MicroRNA-137 in Schizophrenia: A Bioinformatics-Based Marker for Early Detection

Ansh Yadawad

Abstract

Schizophrenia is a serious mental health disorder that affects thinking, emotions, and behavior, but it is often diagnosed only after symptoms appear. Bioinformatics offers a way to find genetic biomarkers that could improve early detection. In this research paper, the National Human Genome Research Institute–European Bioinformatics Institute Genome-Wide Association Studies Catalog (NHGRI–EBI GWAS Catalog) was searched using the term “schizophrenia”. The catalog collates the results of genome-wide association studies, which identify genetic variants contributing to diseases by comparing the DNA of those affected with specific conditions against the DNA of the general population. From this search, three of the most frequently reported genes were found: CACNA1C, GRIN2A, and MIR137HG (miR-137), which appear much more often in schizophrenia studies than in studies of other traits. CACNA1C and GRIN2A are important because they affect specific brain pathways, such as calcium channel function and glutamate signaling. MiR-137 is different because it does not code for a protein but instead regulates hundreds of other genes, including CACNA1C and GRIN2A. This wider influence connects miR-137 to processes such as neuronal growth, learning, and memory which are all areas disrupted in schizophrenia. These findings highlight miR-137 as a promising biomarker candidate and show how bioinformatics can turn large genetic datasets into insights for earlier and more precise mental health care.

Keywords: schizophrenia; miR-137; bioinformatics; genome-wide association studies; GWAS; CACNA1C; GRIN2A; genetic biomarkers; early detection

Introduction

Schizophrenia affects about 24 million people worldwide[1], or roughly 1 in every 100 adults, making it one of the most common and severe mental health disorders. Common symptoms include hallucinations, delusions, memory difficulties, and impaired concentration[2]. The disorder typically begins in late adolescence or early adulthood, a critical period when the brain is still maturing[3]. Although early treatment can greatly improve long-term outcomes[345], detecting schizophrenia before full symptoms appear remains difficult. Early warning signs, such as sleep changes or academic decline, are often dismissed as normal teenage stress. By the time symptoms become clear, significant brain changes may already have occurred[4].

To overcome the difficulty of diagnosing schizophrenia before major symptoms appear, researchers are increasingly turning to bioinformatics. This field makes it possible to analyze

huge amounts of genetic data and find patterns that would be impossible to see by hand. For example, bioinformatics can link DNA changes to diseases, predict how proteins behave, or connect patient health records with genetic information. In this project, I used bioinformatics tools to search the NHGRI-EBI GWAS Catalog for the term “schizophrenia” and then looked at which genes showed up the most across different studies. Bioinformatics can scan thousands of genetic variations at once and reveal subtle patterns associated with disease[6].

Scientists are focusing on using bioinformatics to identify biomarkers, which are measurable signals in the body that can reveal the presence or likelihood of disease. Biomarkers can appear in many forms, such as molecular signals, protein patterns, or imaging features in the brain[7]. In other neurological disorders, such as Alzheimer’s disease and Parkinson’s disease, biomarkers have already proven useful for early detection and monitoring. For instance, abnormal proteins found in spinal fluid and specialized brain scans can identify Alzheimer’s disease years before severe memory loss occurs[7].

Bioinformatics offers new ways to identify genetic markers of schizophrenia. Instead of focusing on a single mutation, it allows scientists to scan across thousands of variations and reveal patterns that repeat across populations[68]. Among these genetic markers, miR-137 stands out because it regulates many different genes at once, especially in the hippocampus and prefrontal cortex, which are two regions strongly affected in schizophrenia[9]. Recognizing these repeated signals lays the foundation for examining how genetic markers, including miR-137, CACNA1C, and GRIN2A, contribute to the disorder.

Recognizing these repeated genetic signals will provide a good basis on which to explore how bioinformatics may study genes that increase the risk of schizophrenia. For this reason, a basic bioinformatics-based search was performed using a publicly available genetic database to identify which genes were most frequently reported in studies related to schizophrenia.

Methods

This study used public genetic data to investigate the most commonly mentioned genes in schizophrenia. I have used the openly available online database NHGRI-EBI GWAS Catalog, which represents a large online collection of results from multiple genetic studies performed worldwide.

I searched with the keyword “schizophrenia” on September 7, 2025, using the GWAS Catalog. It produced a list of genes that showed strong and repeated links to the disorder across many studies. I have looked at the reporting frequency related to the instances of each gene across different studies to identify genes more consistently reported in relation to schizophrenia.From that search came the following: MIR137HG (miR-137), CACNA1C, and GRIN2A, highlighted by 63, 125, and 75 studies, respectively. These numbers do not indicate

the strength of association of the individual gene with schizophrenia but rather the frequency of appearance in the literatures on schizophrenia.

By knowing what these top genes do in the brain through scientific papers from databases like PubMed and Nature, I read how they affect important brain pathways in schizophrenia-like calcium signaling by CACNA1C, glutamate receptor function by GRIN2A, and gene regulation by miR-137, and why those processes matter for schizophrenia.

Such work is called a bioinformatics-based analysis, where instead of laboratory experiments, already available data on genetics and published research are used. It shows how large-scale databases can be utilized for the elucidation of patterns in genetics that would eventually help science understand such a complex mental health disorder like schizophrenia.

Results

To explore genetic markers linked to schizophrenia, I searched the NHGRI-EBI GWAS Catalog using the “schizophrenia” filter. From this search, three genes stood out as the most consistently reported in the literature: MIR137HG (miR-137), CACNA1C, and GRIN2A (Figure 1). These genes appear most often across independent studies, making them top candidates for comparison.

In this study, MIR137HG (miR-137) appeared in 63 studies, CACNA1C in 125, and GRIN2A in 75 (Figure 1).

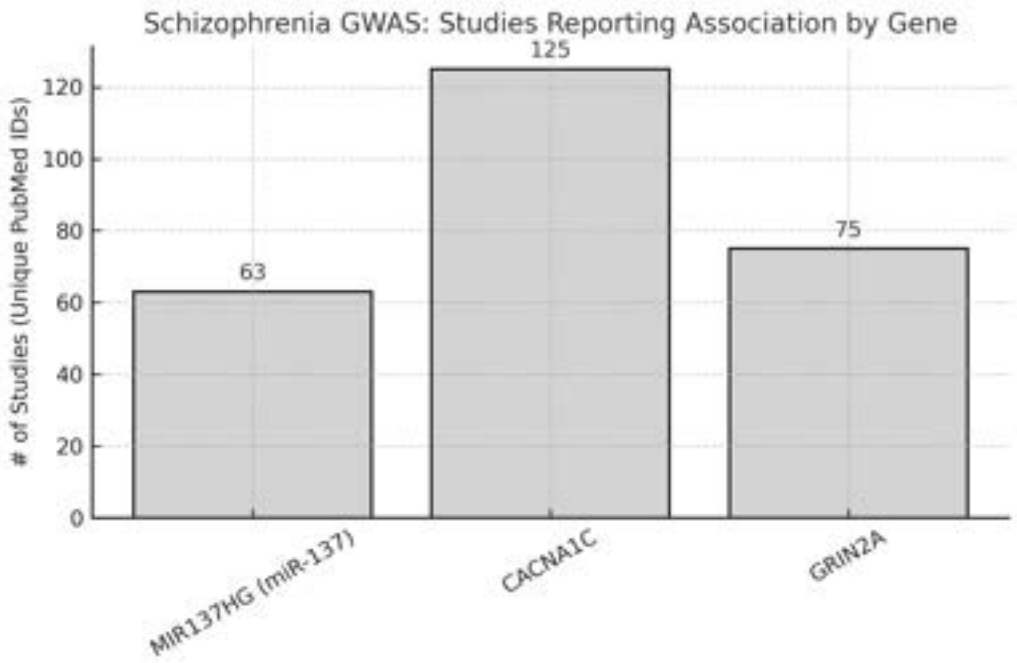

Figure 1 *Number of PubMed-indexed schizophrenia studies linked to MIR137HG (miR-137), CACNA1C, and GRIN2A in the NHGRI-EBI GWAS Catalog (data accessed September 7, 2025). While CACNA1C and GRIN2A were reported more often overall, miR-137 consistently appeared across studies, supporting its role as a broad regulatory signal in schizophrenia*

These counts represent reporting frequency rather than effect size, but they highlight replicated, polygenic risk across multiple genes. While CACNA1C and GRIN2A appear more often overall, miR-137 consistently recurs across studies, supporting its role as a regulatory signal worth deeper investigation.

Discussion

What Are MicroRNAs (miRNAs)

Before focusing on microRNAs, it is helpful to briefly introduce two genes that are often mentioned alongside miR-137 in schizophrenia research. **GRIN2A** is a gene that helps form part of the NMDA glutamate receptor, which is important for learning, memory, and communication between brain cells. Research has shown that changes in GRIN2A can affect how brain cells send signals to one another, a problem commonly seen in schizophrenia. **CACNA1C** is a gene involved in calcium channels, which help control electrical signaling in neurons. Calcium signaling plays an important role in normal brain development and communication between neurons, and disruptions in this process have also been linked to schizophrenia. Because both GRIN2A and CACNA1C are involved in key brain signaling pathways, they are often studied together when researchers investigate the genetic causes of schizophrenia.

MicroRNAs (miRNAs) are small molecules made of RNA. They do not code for proteins themselves but act like “switches” that control whether other genes are turned on or off. Normally, DNA is copied into messenger RNA (mRNA), which is then used to make proteins that carry out cell functions. mRNAs, such as miR-137, can interfere with this process by binding to RNA and blocking protein translation.

This fine-tuning of miR-137 matters most in brain cells, where miR-137 helps neurons grow and communicate. It does this by regulating proteins that are especially important for brain activity. For example, miR-137 can influence N-methyl-D-aspartate (NMDA) receptor genes like GRIN2A, which are needed for learning and memory, and calcium channel genes like CACNA1C, which help brain cells send electrical signals. Because miR-137 helps control both of these major schizophrenia-related genes, it acts like a key coordinator that keeps different brain systems in balance. When this regulation does not work properly, brain signaling can become less efficient, which may affect how information is processed and remembered.

Researchers think the connection between miR-137, GRIN2A, and CACNA1C might explain why changes in miR-137 can have such big effects throughout the brain[89]. Instead of

controlling just one process, miR-137 influences several at the same time, similar to a conductor who keeps different sections of an orchestra in sync. During the teenage and young-adult years, the brain is still wiring and strengthening its networks, so this coordination becomes even more important. If miR-137 fails to properly regulate these target genes, disruptions may occur in synaptic signaling and neuronal development pathways, potentially increasing vulnerability to schizophrenia[89].

Functions of miR-137 Beyond Schizophrenia

Even though miR-137 is often discussed in connection with schizophrenia, it also has many important roles in the healthy brain. One of its main jobs is to guide how neurons grow, make branches (called dendrites), and form strong connections with each other. These connections are what allow us to learn new things, store memories, and make decisions[9]. Because miR-137 helps regulate how cells grow and repair themselves, researchers are also studying its role in areas such as cancer biology and nerve regeneration[3]. There is also evidence that miR-137 may be involved in other brain-related conditions, including Alzheimer's disease and autism spectrum disorders, although this research is still in early stages[7].

Looking at miR-137 in both healthy development and in different diseases shows why it is such a powerful regulator in the brain. Understanding its wide-ranging effects makes it an even stronger candidate for research, since it links everyday brain functions, such as memory and learning, to more complex disorders. These broader roles also explain why changes in miR-137 may have wide effects in disorders like schizophrenia.

Common Presentations of Schizophrenia

Schizophrenia involves a mix of changes in thinking, emotions, and behavior. People with this condition may experience hallucinations, such as hearing voices or seeing things that are not there, and delusions, which are strong beliefs not based in reality. They might also struggle to organize their thoughts, focus on tasks, or speak clearly and logically[2]. Some people show less emotion or lose motivation, making everyday activities like studying or socializing harder. Because these changes affect memory, focus, and emotions, they are closely tied to brain regions such as the hippocampus and prefrontal cortex, where miR-137 activity is especially high[2]. These symptoms usually appear during the late teenage or early adult years, when the brain is still developing important connections[3]. Early signs can sometimes be subtle, such as a drop in school performance, withdrawal from friends, or sleep problems, before more obvious symptoms appear.

MiR-137 and Its Role in Schizophrenia

Because the symptoms of schizophrenia are closely linked to disruptions in brain regions involved in memory, attention, and emotional regulation, researchers study genes such as

miR-137 to better understand the biological processes that may contribute to the disorder[29]. The hippocampus and prefrontal cortex are two brain regions that are strongly affected in schizophrenia and are frequently discussed in research because they help explain many of the cognitive and emotional symptoms of the condition[23]. The hippocampus plays an important role in memory formation and learning, while the prefrontal cortex is responsible for decision-making, attention, emotional regulation, and planning.

When these brain regions do not develop or function properly, individuals may experience memory difficulties, problems organizing thoughts, poor concentration, difficulty making decisions, and emotional changes that are commonly observed in schizophrenia[2]. Disruptions in these areas may also contribute to hallucinations and delusions, as the brain struggles to correctly process and organize information[2]. Since miR-137 is highly active in both the hippocampus and prefrontal cortex, changes in how it regulates gene expression may interfere with normal brain development, particularly during adolescence and early adulthood, when these regions are still maturing[9].

There are several pathways that are regulated by miR-137 that have also been linked to schizophrenia. miR-137 influences genes that guide how neurons grow and form new connections[9]. miR-137 has also been linked to synaptic plasticity through the regulation of NMDA receptor subunits such as GRIN2A, which are critical for learning and memory[9]. Disruptions in NMDA signaling are a well-known feature of schizophrenia[8]. Lastly, miR-137 also affects calcium channel proteins like CACNA1C, which help neurons send electrical signals[9]. Abnormal calcium signaling has been repeatedly observed in schizophrenia patients[8].

By regulating these key pathways, miR-137 connects directly to biological processes that are already known to be dysregulated in schizophrenia. This overlap makes it more than just a “marker” that appears in genetic studies, which suggests that miR-137 could actively shape the brain changes that contribute to the disorder[89].

Bioinformatics

Bioinformatics has transformed how scientists study and detect diseases. In cancer research, computer analysis of tumor genomes helps identify mutations that guide personalized treatments[6]. In Alzheimer’s and Parkinson’s disease, bioinformatics tools are used to find protein markers in spinal fluid and track brain imaging changes, which can signal disease years before major symptoms appear[7]. In infectious diseases, scientists use bioinformatics to sequence viral or bacterial genomes, track outbreaks, and design vaccines faster[7]. These examples show how bioinformatics speeds up discovery, reduces costs, and provides insights that traditional lab methods alone would struggle to achieve.

These successes show the power of bioinformatics, but its role in psychiatry is especially important, since mental health conditions often lack clear physical markers. This project applies those same approaches to schizophrenia, using bioinformatics to highlight genetic signals like miR-137.

Bioinformatics in Schizophrenia

In psychiatric genetics, bioinformatics is especially important because schizophrenia involves hundreds of small genetic changes rather than a single mutation[68]. Large databases like the GWAS Catalog collect results from genome-wide association studies, which compare DNA differences between people with and without the disorder. By pooling results from many studies, researchers can identify consistent genetic markers, including miR-137, CACNA1C, and GRIN2A[8]. Scientists often use tools like R, Python, and BLAST (Basic Local Alignment Search Tool) to scan these datasets, compare DNA, and look for patterns in brain pathways.

Looking ahead, bioinformatics could help doctors recognize schizophrenia risk earlier by identifying genetic markers before symptoms appear[10]. It may also guide personalized medicine, where treatment is chosen based on a patient's genetic profile, improving efficacy and reducing side effects. For example, genetic testing could one day help predict which medications work best for a patient, reducing the trial-and-error process in psychiatry[6]. Genome-wide association studies (GWAS) look at the DNA of very large groups of people to find genetic differences that appear more often in individuals with schizophrenia than in those without the disorder. These studies examine hundreds of thousands to millions of genetic markers across the genome and use statistical methods to detect small but repeated differences between groups. Because each individual genetic variant usually has only a small effect, researchers depend on large sample sizes and results that are repeated across multiple studies to be confident in their findings. The NHGRI-EBI GWAS Catalog collects and organizes these results from many independent studies, making it easier to identify genes that consistently appear in schizophrenia research. Using this approach, large international studies have repeatedly identified miR-137 (MIR137HG), CACNA1C, and GRIN2A as genes associated with schizophrenia, highlighting their contribution to the disorder's polygenic risk[68].

Genetic Markers Beyond MiR-137

MiR-137 appears in many schizophrenia studies and plays an important regulatory role, but it is part of a broader network of genetic factors that contribute to schizophrenia risk. Large genome-wide association studies conducted by the Psychiatric Genomics Consortium identified 108 schizophrenia-associated genetic loci, demonstrating that risk is spread across many regions of the genome rather than concentrated in a single gene[8]. Many of these genes are involved in how brain cells send signals, form connections, and interact with the immune system. Research shows that schizophrenia is not caused by a

single mutation, but instead by many small genetic changes that add up over time. Many of these genes are involved in how brain cells send signals, form connections, and interact with the immune system.

To explore genetic markers linked to schizophrenia, I searched the NHGRI-EBI GWAS Catalog using the “schizophrenia” filter. From this search, three genes stood out as the most consistently reported in the literature: **MIR137HG (miR-137), CACNA1C, and GRIN2A** (Figure 1). These genes appear most often across independent studies, making them top candidates for comparison. CACNA1C is important for calcium channel function in neurons, and GRIN2A plays a role in the glutamate signaling system, both of which are pathways closely tied to brain activity and schizophrenia risk[8].

In this study, MIR137HG (miR-137) appeared in 63 studies, CACNA1C in 125, and GRIN2A in 75 (Figure 1). These counts represent reporting frequency rather than effect size, but they highlight replicated, polygenic risk across multiple genes. While CACNA1C and GRIN2A appear more often overall, miR-137 consistently recurs across studies, supporting its role as a regulatory signal worth deeper investigation.

What makes miR-137 stand out compared to CACNA1C and GRIN2A is the way it controls other genes. Both CACNA1C and GRIN2A affect very specific brain functions. miR-137 is different because it does not make a protein at all; instead, it works more like a “master switch” that can fine-tune hundreds of other genes at once. Some of the genes it regulates are directly connected to brain growth and communication, including CACNA1C and GRIN2A themselves[68]. As miR-137 is upstream of these pathways, helping to decide how strongly they function during brain development. A single change in miR-137 can ripple across many systems at once, while CACNA1C and GRIN2A mainly act in one pathway each. That broader reach may explain why, even though miR-137 shows up in fewer studies than CACNA1C, it is still one of the most important genetic signals linked to schizophrenia risk.

Implications for Treatment Strategies

Using bioinformatics and genetic testing in medical practice could improve how schizophrenia risk is identified and managed. At present, schizophrenia is mainly diagnosed through behavioral symptoms, which often appear after changes in the brain have already begun. Research suggests that genetic markers may help identify individuals who are at higher risk earlier in life, before symptoms become severe[8 12]. Instead of replacing traditional diagnosis, genetic markers could support earlier monitoring and intervention when combined with clinical observations.

The genes discussed in this paper, miR-137, CACNA1C, and GRIN2A, are especially relevant because they are linked to important brain pathways involved in schizophrenia.

CACNA1C plays a role in calcium signaling, which affects how neurons communicate, while GRIN2A is involved in NMDA and glutamate signaling, which are important for learning and memory. miR-137 is particularly important because it helps regulate many genes related to brain development and synaptic function, including genes associated with schizophrenia risk. Because miR-137 influences multiple pathways, it may serve as a useful biomarker for identifying individuals who could benefit from closer monitoring or early support (Figure 2).

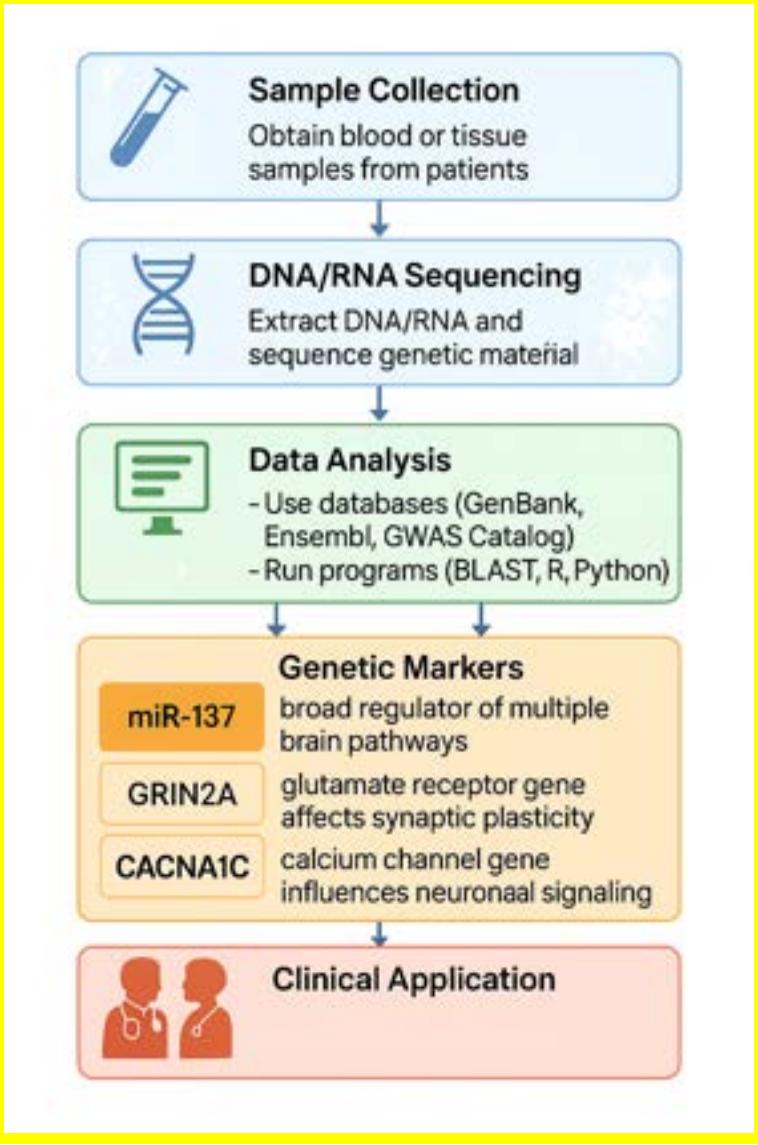

Figure 2. *How bioinformatics and genetic testing could be integrated into medical practice for schizophrenia. Genetic data from patients are analyzed through bioinformatics pipelines to*

identify biomarkers such as miR-137, CACNA1C, and GRIN2A. Results could help clinicians predict risk and personalize treatments.

If validated through repeated studies, a genetic panel including miR-137, CACNA1C, and GRIN2A could help clinicians better understand individual risk and tailor early intervention strategies[5 10].

Despite this potential, several challenges must be addressed before these biomarkers can be used routinely in clinical settings. Genetic testing can be expensive and is not equally available to all patients. In addition, schizophrenia risk is influenced by many genes, meaning that no single gene can be used as a diagnostic tool on its own. Privacy is also an important concern, since genetic information related to mental health may be sensitive and could be misunderstood or misused if not properly protected[11]. Larger and more diverse studies are still needed to confirm how reliably miR-137, CACNA1C, and GRIN2A predict schizophrenia risk and whether their use leads to better clinical outcomes[13]. Ethical guidelines and regulatory approval will also be necessary, especially if screening is considered for adolescents[10 14]. If these challenges are addressed, biomarker-informed screening could help psychiatry focus more on early intervention and prevention, reducing the impact of schizophrenia on education, work, and daily life.

Conclusion

This study used data from the NHGRI-EBI GWAS Catalog to identify genetic markers that have been repeatedly associated with schizophrenia. Through comparison of reported associations, miR-137 (MIR137HG), CACNA1C, and GRIN2A emerged as key genes of interest, with miR-137 standing out due to its regulatory role across multiple schizophrenia-related pathways. These findings support the idea that examining regulatory molecules alongside protein-coding genes can provide a broader view of genetic risk.

The significance of this study lies in showing how existing bioinformatics resources can be used to explore complex psychiatric disorders without generating new genetic data. By focusing on frequently reported GWAS associations, this project highlights miR-137 as a potential upstream biomarker that may help connect different biological pathways involved in schizophrenia. This approach supports ongoing efforts to move toward earlier risk identification and more personalized mental health care.

A major strength of this study is its use of a large, well-curated public database that integrates findings from many independent genetic studies, increasing the reliability of the identified associations. However, the study also has limitations. GWAS data show correlations rather than direct causes, and schizophrenia risk is influenced by many genes as well as

environmental factors. In addition, this analysis did not examine gene expression levels or clinical outcomes, which limits how directly the findings can be applied to patient care.

Future research could build on this work by combining GWAS data with gene expression studies, functional experiments, or clinical data to better understand how miR-137, CACNA1C, and GRIN2A influence disease development. Further studies could also explore how these markers interact with environmental risk factors and whether they can help guide early monitoring or intervention strategies. Together, these steps would help clarify the role of genetic biomarkers in improving early detection and treatment of schizophrenia.

References

1. World Health Organization. Schizophrenia. https://www.who.int/news-room/fact-sheets/detail/schizophrenia, 2023.
2. M. J. Owen, A. Sawa, P. B. Mortensen. Schizophrenia. The Lancet. Vol. 388, pg. 86–97, 2016, https://doi.org/10.1016/S0140-6736(15)01121-6.
3. R. Birnbaum, D. R. Weinberger. Genetic insights into the neurodevelopmental origins of schizophrenia. Nature Reviews Neuroscience. Vol. 18, pg. 727–740, 2017, https://doi.org/10.1038/nrn.2017.125.
4. J. A. Lieberman, S. Stroup, D. Perkins. Early intervention in psychosis: A review. American Journal of Psychiatry. Vol. 177, pg. 1–10, 2020, https://doi.org/10.1176/appi.ajp.2020.20020147.
5. P. D. McGorry, A. R. Yung. Early intervention in psychosis: An overview. Australian & New Zealand Journal of Psychiatry. Vol. 46, pg. 607–616, 2012, https://doi.org/10.1177/0004867412435327.
6. P. F. Sullivan, M. J. Daly, M. O'Donovan. Genetic architectures of psychiatric disorders: The emerging picture and its implications. Nature Reviews Genetics. Vol. 13, pg. 537–551, 2012, https://doi.org/10.1038/nrg3240.
7. S. Singh, S. K. Gupta, P. K. Seth. Biomarkers for detection, prognosis and therapeutic assessment of neurological disorders. Reviews in Neuroscience. Vol. 29, pg. 771–789, 2018, https://doi.org/10.1515/revneuro-2017-0097.
8. Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. Nature. Vol. 511, pg. 421–427, 2014, https://doi.org/10.1038/nature13595.
9. S. Siegert, J. Seo, E. J. Kwon, A. Rudenko, S. Cho, W. Wang, L. H. Tsai. The schizophrenia risk gene product miR-137 alters presynaptic plasticity. Nature Neuroscience. Vol. 18, pg. 1008–1016, 2015, https://doi.org/10.1038/nn.4023.
10. J. A. Lieberman, S. A. Small, R. R. Girgis. Early detection and preventive intervention in schizophrenia: From fantasy to reality. American Journal of Psychiatry. Vol. 176, pg. 794–810, 2019, https://doi.org/10.1176/appi.ajp.2019.19080865.

11. M. J. Gandal, J. R. Haney, N. N. Parikshak, V. Leppa, G. Ramaswami, C. Hartl, D. H. Geschwind. Shared molecular neuropathology across major psychiatric disorders parallels polygenic overlap. Nature Neuroscience. Vol. 21, pg. 725–734, 2018, https://doi.org/10.1038/s41593-018-0114-9.
12. M. P. Vawter, F. Mamdani, F. Macciardi. An integrative functional genomics approach for discovering biomarkers in schizophrenia. Briefings in Functional Genomics. Vol. 10, pg. 387–399, 2011, https://doi.org/10.1093/bfgp/elr036.
13. L. Zhang, J. Zhang. Bioinformatics-based identification of CTSS, DOK2, and ENTPD1 as potential blood biomarkers of schizophrenia. BMC Psychiatry. Vol. 25, pg. 157, 2025, https://doi.org/10.1186/s12888-025-06512-0.
14. P. D. McGorry, E. Killackey, A. R. Yung. Early intervention in psychosis: concepts, evidence and future directions. World Psychiatry. Vol. 7, pg. 148–156, 2008, https://doi.org/10.1002/j.2051-5545.2008.tb00182