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テトランドリンは P-糖タンパク質および MAPK の阻害を介して活性化ヒト末梢血単核細胞におけるグルココルチコイドの作用を増強する

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[Purpose] Glucocorticoids (GC) play significant roles in treatments of inflammatory and autoimmune diseases. However some patients show a poor or absent response to use GC. The purpose of this study was to explore whether tetrandrine (TET) combined with GC could be a new treatment strategy to resolve GC resistance.

[Methods and Results] Human peripheral blood mononuclear cells (PBMCs) was chosen as a model to study the synergic effect of TET with methylprednisolone (MPSL), including the underlying action mechanisms. TET decreased the IC_{50} value of MPSL significantly, but it showed little toxic effect on the concanavalin A-activated PBMCs. Both TET and MPSL inhibited the secretion of pro-inflammatory cytokines TNFα and IL-6 significantly and the synergic inhibitory effect could be observed. TET and/or MPSL did not increase the percentage of $CD4^+$ $CD25^+$ $Foxp3^+$ regulatory T cells in $CD4^+$ T cells. However TET with or without MPSL significantly inhibited the function of drug efflux pump P-glycoprotein 170 (P-gp) of $CD4^+$, $CD8^+$ T cells and lymphocytes. TET suppressed the phosphorylation of MAPK and this effect was potentiated by MPSL. These TET effects were suggested to be beneficial for improving the immunosuppressive efficacy of GC. GC combined with TET could be a new therapeutic approach to resolve GC-resistance via inhibiting the function of P-gp and blocking MAPK signaling pathway but not affecting on $CD4^+$ $CD25^+$ $Foxp3^+$ regulatory cells.