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## 5.04.2 The Effect of Childhood Trauma on Blood Transcriptome Expression in Major Depressive Disorder.

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**Background** Childhood trauma (CT) increases the likelihood of developing severe mental illnesses, such as major depressive disorder (MDD), during adulthood. Several studies have suggested an inflammatory immune system dysregulation as a biological mediator; however, the molecular mechanisms underlying this relationship remain largely undetermined. Moreover, different types of CT, in particular, emotional abuse and neglect, confer a higher risk of developing MDD, and recent meta-analyses showed that each CT can be associated with different pro-inflammatory biomarkers. However, no studies using a hypothesis-free approach have been performed. For this reason, we carried out a reanalysis of transcriptome data from a large mRNA sequencing dataset to investigate different types of CT in MDD patients.

**Methods** Likelihood ratio tests and principal component and gene-set enrichment analyses were carried out to identify genes and pathways differentially expressed in patients who experienced different types of CT.

**Results** Expression analysis of single genes revealed a significant association between the neglect CT and the *MED22* gene ( $p=1.11 \times 10^{-6}$ ;  $FDR=0.016$ ) that apparently was not mediated by *MED22* expression quantitative trait loci (eQTLs). Furthermore, analyses of the principal components of expression data support a dysregulation of cytokine system pathways, such as interferon (IFN)  $\alpha/\beta$  and  $\gamma$  signaling, as a consequence of emotional abuse in depressed patients.

**Conclusions** Our results corroborate the hypothesis that specific types of CT affect distinct molecular pathways. Moreover, this study provides biological evidence in support of clinical literature regarding the impact of emotional abuse and neglect on the development of MDD.