specifically responding to a certain drug. Despite decades of efforts though, pharmacogenetics appears to be still in its infancy.
Aim A clearer understanding of the pharmacodynamics and pharmacokinetics events in combination with the genetic and epigenetic controls of cells and molecular cascade must inform the future of personalised medicine.
Objectives To systematically review the current cutting edge knowledge about pharmacognetics in the search for the next groundbreaking biological key events that may provide the keys to future treatments.
Methods The major online databases are systematically searched with common keywords by two independent researchers and conflicting findings are solved during regular meetings dedicated to the topic in object. Manual searching of single bibliographies is also put in place.
Results Genes belonging to the serotoningeric, dopaminergic, glutamatergic and GABAergic systems are classic candidates for pharmacogenetics whose role was not confirmed by GWAS analyses, which, on the other hand, identified genes related to molecular pathways not associated with direct target of drugs used for the treatment of depression.
Conclusion Both hypothesis driven candidate genetic investigations and GWAS analyses have been conducted so far, leading to the identification of a handful of potential good candidates, but the replication rate of the positive association findings lags behind expectations. The current knowledge about the pharmacodyncamic and pharmacokinetic genetic determinants of antidepressant response is critically analysed and new candidates are presented discussed.
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EW0176

A molecular pathway analysis informs the genetic risk for arrhythmia during antipsychotic treatment

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Background Arrhythmia is a potentially fatal side effect of antipsychotics. A biologic predictive tool to prevent it is missing.
Aim Identification of a genetic profile at risk for antipsychotic induced arrhythmia.
Objective Identifying a molecular pathway enriched for antipsychotic induced QT-modifications.
Methods Seven hundred and sixty-five SKZ individuals, $M = 556$, age = 40.93 ± 11.03 were included. QT-variation was a phase-specific created variable. A nested mixed regression served in R for clinical and molecular pathway analyses. Plink served for genetic analyses. Quality checking was standard, inflation factor was controlled by lambda values.
Results Quetiapine and Perphenazine were associated with QT variation ($P = 0.002$; Estimate = 5.79 and $P = 5.67e\text{-}06$; Estimate = 8.96 respectively). No other significant association was detected. No inflation was detected. Axon guidance and Collagen biosynthesis (Table 1) were associated with QT variation at a conservative (adjusted) P value < 0.01.
Conclusions Two molecular pathways were identified as possibly involved in QT modifications during antispsychotic treatment in SKZ patients. Previous evidence supports a role of the same pathways in cardiac disorders [1,2]. Interaction of specific SNPs with the drugs will be focus of further research.

Table 1 Molecular pathways enriched in association with QT modifications.

ID	Description	Gene Ratio	BgRatio	*P*-value	*P*.adjust	Qvalue
422475	Axon guidance	19/135	292/6750	4.6e–06	0.0022	0.0021
1650814	Collagen biosynthesis and modifying enzymes	8/135	59/6750	1.9e–05	0.0047	0.0044

Disclosure of interest The authors have not supplied their declaration of competing interest.
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A molecular pathway analysis stresses the role of inflammation towards cognition in Schizophrenia

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Background Cognitive processes are impaired in Schizophrenia (SKZ). The nature of such impairment escapes definition.
Aim Identification of a genetic profile at risk of cognitive impairment.
Object Identifying a molecular pathways enriched for mutations associated with cognitive impairment.
Methods Seven hundred and sixty-five individuals from the CATIE, $M = 556$, mean age = 40.93 ± 11.03 were included. Verbal memory was outcome. R and Plink served for the analyses. Inflation factor was controlled by lambda values. Input for the pathway analysis were SNPs associated with outcome ($P < 0.05$) genomewide.
Results Gender (male, $P = 2.34e{-}05$; $t = -4.26$) and years of education ($P = 1.57e{-}03$; $t = 6.502$) were associated with verbal memory. Inflammation and oxidation were associated with outcome (Table 1, adj_$P < 0.01$).
Conclusions Being male and poorly educated were associated with poorer verbal memory. Inflammation and the arachidonic acid pathway were enriched in mutations associated with poorer verbal memory. This finding is in line with previous reports [1,2,3].

Table 1 Pathways enriched in association with verbal memory.

Description	GeneRatio	BgRatio	*P*value	*P*.adjust
Synthesis of Leukotrienes	5/105	17/6750	4.42E–06	0.0009
Arachidonic acid metabolism	7/105	45/6750	5.03E–06	0.0009
Glutathione synthesis and recycling	4/105	11/6750	1.68E–05	0.0021

Disclosure of interest The authors have not supplied their declaration of competing interest.
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