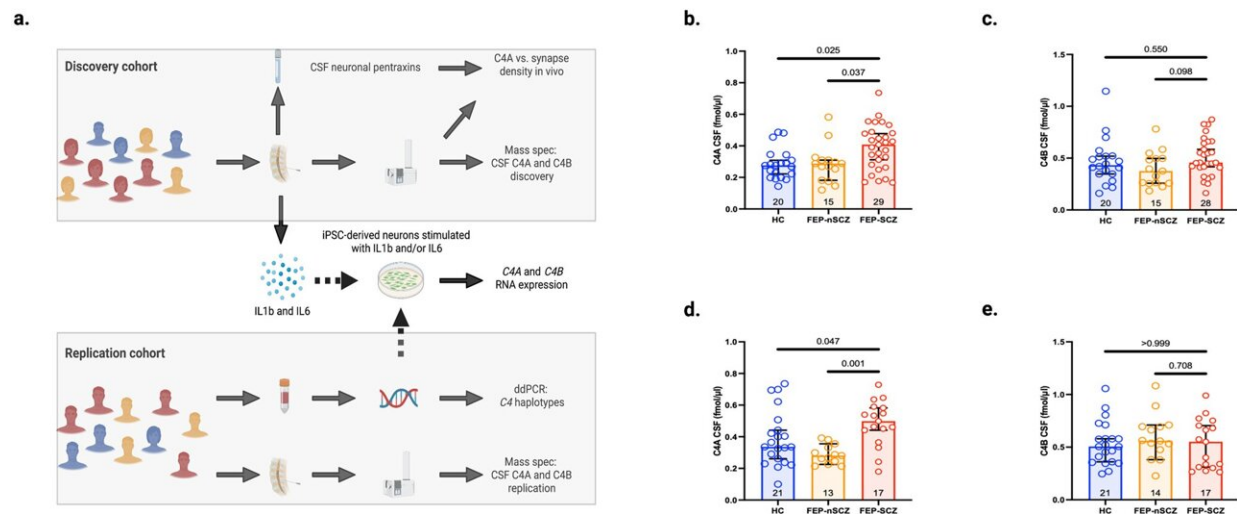


# Inflammation may amplify effect of genetic risk variants for schizophrenia

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Cerebrospinal fluid levels of C4A are increased in patients with first-episode psychosis who develop schizophrenia. **a** Overview of the study design. **b** In the discovery cohort (KaSP), patients with first-episode psychosis (FEP) who developed schizophrenia (FEP-SCZ;  $n = 29$ ) displayed significantly higher cerebrospinal fluid (CSF) C4A concentrations as compared to healthy controls (HCs;  $n = 20$ ) or patients with FEP who did not develop SCZ (FEP-nSCZ;  $n = 15$ ) (HCs: 0.28 fmol/ul; 95% confidence interval [CI] = 0.24–0.33, FEP-nSCZ: 0.29 fmol/ul; CI = 0.22–0.35, FEP-SCZ: 0.41; CI = 0.34–0.45, adjusted  $P$  [FEP-SCZ vs. HCs]=0.025, adjusted  $P$  [FEP-SCZ vs. FEP-nSCZ]=0.037). **c** CSF C4B concentrations were similar across groups (HCs [ $n = 20$ ]: 0.43 fmol/ul; CI = 0.36–0.57, FEP-nSCZ [ $n = 15$ ]: 0.38 fmol/ul; CI = 0.30–0.49, FEP-SCZ [ $n = 28$ ]: 0.46 fmol/ul; CI = 0.44–0.58, adjusted  $P$  [FEP-SCZ vs. HCs]=0.550, adjusted  $P$  [FEP-SCZ vs. FEP-nSCZ]=0.098). **d** In the replication cohort (GRIP), patients with FEP-SCZ ( $n = 17$ ) displayed significantly higher CSF C4A concentrations as compared to HCs ( $n = 21$ ) or patients with FEP-nSCZ ( $n = 13$ )

(HC: 0.34 fmol/ul; CI: 0.31–0.47, FEP-nSCZ: 0.28 fmol/ul; CI: 0.25–0.33, FEP-SCZ: 0.50 fmol/ul; CI: 0.41–0.56, adjusted P [FEP-SCZ vs. HCs]= 0.047, adjusted P [FEP-SCZ vs. FEP-nSCZ]=0.001), while (e) CSF C4B concentration were similar across groups (HCs [n = 21]: 0.51 fmol/ul; CI = 0.44–0.63, FEP-nSCZ [n = 14]: 0.56 fmol/ul; CI = 0.47–0.72, FEP-SCZ [n = 17]: 0.55 fmol/ul; CI = 0.41–0.65, adjusted P [FEP-SCZ vs. HCs]=0.999, adjusted P [FEP-SCZ vs. FEP-nSCZ]=0.708). Bar graphs represent medians and error bars represent 95% CIs. Data were analyzed using Kruskal–Wallis H tests followed by post-hoc tests. Significance was set to P

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