analysis suggested that the benefit of AOM 400 versus placebo was driven by a significantly lower proportion of patients experiencing a YMRS total score ≥15 (18–32 years: 5.60% versus 44.10%, p<0.001; disease duration ≤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 ≤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

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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 (STARD) 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.

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

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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 TM" 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