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The natural drug DIAVIT is protective in a type-2 mouse model of diabetic nephropathy

Statement of the Problem: There is evidence to suggest that abnormal angiogenesis, inflammation and fibrosis drive diabetic nephropathy (DN). However, there is no specific treatment to counteract these processes. We aimed to determine whether DIAVIT, a natural Vaccinium myrtillus (blueberry) and Hippophae rhamnoides (sea buckthorn) extract, is protective in a model of type-2 DN.

Methodology & Theoretical Orientation: Diabetic db/db mice were administered DIAVIT in their drinking water for 14 weeks. We assessed the functional, structural and ultra-structural phenotype of three experimental groups (lean+vehicle, db/db+vehicle, db/db+DIAVIT) and the angiogenic and fibrotic pathways involved in the DIAVIT mechanism.

Findings: Diabetic db/db mice developed hyperglycemia, albuminuria and an increased glomerular water permeability; the latter two were prevented by DIAVIT. db/db mice developed fibrotic glomeruli, endothelial insult and glomerular ultra-structural changes, which were absent in DIAVIT-treated mice. VEGF-A splicing was altered in the db/db kidney cortex, increasing pro-angiogenic VEGF-A165 relative to anti-angiogenic VEGF-A165b. This was partially reversed with DIAVIT. TNFα-induced nuclear translocation of p65-NFκB in cultured glomerular endothelial cells was also prevented by DIAVIT.

Conclusion & Significance: In conclusion, DIAVIT alters VEGF-A splicing and p65-NFκB activation, rescuing the DN phenotype. This study highlights the therapeutic potential of natural drugs in DN through the manipulation of gene splicing and expression.

Biography

Megan Stevens is currently working as a Research Fellow at the University of Exeter, UK as part of Dr. Sebastian Oltean's group. Her research focuses on the background in the alternative splicing of VEGF-A as a therapeutic in chronic kidney disease and her current focus is on exploring alternative splicing events in diabetic nephropathy and how DIAVIT and other small molecules can be used to modulate splicing in a therapeutic manner.

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