Agrin is a major heparan sulfate proteoglycan in the human glomerular basement membrane

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Agrin is a heparan sulfate proteoglycan (HSPG) that is highly concentrated in the synaptic basal lamina at the neuromuscular junction (NMJ). Agrin-like immunoreactivity is also detected outside the NMJ. Here we show that agrin is a major HSPG component of the human glomerular basement membrane (GBM). This is in addition to perlecan, a previously characterized HSPG of basement membranes. Antibodies against agrin and against an unidentified GBM HSPG produced a strong staining of the GBM and the NMJ, different from that observed with anti-perlecan antibodies. In addition, anti-agrin antisera recognized purified GBM HSPG and competed with an anti-GBM HSPG monoclonal antibody in ELISA. Furthermore, both antibodies recognized a molecule that migrated in SDS-PAGE as a smear and had a molecular mass of approximately 200-210 kD after deglycosylation. In immunoelectron microscopy, agrin showed a linear distribution along the GBM and was present throughout the width of the GBM. This was again different from perlecan, which was exclusively present on the endothelial side of the GBM and was distributed in a nonlinear manner. Quantitative ELISA showed that, compared with perlecan, the agrin-like GBM HSPG showed a sixfold higher molarity in crude glomerular extract. These results show that agrin is a major component of the GBM, indicating that it may play a role in renal ultrafiltration and cell matrix interaction.
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