Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

Nucleoside Diphosphate Kinase B deficiency leads to endothelial damage through Angiopoietin-2

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Nucleoside diphosphate kinase B (NDPK B) is a ubiquitously expressed enzyme required for nucleotide triphosphate (NTP) synthesis. Data from NDPK B deficient mice demonstrated the significantly increased pericyte loss and the formation of acellular capillaries in the retina, mimicking the pathology of diabetic retinopathy (DR). Endothelial Ang2 has been reported to be crucial for the initiation of pericyte loss in DR. This study was designed to explore the contribution of NDPK B depletion to the endothelial damage by assessing Ang2 expression and protein GlcNAcylation in endothelial cells (ECs). NDPK B deficiency increased Ang2 expression and protein GlcNAcylation in ECs, mimicking the impact of high glucose. Ang2 depletion partially inhibited the increased protein GlcNAcylation level induced by high glucose. In addition, Ang2 depletion could counteract increased protein GlcNAcylation induced by NDPK B depletion in ECs. In addition, the expression of NDPK B did not alter under high glucose and Ang2 depletion. We thus speculate that Ang2 plays a central role in NDPK B induced EC damage through NDPK B-Ang2-protein GlcNAcylation cascade. The expression of Tie2, the tyrosine receptor of Ang2, increased in single Ang2- or NDPK B-depleted ECs, but markedly decreased in double Ang2 and NDPK B depletion in ECs, indicating complicated mechanisms underlying NDPK B deficiency induced EC damage.
In conclusion, NDPK B deficiency induces EC damage by increasing Ang2 expression and protein GlcNAcylation, thus mimicking the pathology of DR. Ang2 is likely playing a central role in mediating the vasoregression in NDPK B depletion. Our data suggest that NDPK B is a protective factor in ECs, thus could be a novel therapeutic approach to DR.