

analysis suggested that the benefit of AOM 400 versus placebo was driven by a significantly lower proportion of patients experiencing a YMRS total score  $\geq 15$  (18–32 years: 5.60% versus 44.10%,  $p < 0.001$ ; disease duration  $\leq 4.6$  years: 6.10% versus 41.20%,  $p < 0.01$ ) or clinical worsening (18–32 years: 8.30% versus 38.20%,  $p < 0.01$ ; disease duration  $\leq 4.6$  years: 6.10% versus 38.20%,  $p < 0.01$ ).

**Conclusion.** The efficacy of AOM 400 was demonstrated in the earlier BP-I population.

**Study registration number:** NCT01567527 (ClinicalTrials.gov)

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## Using Patient iPSC-Derived Neurons to Uncover Mechanisms Associated with Response to Antidepressant Drugs: A Framework for Precision Medicine in Depression

Aleksandra Kugel, Dana Kroitorou, Claudia Albeldas, Talia Cohen Solal and Daphna Laifenfeld

**Introduction.** Depression is a leading cause of disability worldwide affecting over 300 million individuals globally. Despite the abundance of approved antidepressants, the majority of depressed patients do not respond to their first prescribed antidepressant, with over 30% not responding to subsequent drugs. This is largely attributed to individual differences in the underlying pathophysiology of the disease, which make some medications efficacious for some patients while ineffective for others. Multiple studies have been conducted with the aim of identifying patient subgroups associated with drug response, with a large focus on variations in genetic and gene expression levels that may underlie response to specific drugs. However, these studies yielded mostly inconsistent results, with robust genetic effects largely related to drug pharmacokinetics and gene expression level associations poorly reproducible. In this study, we assessed gene expression levels in iPSC-derived neurons from depressed patients with a known response profile to various medications, alongside genetic variations. iPSC-derived neurons have the potential to unravel mechanisms that are neuronal specific and thus not observed in patient whole blood molecular analysis.

**Methods.** Patient-derived lymphoblastoid cell lines from the Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) study with known response to Citalopram or Bupropion were reprogrammed and then differentiated to cortical neurons. Analysis of genetic variants and differential gene

expression was performed on the derived neurons to identify variants and gene expression levels that are associated with drug response.

**Results.** Significant differential gene expression was shown between Bupropion responders and non-responders as well as between Citalopram responders and non-responders. Functional enrichment analysis revealed biologically relevant pathways that differ between responders and non-responders in Bupropion and in Citalopram. In addition, we found an interplay between genetics and neuronal gene expression, that is associated with patient drug response. This was specifically observed in genes implicated in drug mechanism of action, including COMT and BDNF.

**Conclusions.** Patient-derived neurons have utility in mechanistic disease and drug modeling, and can elucidate mechanisms that cannot be read out from systemic whole blood analysis. In addition, combining genetics and target organ gene expression levels has the potential to be used as biomarkers for drug response. Together, these findings support a novel framework for precision medicine in depression.

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## Pollock's Abstract Images in Paintings Prior to His Drip Paintings

Debbi Ann Morrissette, PhD<sup>1</sup>,  
Stephen M. Stahl, MD, PhD<sup>1,2</sup> and Jon A. Gates

<sup>1</sup>Neuroscience Education Institute, Carlsbad, CA and <sup>2</sup>Dept of Psychiatry, University of California San Diego and Riverside, CA

Although Jackson Pollock is most famous for his drip drawings, these occurred late in his career, starting around 1947. Prior to that he produced some “surrealist inflected” paintings and “gestural abstraction.” *Troubled Queen* in 1945 is considered Pollock’s masterful transitional work from the regionalist figurative paintings of his early years to the passionate “drip paintings” for which he is best known. As stated by Elliot Bostwick Davis et al (mfashop.com/9020398034), “As *Troubled Queen* shows, Pollock had begun to work in a very large scale by this time; his paint was dragged over, dripped on, and flung at the canvas. His subject matter was no less highly wrought: emerging from the churning coils and jagged lines of this life-sized canvas are two facelike forms, one a leering mask, the other a one-eyed diamond shape. Their nightmarish presences reflect not only Pollock’s agitated psyche but also the years of violence that had torn the world apart through war.” Thus, *Troubled Queen* shows that Pollock included images in his painting prior to his “drip paintings,” rendering it feasible that he continued to include images in his “drip paintings” using that new technique. We have coined the term “Polloglyphs™” to name the images that are encrypted in his “drip paintings” and that tell a story about Pollock’s inner being, camouflaged yet hiding in plain sight.

Here, in order to establish the basis for Polloglyphs in his later “drip paintings,” we have deconstructed the multiple images in *Troubled Queen* by first showing the image on a white

background and then transposing it upon the painting. In this way, the observer can begin to see how images were incorporated into Pollock's pre-drip paintings. These are not Rorschach ink blots with fractal edges that are fooling the eyes and only in the mind of the viewer, but images purposely put on canvas as the observer can see. Clearly, there is a "troubled queen" in *Troubled Queen*. Beyond that there are images of war possibly inspired by Picasso's famous *Guernica* painted in 1937 and first seen by Pollock in 1939. A character is also seen to her left. Pollock had a trick that can be used to better visualize and uncover his images by rotating this painting 90 degrees counterclockwise. In this case, a small angel of mercy with her sword can be seen in the upper left quadrant. Another character, possibly a soldier with a hatchet and gun with bullet in the barrel can also be seen. Several other images can also be deciphered including a Picasso-like rooster and many others. Together, these images suggest a theme of war during the midst of World War II and may have triggered Pollock's long standing feelings of inadequacy as his psychiatrist and his draft board found him unfit to serve as a soldier and he was exempted from serving. We encourage the observer to look carefully at *Troubled Queen* and to develop an opinion on which if any of the images are seen and to ponder as well what they may mean.

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## Psychiatric Consultations at an Academic Medical Center in the Initial Weeks of the COVID-19 Pandemic: A Clinical and Sociodemographic Comparison of COVID-Positive and COVID-Negative Consultations

Emily Groenendaal, MD<sup>1</sup>, Sean Lynch, MD<sup>2</sup>,  
Sivan Shahar, MD<sup>2</sup>, Rhea Dornbush, PhD, MPH<sup>1</sup>,  
Lidia Klepacz, MD<sup>1</sup> and Stephen J. Ferrando, MD<sup>1</sup>

<sup>1</sup>Westchester Medical Center, New York Medical College, NY and <sup>2</sup>Mount Sinai, New York Medical College, NY

**Background.** During the initial weeks of the COVID-19 pandemic, the overall number of psychiatric consultations decreased; however, the consultations that were placed appeared to be heavily related to either COVID-19 infection or a stressor secondary to the pandemic. New onset neuropsychiatric symptoms have been seen and described in prior reports among patients with acute COVID-19 infection. This study aimed to examine the sociodemographic and clinical characteristics of psychiatric consultations in the early portion of the pandemic, and compare patients who were COVID-19-positive with those who were negative.

**Methods.** This IRB-approved retrospective chart review involved all psychiatric consultations for COVID-19-positive patients admitted to a medical floor at an academic medical center from

March 1 2020 until May 31 2020. Sociodemographic, medical (including diagnoses and laboratory values), and psychiatric information was collected from all consultations, and patients who were COVID-19 positive were matched with a COVID-negative comparison group by age (+/- 3 years) and gender. Statistical analyses to compare these groups were performed.

**Results.** There were 80 consultations for COVID-positive patients identified in the given time period. These were matched with a comparison group of 80 patients who had been listed as COVID-negative; however on review of medical records only 64 were truly negative, so 16 were excluded. Significant differences existed between groups in terms of reason for psychiatric consultation ( $p=0.04$ ) and billing diagnosis ( $p<0.01$ ), with COVID-positive patients appearing to have a greater likelihood of presenting with psychosis or delirium, and less likelihood for mood, anxiety, or substance use. D-dimer levels were higher in COVID-positive patients, and patients with COVID had a higher mortality rate. COVID-positive patients were more likely to receive a "second-generation antipsychotic". Differences between groups in terms of specific psychiatric symptoms were explored. No other sociodemographic or medical differences were found between groups.

**Discussion/Conclusion:** Patients with COVID-19 infection may be at an increased rate for delirium and for symptoms of psychosis. Multiple studies have speculated on mechanisms for such symptoms, though findings are inconclusive. This study suggests that simply increased stress during the pandemic is not the driving factor for these symptoms. Patients admitted to medical floors with COVID-19 infection should be screened for delirium and for new-onset neuropsychiatric symptoms.

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## IDgenetix-Guided Medication Management for Major Depressive Disorder: Confirmation of Randomized Controlled Trial Outcomes by Real-World Evidence

Feng Cao, PhD, Andrea Hanson, PhD and  
Robert Cook, PhD

Castle Biosciences, Friendswood, TX

**Introduction.** IDgenetix is an advanced multi-gene pharmacogenomic (PGx) test that incorporates drug-gene interactions, drug-drug interactions, and lifestyle factors to guide medication management for patients diagnosed with major depressive disorder (MDD), anxiety, or other mental illnesses. In a previously published randomized controlled trial (RCT), IDgenetix significantly improved patient response and remission rates (Bradley et al., 2018). In this analysis, we aimed to compare the clinical outcome results from the RCT with real-world evidence from an open-label study (Cao et al., 2023).