Symposium | Schizophrenia：[Symposium 56] Current status of psychiatric research using genetic medicine and genomic medicineImportance of collaborative research among East Asians

Sat. Sep 27, 2025 9:00 AM - 10:30 AM JST | Sat. Sep 27, 2025 12:00 AM - 1:30 AM UTC Session Room 3 (Large Hall A)

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Moderator: Nakao Iwata (Fujita Health University School of Medicine), Hailiang Huang (The Broad Institute of MIT and Harvard)

[SY-56]

Current status of psychiatric research using genetic medicine and genomic medicine Importance of collaborative research among East Asians

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[SY-56-01]

Pharmacogenomic Research on Antipsychotic Therapy in Chinese Han Population

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[SY-56-02]

Multimodal Genomic and Mobile Sensing Reveals Genetic and Behavioral Signatures in Mood Disorder Phenotypes

*Po-Hsiu Kuo[1,5,8], Chiao-Erh Chang[1], Ting-Yi Lee[1], Shiau-Shian Huang[2,3], Ying-Ting Chao[1,4], Hsi-Chung Chen[5], Ming-Chyi Huang[6], I-Ming Chen[5], Chuhsing Kate Hsiao[1,7] (1. Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University (Taiwan), 2. Department of Psychiatry, Taipei Veterans General Hospital (Taiwan), 3. College of Medicine, National Yang Ming Chiao Tung University (Taiwan), 4. Department of Medical Research, National Taiwan University (Taiwan), 5. Department of Psychiatry, National Taiwan University Hospital (Taiwan), 6. Department of Psychiatry, Taipei City Psychiatric Center, Taipei City Hospital (Taiwan), 7. Institute of Health Data Analytics and Statistics, College of Public Health, National Taiwan University (Taiwan), 8. Psychiatric Research Center, Wan Fang Hospital (Taiwan))

[SY-56-03]

Contribution of common and rare variants to schizophrenia risk in East and South Asian ancestries

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Keywords：genetics and epidemiology、pharmaogenetics、schizophtenia、bipolar disorder

Despite various efforts to elucidate the biological pathogenesis of major mental disorders, much remains unclear at present. No clear biomarkers have been identified, and since the disease entity is the brain, which is extremely difficult to access in vivo, current medical science approaches cannot easily elucidate the pathogenesis.
Genetic factors in major mental disorders such as schizophrenia and bipolar disorder have been observed for a long time. If Mendel's laws are true, clues to the pathogenesis of mental disorders are certainly recorded in genetic information.
Recent advances in genomic medicine research, particularly the development and low-cost availability of whole-genome sequencing technology and the advancement of computer technology enabling rapid analysis of large amounts of data, have yielded significant results in genomic medicine research.
In schizophrenia and bipolar disorder, hundreds of associated gene loci and genes have been identified. By combining various analytical techniques with image and multiomics analysis data, findings that shed light on the pathogenesis of these disorders based on genomic information are gradually accumulating.
In this symposium, we will introduce and discuss the latest findings in genetic epidemiology, genomic medicine, and pharmacogenetics aimed at elucidating the pathophysiology of mental disorders, based on collaborative research across Japan, China, Taiwan, and various other ethnic groups around the world.

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[SY-56-01] Pharmacogenomic Research on Antipsychotic Therapy in Chinese Han Population

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Keywords：Schizophrenia、Pharmacogenomics、Antipsychotics

Schizophrenia (SCZ) is one of the most complex diseases with high heterogeneity in mechanism or clinical phenotype. Without any specific or effective biomarkers, this is a very difficult issue for the clinicians to solve the key clinical issues about subjective diagnosis, or experiential therapy of schizophrenia. The strategy of genetics has been proven to be effective and helpful to explore the mechanism of schizophrenia and the molecular basis of antipsychotic medications. The speaker has been committed to finding the susceptibility genes of schizophrenia in Chinese Han population. The major topic are as follows: 1) Using the genome-wide association study (GWAS) and meta-analysis, her group has found several novel susceptible loci of schizophrenia. Combined clues of bioinformatics data and functional experiments, they further explored the potential function of the novel susceptible genes. 2) Using the multi-omics approaches, they found there were very important interactive effects on genetic polymorphisms or variants, on transcriptional levels or neuroimaging characters in schizophrenia patients. 3) With a relatively large sample size of pharmacogenomics, her group reported several susceptible genes associated with individual differences in therapeutic or side effects of common antipsychotic medicines. Based on the genetic, clinical-environmental, brain structure or function, molecular pathway, her group explored the potential objective biomarkers for diagnosis and biotypes with clinical implications of efficacy prediction for schizophrenia.

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[SY-56-02] Multimodal Genomic and Mobile Sensing Reveals Genetic and Behavioral Signatures in Mood Disorder Phenotypes

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Keywords：antidepressant induce mania、unipolar mania、digital phenotyping

Mood disorders span diverse phenotypes. We integrate genome-wide analyses and digital phenotyping to clarify how inherited risk and real-world mobility inform mood disorder classification and prediction. Among 772 Han Chinese patients with unipolar depression, 145 (19.7%) developed antidepressant-induced mania (AIM) within 28 days of antidepressant exposure or discontinuation. Genome-wide testing identified eight suggestive SNPs, and higher bipolar polygenic risk scores significantly predicted AIM (OR $\approx$ 1.25, $p < .05$). Clinical risk factors included female sex, postpartum depression, OCD, severe episodes, substance use, and psychoses. Additionally, bipolar patient with unipolar mania (UM) were compared to 1,041 with depressive-manic (D-M) presentations. A genome-wide locus (rs149251101, *THSD7A*) differentiated UM from D-M cases ($p = 5.3 \times 10^{-8)}$. PRS for bipolar disorder, major depression, and suicide attempt were positively associated with UM, while insomnia liability was inversely linked. Lastly, in two smartphone cohorts (n=107), passive GPS and mood data over six months revealed over 10,000 person-days. Homestay predicted next-day fatigue, depressed mood, and irritability; higher location variance predicted lower depression. Depressive symptoms, in turn, predicted reduced mobility. Spectral and diurnal analyses identified mood-linked movement cycles and evening mobility declines as digital markers of depression. These multimodal approaches reveal overlapping genetic and behavioral markers in mood disorders, enabling future personalized, movement-informed interventions.

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[SY-56-03] Contribution of common and rare variants to schizophrenia risk in East and South Asian ancestries

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Keywords：Schizophrenia、Genetics、Sequencing

Schizophrenia genetic studies have primarily focused on European ancestries, leaving variants in other populations underexplored and potentially increasing health disparities. Here, we report initial findings from the first large-scale schizophrenia sequencing study examining both common and rare variants in East and South Asian populations (EAS and SAS), using the Blended Genome Exome (BGE), a technology combining low-pass whole-genome and deep whole-exome sequencing.

We ascertained 98,739 East Asian (cases: 45,925, controls: 52,814) and 17,697 South Asian individuals (cases: 8,843, controls: 8,854), and conducted genotyping, WES, and BGE. We also incorporated European (EUR) cohorts (cases: 53,386, controls: 77,258), achieving a total sample size of 247,080. In GWAS, we identified 41 schizophrenia-associated loci in EAS—a 5x increase over the largest previous EAS study. In SAS, we found 7 genome-wide significant loci, marking the first large-scale GWAS in this population. We observed high genetic correlations across the three populations: 0.86-1.08. A multi-ancestry meta-analysis across EUR, EAS, and SAS revealed 461 loci significantly associated with schizophrenia, 131 of which are novel, with SNP-based heritability of 23%.

For RVAS, we identified 12 exome-wide significant genes (29 at FDR 5%), including four novel genes. Schizophrenia RVAS signals were significantly enriched in schizophrenia GWAS loci compared to loci for a non-psychiatric trait. By integrating both common and rare variants, we prioritized genes strongly associated with schizophrenia, such as SCAF1, FYN, and KLC1.

This study provides, for the first time, insights into the genetic architecture in the SAS population and the integrative contribution of both common and rare variants to schizophrenia in three major populations. These novel findings will enable future investigations and uncover the pathogenesis of schizophrenia, ultimately contributing to the reduction of its disease across ancestries.