Mini Review

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New paradigms in cell death in human diabetic nephropathy

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ABSTRACT

Cell death is thought to contribute to progressive renal cell depletion in diabetic nephropathy. Unbiased gene expression profiling identified novel cell death molecules in human diabetic nephropathy. The expression of TNF-related apoptosis-inducing ligand (*TRAIL*), its decoy receptor osteoprotegerin, and receptors Fas (a Fas ligand receptor) and CD74 (a migration inhibitory factor (MIF) receptor) were induced in human diabetic nephropathy. Cell culture studies supported the functional relevance of this observation and the relationship to a high glucose environment. To define novel proapoptotic proteins upregulated in diabetic nephropathy, functional genomic screens for novel apoptosis mediators were integrated with genome-wide expression profiling and identified candidates for further functional analysis, including brain acid-soluble protein 1 (*BASP1*). Several lines of evidence point toward induction of endoplasmic reticulum stress response in human diabetic nephropathy. Functional studies defining an unequivocal contribution of endoplasmic reticulum stress to cell death in this setting are still needed. Further comparative studies will be required to define whether there is a specific aspect of apoptosis in progressive human diabetic nephropathy or whether the mechanisms are shared among all patients with chronic kidney disease. The next challenge will be to define the consequence of therapeutic interference of the apoptosis pathways in diabetic nephropathy and chronic kidney disease.

Keywords: apoptosis; BASP1; CD74; diabetic nephropathy; MIF; TRAIL

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