

Gangliosides as a Pathophysiological Modulator of Cell Proliferation in Cultured Rat Mesangial Cells

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Proliferation of glomerular mesangial cells (GMCs) is a common feature in the early stage of diabetic nephropathy, and sialic acid-conjugated gangliosides are known to regulate the differentiation and growth of many cell types. Using cultured GMCs originated from rat glomeruli, this study examined whether gangliosides act as a modulator of cell proliferation occurring in physiological and pathological conditions. GMCs were exposed to normal (5.6 mM) or high (25 mM) glucose for 24hrs, and following results were obtained. High glucose, TGF- β 1 (10 ng/mL) and PDMP (20 μ M), an inhibitor of ganglioside synthesis, significantly stimulated the proliferation of GMCs. In contrast, exogenous gangliosides, especially ganglioside GM3, conspicuously inhibited the proliferation of GMCs in both normal and high glucose-condition, and the inhibitory rate in high-ambient glucose was much higher than that in normal glucose. Based upon the motility on HPTLC, GMCs showed a complex pattern of ganglioside expression that consisted, at least, of three different components of gangliosides, mainly ganglioside GM3, and high-ambient glucose and TGF- β 1 caused a dramatic reduction of ganglioside expression. A prominent immunofluorescence microscopy showed that these conditions also caused a dramatic disappearance of immunoreactivity produced by anti-ganglioside GM3 antibody. High glucose, TGF- β 1 and PDMP significantly decreased the intracellular sialic acid contents and ganglioside GM3 synthase activity. These results provide a pathophysiological role of gangliosides in the proliferation of rat mesangial cells, indicating that gangliosides negatively regulate the high glucose- and TGF- β -induced mesangial proliferation, and this mechanism may play an important role in the development of diabetic glomerular injury.