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Anti-inflammatory effect of PDE5 inhibition in diabetic cardiomyopathy

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In patients with type 2 diabetes PDE5 inhibition (PDE5i) is associated with cardiac remodeling and reduced inflammatory cytokines[1]. In this study it was investigated if PDE5 inhibition prevents the development of cardiomyocyte hypertrophy associated with diabetes by modulation of specific subsets of circulating monocytes and tissue macrophages.

Leptin receptor–deficient *db/db* mice develop diabetes mellitus and cardiac hypertrophy. The *db/db* mice were treated with the PDE5 inhibitor sildenafil (SILD) for 8 weeks. In the hearts of SILD treated mice cardiomyocyte showed a reduced cross-sectional area compared to the cardiomyocyte of untreated mice. Expression of the hypertrophic marker β-myosin was up-regulated in db/db mice hearts and this increase was prevented by SILD treatment. Circulating pro-inflammatory $CD11b^{+}Gr\text{-}1^{+}$ myeloid cells and the $CD11b^{+}Gr\text{-}1^{-}$ monocyte cells, were monitored during SILD treatment. $CD11b^{+}Gr\text{-}1^{+}$ cells were reduced after SILD treatment in db/db mice compared with untreated ones. No significant changes of $CD11b^{+}Gr\text{-}1^{-}$ cells were detected in both control and SILD treated animals. After tissue dissociation, cardiac macrophages infiltration was characterized using specific markers such as F4/80 and TIE2. $F4/80^{+}$ macrophages in diabetic mice were 2-fold increased compared to untreated mice and they were reduced by SILD treatment. Proangiogenic TIE2 expressing monocytes/macrophages (TEMs) percentage was highly increased in SILD treated db/db mice and correlated with an increase of vessel density, measured by the expression of the endothelial marker CD31.

These data suggest that PDE5 inhibition attenuates inflammation in diabetic cardiomyopathy reducing pro-inflammatory monocytes and in parallel increasing TEMs percentage and tissue vascularization.

References

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Keywords
Macrophages; cardiac hypertrophy; phosphodiesterase-5 inhibitor; diabetic mouse.