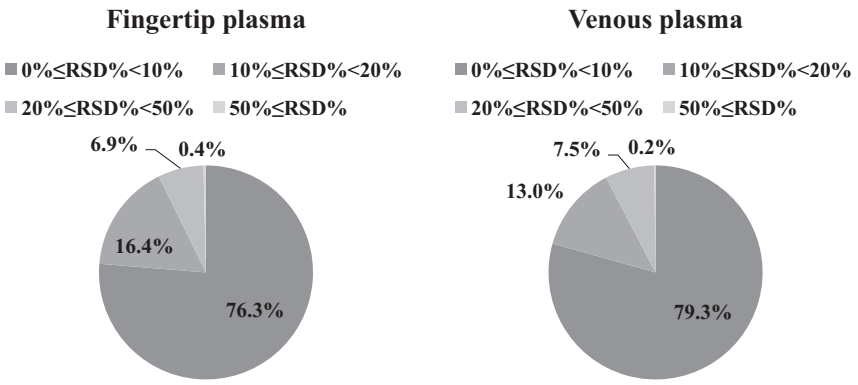

Fig. 1. The analytical stability of the proteins detected in venous or fingertip plasma by an LC/MS-based protein-analyzing platform. The analytical stability of the proteins detected in venous or fingertip plasma by an LC/MS-based protein-analyzing platform was evaluated on the basis of their RSD% values. The percentage (%) values shown on each pie chart represent percentages of all of the proteins detected by the LC/MS-based protein-analyzing platform.

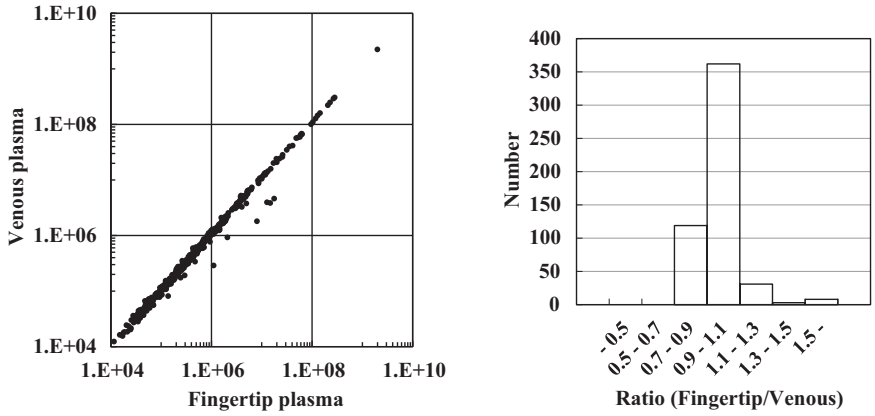

Fig. 2. The correlations between the levels of proteins in venous and fingertip plasma according to an LC/MS-based protein-analyzing platform. The correlation between the proteins levels of venous and fingertip plasma was investigated using an LC/MS-based protein-analyzing platform. A correlation diagram is shown on the left side, and the numbers of proteins in each fingertip:venous ratio category (fingertip:venous: ≤ 0.5, 0.5–0.7, 0.7–0.9, 0.9–1.1, 1.1–1.3, 1.3–1.5, > 1.5) are indicated in the graph on the right side.

Table 1
The List of proteins with the higher and lower ratio (Fingertip/Venous).

Accession No.	Protein Name	Ratio (Fingertip/Venous)
sp|P49908|SEPP1_HUMAN	Selenoprotein P	0.72
sp|A0A075B6S2|KVD29_HUMAN	Immunoglobulin kappa variable 2D-29	0.72
sp|P04196|HRG_HUMAN	Histidine-rich glycoprotein	0.74
sp|Q9NXG0|CNTLN_HUMAN	Centlein	0.75
sp|Q14676|MDC1_HUMAN	Mediator of DNA damage checkpoint protein 1	0.75
sp|P06312|KV401_HUMAN	Immunoglobulin kappa variable 4-1	0.76
sp|Q9BQG0|MBB1A_HUMAN	Myb-binding protein 1A	0.77
sp|Q8NI35|INADL_HUMAN	InaD-like protein	0.79
sp|Q9UIA9|XPO7_HUMAN	Exportin-7	0.79
sp|A0A0B4J1U3|LV136_HUMAN	Immunoglobulin lambda variable 1–36	0.79
sp|A0A0A0MS15|HV349_HUMAN	Immunoglobulin heavy variable 3–49	0.79
sp|P0DOY2|IGLC2_HUMAN	Immunoglobulin lambda constant 2	1.31
sp|O75808|CAN15_HUMAN	Calpain-15	1.40
sp|O95714|HERC2_HUMAN	E3 ubiquitin-protein ligase HERC2	1.41
sp|Q5SZD4|GLYL3_HUMAN	Glycine N-acyltransferase-like protein 3	1.54
sp|P02775|CXCL7_HUMAN	Platelet basic protein	1.70
sp|P02766|TTHY_HUMAN	Transthyretin	2.25
sp|P69905|HBA_HUMAN	Hemoglobin subunit alpha	3.21
sp|P02042|HBD_HUMAN	Hemoglobin subunit delta	3.83
sp|P02008|HBAZ_HUMAN	Hemoglobin subunit zeta	3.83
sp|P68871|HBB_HUMAN	Hemoglobin subunit beta	3.84
sp|P02751|FINC_HUMAN	Fibronectin	4.45

The proteins with the ratio (The value in fingertip plasma/The value in venous plasma) more than 1.3 (higher) and less than 0.8 (lower) were listed in Table 1.

biomarker research, proteomics and metabolomics have been widely utilized as analytical procedures [2–4]. Proteomics (proteome analysis) is one of the omics, and it involves the large-scale study of the proteome, which is the set of proteins produced in an organism or biological material. Metabolomics (metabolome analysis), which is another of the omics, involves the analysis of the metabolome; i.e., the low-molecular-weight metabolites, in an organism or biological material. Previous biomarker studies involving proteomics and/or metabolomics have analyzed the proteomes and metabolomes present in serum/plasma, saliva, urine, feces, or tissues, and a particularly large number of studies have evaluated the proteomes and metabolomes found in serum and plasma. In research based on proteomics and metabolomics, serum/plasma is separated from blood collected using the standard venous blood sampling protocol and then the levels of the target substances are measured. However, there have only been a few reports about the analysis of blood obtained from the fingertip using proteomics and/or metabolomics. Therefore, understanding the proteomic and metabolomic information in fingertip blood would aid the practical use of protein/metabolite blood biomarkers in the future. In this study, the proteomes and metabolomes in venous and fingertip plasma were compared via liquid chromatography/mass spectrometry (LC/MS)-based non-targeted proteomics and metabolomics, respectively.

2. Materials and methods

2.1. Sample collection

The human samples were collected in accordance with the guidelines of Kobe University Hospital. The fingertip plasma samples were collected using the 'KANTAN SAIKETSU SET EIKEN', which is a finger-prick blood sample collection kit (EIKEN CHEMICAL, Tokyo, Japan). Specifically, each subject put a few drops of blood from their fingertip onto the pad contained in the finger-prick blood sample collection kit. The centrifugation machine included with the kit was then used to