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CCN3-based therapy: A first-in-class preventative and treatment to block and reverse renal and other organ fibrosis complicating diabetes

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We first demonstrated a role for the matricellular protein CCN2 (formerly CTGF) as a critical downstream pro-fibrotic element in renal fibrosis. Then, in 2009 we published the first work identifying a role for CCN3 (NOV), another family member, as a co-regulating molecule working in a yin/yang manner to block mesangial cell transformation to a fibroblast phenotype and the over-production of collagen. Recently, we conducted pharmacokinetic and proof-of-principle efficacy studies in the BT/BR ob/ob mouse as a best rodent model of human diabetic nephropathy (DN). We showed that IV and IP dosing resulted in primary drug targeting to the kidney and a suitable half-life. A 3x/week treatment for 8 weeks, beginning in established DN, completely blocked and returned to normal the overexpression of key pro-fibrosis genes. Further, it completely blocked and reversed podocyte cell loss, glomerular fibrosis, reduction of kidney function and albuminuria. We therefore elucidated mechanisms operating at multiple therapeutic levels or pathways; both upstream (protecting against cell injury) and downstream (regulating CCN2 activity and ECM metabolism/accumulation. The unexpected protection from podocyte injury and glomerular hypertrophy is extremely important, since it is a key early marker of DN and thought to be critical to the development of proteinuria and glomerular/interstitial fibrosis. Most recently, we have identified key regions on the CCN3 protein, and created small peptide mimetics to specifically replicate the anti-fibrotic activity of CCN3 without additional unrelated functions. We have similarly tested these therapeutics in the BT/BR ob/ob mouse and other models of fibrosis with very positive results. BLR Bio is currently developing this as a platform for the treatment of renal disease.

Biography

Bruce L Riser was a Senior Staff Member and Director of the Renal Research Program in the Nephrology Division at Henry Ford Hospital, Detroit for 13 years then Director of R&D at Baxter Healthcare, Renal Division, for 11 years. In 2013 he founded BLR Bio an emerging biotechnology company focused on the diagnosis, prevention, and treatment of renal and other forms of fibrosis. The technology was created at Rosalind Franklin University of Medicine and Science in a laboratory effort he led over the last 12 years while also at Baxter. He holds an MS in Public Health and a PhD in cell/molecular biology both from the School of Public Health, and a Post-doctoral degree in Pathology from the Medical School, all at The University of Michigan.

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