News Release

Title

Proteomic Analysis of Lymphoblastoid Cell Lines from Schizophrenic Patients

Key Points

- **There is no objective biomarker for schizophrenia (SCZ) as it is difficult to detect molecular aberrations in the brain.**
- **To explore potential biomarker for SCZ, comprehensive protein expression analysis of lymphoblastoid cell lines (LCLs) was performed, and 22 candidate proteins were identified.**
- **Prediction models for SCZ comprised of 4- and 6-markers were constructed with good discriminative ability.**

Summary

Prof. Kenji Kadomatsu (Dean of Nagoya University Graduate School of Medicine), Prof. Norio Ozaki, Assoc. Prof. Branko Aleksic, Dr. Shohko Kunimoto (Department of Psychiatry), Assoc. Prof. Taku Nagai (Department of Neuropsychopharmacology and Hospital Pharmacy), Prof. Yukihiro Noda, Dr. Akira Yoshimi, Dr. Shinnosuke Yamada (Faculty of Pharmacy, Meijo University), *et al.* have conducted comprehensive protein expression analysis of lymphoblastoid cell lines from schizophrenic patients (SCZ) and control subjects, and identified 22 candidate biomarkers for SCZ. Multivariate logistic regression analysis was performed to identify an optimal combination of biomarkers and prediction models for SCZ comprised of 4- and 6-markers were constructed with good discriminative ability. Molecular function of identified proteins was involved in pathophysiology of SCZ such as neuroinflammation and dysregulation of immune system. Moreover, proinflamatory genes were also up-regulated in animal model of SCZ (poly I:C-treated mice). Differentially expressed proteins might be associated with molecular pathophysiology of SCZ, including dysregulation of immunological reactions and potentially provide diagnostic and prognostic biomarkers.
The results of this research was published online in the international scientific journal "Translational Psychiatry" dated April 22, 2019 (1 a.m. UK time).

Research Background

Although a number of studies have identified several convincing candidate genes or molecules, the pathophysiology of SCZ has not been completely elucidated. Therapeutic optimization based on pathophysiology should be performed as early as possible to improve functional outcomes and prognosis. Therefore, the identification of biomarkers for SCZ which reflect pathophysiology is necessary to provide timely diagnosis and effective therapy.

Research Results

Twenty protein spots were differentially expressed between SCZ and control subjects (CON) in fluorescence two-dimensional differential gel electrophoresis and 22 unique proteins were identified by liquid chromatography tandem-mass spectrometry. Differential expression of 8 proteins was confirmed by Western blotting (WB). Among the 8 candidate proteins (HSPA4L, MX1, GLRX3, UROD, MAPRE1, TBCB, IGHM, and GART), we successfully constructed logistic regression models comprised of 4- and 6-markers with good discriminative ability between SCZ and CON. In both WB and gene expression analysis of LCL, MX1 showed reproducibly significant associations. Moreover, *Mx1* and its related proinflamatory genes (*Mx2*, *Il1b*, and *Tnf*) were also up-regulated in poly I:C-treated mice.

Research Summary and Future Perspective

Differentially expressed proteins might be associated with molecular pathophysiology of SCZ, including dysregulation of immunological reactions and potentially provide diagnostic and prognostic biomarkers. Future follow-up studies, which investigate molecular mechanisms of identified markers, could provide insight into the pathophysiology of SCZ and potentially provide novel molecular targets and diagnostic/prognostic biomarkers.

Publication

Akira Yoshimi, Ph.D.[1,2,3¶], Shinnosuke Yamada, Ph.D.[1,2,¶], Shohko Kunimoto, Ph.D.[3,¶], Branko Aleksic, M.D., Ph.D.[3,*], Akihiro Hirakawa, Ph.D.[4], Mitsuki Ohashi[1], Yurie Matsumoto[1,3], Kazuhiro Hada[2], Norimichi Itoh, Ph.D.[2], Yuko Arioka, Ph.D.[3,5], Hiroki Kimura, M.D., Ph.D.[3,6], Itaru Kushima, M.D., Ph.D.[3,6,7], Yukako Nakamura, Ph.D.[3], Tomoko Shiino, Ph.D.[3,8], Daisuke Mori, Ph.D.[3,9], Satoshi Tanaka, M.D., Ph.D.[6], Shuko Hamada, Ph.D.[3], Yukihiro Noda, Ph.D.[1,2,3], Taku Nagai, Ph.D.[2], Kiyofumi Yamada, Ph.D.[2] and Norio Ozaki, M.D., Ph.D.[3,6]

[1]Division of Clinical Sciences and Neuropsychopharmacology, Faculty and Graduate School of Pharmacy, Meijo University, Nagoya 468-8503, Japan; [2]Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya 466-8550, Japan; [3]Department of Psychiatry, Nagoya University Graduate School of Medicine, Nagoya 466-8550, Japan; [4]Department of Biostatistics and Bioinformatics, Graduate School of Medicine, University of Tokyo, 113-0033, Japan; [5]Center for Advanced Medicine and Clinical Research, Nagoya University Hospital, Nagoya 466-8550, Japan; [6]Department of Psychiatry, Nagoya University Hospital, Nagoya 466-8550, Japan; [7]Institute for Advanced Research, Nagoya University, Nagoya 464-8601, Japan; [8]Department of Pathology of Mental Diseases, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo 187-8553, Japan

[9]Brain and Mind Research Center, Nagoya University, Nagoya 466-8550, Japan

[¶]These authors contributed equally to this work.

Translational Psychiatry
April 22, 2019 (1 a.m. UK time)

DOI: https://doi.org/10.1038/s41398-019-0461-2

Japanese ver.
https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Tran_Psy_20190419.pdf