



MEDIA RELEASE

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New Study Reveals Immune System Changes Linked to Schizophrenia and Treatment Resistance

1. Researchers from the National Healthcare Group (NHG)'s Institute of Mental Health (IMH) and Agency for Science, Technology and Research (A*STAR) have made strides in understanding the connection between the immune system and resistance to antipsychotic medications in schizophrenia, using changes in immune cell populations to predict potential treatment resistance and initiate the most appropriate treatment sooner. Their paper, "Immunophenotyping schizophrenia subtypes stratified by antipsychotic response", published in leading psychoneuroimmunology journal *Brain, Behaviour and Immunity*¹ adds to a growing body of research suggesting that immune system dysregulation may underlie the development of the mental disorder. The study was supported by the Singapore Ministry of Health through the National Medical Research Council (NMRC) Office, MOH Holdings Pte Ltd under the NMRC Clinician Scientist Award (MOH-000013).
2. The exact cause of schizophrenia — a psychotic disorder affecting around 24 million people worldwide² and 1 in 116 individuals in Singapore³ — remains unclear even today. While imbalances in dopamine levels in the brain are commonly observed in people with schizophrenia, not all patients with schizophrenia respond to standard antipsychotic drugs that target the dopamine pathway. In recent years, scientific studies on changes in the immune system and their association with the development of mental health conditions have emerged as a promising area of research.
3. Globally, around 30% of individuals diagnosed with schizophrenia are treatment-resistant. This means they do not achieve remission of symptoms, such as hallucinations and delusions, despite treatment. This debilitating condition affects both individuals (who also experience difficulties with their cognitive or thinking skills and have higher risks of poor health and poor quality of life), and their families in terms of caregiving burden. Currently, clozapine is the only psychiatric medicine indicated for treating treatment-resistant schizophrenia.
4. "With this study, we aimed to explore the relationship between the immune system, schizophrenia and treatment resistance. Our goal was to identify immune cell changes that could potentially be used to predict treatment resistance, allowing for earlier and more targeted interventions such as initiating clozapine treatment sooner for better clinical outcomes. A better understanding of how the immune system is involved can also help in developing immune-targeted therapies as additional treatment options for schizophrenia in future," said Dr Li Yanhui, NHG Psychiatry Resident at IMH, and lead author of the paper.
5. In this study, blood samples of 196 healthy participants and individuals with schizophrenia with varying degrees of treatment resistance were collected. Proportions of different immune cell types were compared across these groups, to identify possible biomarkers (markers that are

¹ <https://www.sciencedirect.com/science/article/pii/S0889159124006603#s0155>

² World Health Organization

³ Singapore Mental Health Study 2016

associated with and may predict) for schizophrenia or treatment resistance. The researchers identified and compared 66 immune cell populations in the blood of 147 people with schizophrenia and 49 healthy individuals to explore the immune cell populations associated with the disorder and treatment resistance. They found significant differences in certain immune cell populations between healthy individuals and people with schizophrenia.

6. Furthermore, those changes in immune cell populations also correlate with how resistant a patient with schizophrenia might be to treatment. Specifically, the researchers found that the ratio of CD4 to CD8 T cells was much higher, while the levels of mucosal-associated invariant T (MAIT) cells were much lower in individuals with schizophrenia, especially in those with greater treatment resistance. Hence, the CD4/CD8 ratio has emerged as a potential biomarker to predict how well someone with schizophrenia might respond to treatment; whereas for MAIT cells, which are predominantly found in the gut where they contribute to immune defence and are closely linked to autoimmune processes, their lower numbers may signify immune dysregulation in schizophrenia.
7. “The findings support the role of immune dysregulation in schizophrenia and in treatment resistance. It is also pertinent in making headway in precision medicine, with the potential to utilise certain immune markers as predictors of future treatment resistance. This offers hope in early identification of patients likely to be treatment-resistant, and guides clinicians in selecting more effective treatment strategies to achieve better outcomes,” said Associate Professor Jimmy Lee, Senior Consultant with the Department of Psychosis, IMH, who led the study.
8. “The complexity of schizophrenia and how variably it manifests in each individual make it a difficult disorder to diagnose, much less to administer the most suitable treatment on time. Through our collaborative efforts with IMH, we were able to bridge scientific methodologies with clinical practice, bringing to light immunological findings that may enable more decisive treatment applications to better meet patient needs and alleviate their burdens,” said Dr Anand Kumar Andiappan, Principal Investigator, A*STAR Singapore Immunology Network (A*STAR SigN), who co-led the study with Assoc Prof Lee.

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About the Institute of Mental Health (IMH)

The Institute of Mental Health (IMH), a member of the National Healthcare Group, is the only tertiary psychiatric care institution in Singapore. Located on the sprawling 23-hectare campus of Buangkok Green Medical Park in the north-eastern part of Singapore, IMH offers a multidisciplinary and comprehensive range of psychiatric, rehabilitative and therapy services in hospital-based and community-based settings. The 2,000-bedded hospital aims to meet the needs of three groups of patients – children and adolescents (aged below 19 years), adults and the elderly. Besides providing clinical services, IMH dedicates resources to carry out mental health promotion and raise mental health literacy. IMH also leads in mental health research and training the next generation of mental health professionals in Singapore. For more information, please visit www.imh.com.sg.

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English-Chinese Glossary

Institute of Mental Health (IMH)	心理卫生学院
National Healthcare Group (NHG)	国立健保集团
Agency for Science, Technology and Research (A*STAR)	新加坡科技研究局
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Dr Anand Kumar Andiappan Principal Investigator, A*STAR Singapore Immunology Network (A*STAR SIgN)	(No Chinese Translation) 首席研究员 新加坡免疫学组