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LETTER TO THE EDITOR

DISCovery in psychiatric genetics

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The Guest Editorial by Sullivan[1] on DISC1 reflects not only his limitations in understanding biology, but more broadly reflects those of a group of statistically trained non-biologists who are currently very active (and vocal) in psychiatric genetics. Illness works through alterations in biology. Biology works at a gene level and not at a single-nucleotide polymorphism (SNP) level. Biologically important genes such as *DISC1* (or *BDNF* or *COMT*) have more SNP heterogeneity and diversity in the population[2] likely owing to the need to evolutionarily adapt and fine-tune the interface between organism and environment.[3] Integrative approaches at a gene level clearly demonstrate their involvement and show reproducibility[4] as opposed to the statistically driven SNP-focused Genome-Wide Association Study (GWAS) approaches of Sullivan and colleagues[5] that have identified primarily housekeeping genes to date (such as *ANK3*, *CACNA1C* and *ODZ*). In fact, SNP-focused GWAS approaches miss the boat on their own data. The overlap between GWAS studies is 100-fold greater at a gene level than at a nominally significant SNP level[4]. Moreover, what non-biologists do not understand is how the brain (or for the matter, the body) works. Schizophrenia, like other complex disorders, is a broad entity overlapping with other disorders. Genes and their products are building blocks that in different combinations, and in different environmental contexts, give different psychiatric and non-psychiatric syndromes. In the sporting tradition of years past in science, before things became rather boring and politically correct, I would like to wager with Sullivan[1] the following: whomever is wrong between the two of us on this subject should write a Letter to Molecular Psychiatry in 2020, titled *Mea Culpa on DISC1*.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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