# Study of Dopamine and Glutamate Receptor Oligomerization on the Effect of Antipsychotic Drugs in an *In Vitro* Phenotypic Model of Schizophrenia.

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## ABSTRACT

Schizophrenia is a chronic psychotic illness that affects more than 1% of the world population. Its symptoms are heterogeneous and vary markedly from one individual to another, usually appearing during late adolescence and continuing throughout adulthood, the symptoms can be divided into three categories: positive symptoms, characterized by hallucinations and delusions; negative symptoms, such as loss of motivation, anhedonia and abulia; and cognitive deficits, related to attention and concentration problems[1,2].

Although much of its etiopathogenesis remains unknown due to the multiple molecular mechanisms involved in its onset, it has been shown that there is dysregulation in the dopaminergic, glutamatergic and serotonergic neurotransmitter systems, in which several pharmacological targets are involved. Several studies have identified different G-protein-coupled membrane receptors (GPCRs) as key targets, with the D2, D3, 5-HT2A, and mGlu2 receptors being the most relevant, being the main targets of typical and atypical antipsychotics used in the clinic of schizophrenia. Moreover, there are indications that these receptors may act as dimers, giving rise to signaling different from that of their monomeric forms, and to the possibility of cross-signaling between these receptors[3,4].

Therefore, the aim of this research was to study the oligomerization of dopaminergic (D2) receptors and metabotropic glutamatergic type 2 (mGlu2) receptors in an *in vitro* phenotypic model of schizophrenia, and to determine whether they can assemble into a functional heteromeric complex that allows modulating the function of the other. To this end, functional cAMP assays were performed to evaluate the expression and functionality of D2 receptors in SH-SY5Y cells after the differentiation process. Subsequently, intracellular calcium mobilization assays were performed to verify the presence of the mGlu2 receptor and to evaluate the response of both receptors when exposed to different modulators. The results showed that there is interference of the D2 receptor agonist on mGlu2 receptor signaling, as well as changes in the dopamine response in the absence and presence of glutamate.

## REFERENCES

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