Progress in CD80 and Glomerular Micropathy

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Keywords: Nephrotic syndrome, Glomerular, CD80.

Abstract. Small lesion is a common pathological type nephrotic syndrome, especially in high-risk children; common complications include infection, thrombosis, and acute renal failure and protein and lipid metabolism disorders. The pathogenesis of this disease is still not clear, and the current research focus has been turned to the study of foot cells by the study of T cell immune disorders. However, CD80 is expressed in the foot cells in small glomerular lesions, and is related to the formation of egg white urine. This article reviews the relationship between CD80 and glomerular micropathy.

Introduction

CD80 called B7\textsuperscript{1} again, it is total stimulus molecule B7 one important member in the family, as a kind of stimulus signal, expressed in antigen presented cells (Antigen present cell, APC) surface, the stimulation with T cell surface receptors, two-way regulating T cell immune. In recent years, there is increasing evidence that CD80 is involved in the pathogenesis of proteinuria, especially in the pathogenesis of minimal change disease, so we have summarized the relationship between the two.

CD80 Overview and Physiological Function

In the process of antigen recognition, activation, proliferation and differentiation, T cells need double signal participation, and both signal stimulation is provided by APC.

The first signal comes from APC surface antigen peptide - the main histocompatibility complex and T cell receptor (TCR) \textsuperscript{[1]}. The second signal comes from the combination of co-stimulators and T-cell surface specific receptors on APC surface. Without a second signal, the T cell activation process weakens or even induces cell death. CD80 / B7-1. CD86 / B7-2 is an important stimulus, CD28, Cytotoxic T and T cell surface receptors related molecules - 4 (CTLA 4) combined with, regulating cellular and humoral disease free \textsuperscript{[2]}. CD80 transmembrane glycoprotein, is a kind of monomer is composed of 19 amino acids belong to avoid immune globulin than members of the family. It can express in B cells, dendritic cells, chronic granulomatous inflammation of invasive monocyte chemotactic cells, sertoli cell and...
renal tubular epithelial cells such as APC surface. CD80 molecule binds to a CD28 points of homologous dimers, crosslinking polymerization play a stimulating [3], can combine with slow and persistent CTLA - 4 play the role of inhibiting T cell activation [4].

**CD80 Expression in the Foot Cells**

Foot processes(FPs) and slit diaphragm(SD) are a barrier to urinary protein leakage. All patients with renal retic syndrome(NS) disappeared and SD was reorganized. The disappearance of FPs includes the structural changes of the cell cytoskeleton, FPs movement and SD reconstruction [5]. Reiter [6], nephropathy rat model induced by knockout and puro, glomerular podocyte CD80 clearly expressed, actin reorganization, podocyte structure change. With LPS stimulation in vitro cell and LPS intravenous wild type mice, CD80 observed sertoli cell produced significant increases, which in turn lead to foot cell morphology change (FPs fusion, SD fracture) and transient proteinuria. LPS stimulation of CD80 gene knockout mouse model did not occur in glomerular foot cell morphological changes and proteinuria, demonstrating that CD80 expression was associated with foot cell morphology and proteinuria. In addition, the LPS stimulation of severe combined immunodeficiency mice also produced proteinuria and CD80, indicating that CD80 molecules can express the pathogenesis of the enhancement and involvement of proteinuria in the absence of cellular immunity [6].

In PHN and PAN two podocyte lesion nephritis model in the study found that in before the start of proteinuria, SD gene has no obvious change, after in proteinuria, start CD80 gene expression enhancement and earlier than SD protein gene of egg white (kidney disease genes and FAT1) expression changes [7]. LPS can through toll-like receptor 4 (TLR - 4) [6], TLR3 ligand PolyIC by activating cultured human glomerular TLR3 sertoli cell surface receptors, SBE TLR2 ligand activated receptors TLR2, stimulate cells express CD80, and raised a dose and time dependent on sex, cathepsin L cut synaptic protein expression and reduce the tension of fiber, muscle protein restructuring [7]. Nf-kappa B is an important molecule in many signal transduction pathways, such as Shiraada [8] in research TLR receptor and the ligand signaling pathways in the process, using the nf-kappa B inhibitor PDTC blocked cells express CD80, from and inhibit its shape change, therefore the nf-kappa B signal transduction pathways involved in the process. Gurkan etc. [9], the study found to induce foot TLR ligands - receptor cells to produce the inflammation factor such as IL - 6, TNFa and type I IFN - p table, interferons alpha/beta cells can stimulate the foot CD80 expression, fine actin caused by the change of cell skeleton and proteinuria, CD80 RNA knockout cells can block under hypoxic stimulus of the above changes [10].

**CD80 and Glomerular Micropathy**

MCD is a common pathological type of NS, which is high in children. In more clinical studies, it was found that the expression of CD80 in patients with MCD onset was significantly higher than that in the convalescence MCD and healthy control group, while there was no significant difference in CD80 in blood [11-14]. Consider CD80 molecule may comes from the kidney and acyclic molecules CD80, Eduardo H precipitation method - western blot method analysis of urine excretion of 53 kd CD80 molecule, rather than the cycle of 23 kd molecules CD80 [12]. CD80 can be made of podocyte skin cells, renal tubular, immunofluorescence technique shown in MCD episodes in patients with glomerular podocyte CD80 positive
staining, renal tubular no coloring, confirmed urine CD80 produced by foot cells (rather than the renal tubules)\textsuperscript{[11]}, by SD protein adhesion molecules CD80 urine after\textsuperscript{[15]}.

The second: Both the cytokines and pathogenic microorganisms caused the overexpression of proteinuria, so the presence of the secondary attack caused CD80 to persist and the proteinuria persisted. One is the absence of T cell function. T helper cells do not directly affect the podocytes, ctl\textsuperscript{a}-4 is CD80 negative regulator, and il-10 can inhibit the expression of CD80. Foxp\textsuperscript{3} + T cells can stimulate the production of ctl\textsuperscript{a}-4 and il-10, which can play a role in the binding of CD80 molecules in the glomerular basement membrane and the foot cell. NS, abnormal function of Treg cells, leading to reduced secretion of IL - 10 expression, secretion reduce, then CTLA - 4 episodes MCD patients with urinary CD80 / CTLA 4 ratio significantly higher, the remission patients CTLA 4 cannot suppress CD80, showing a continuous protein urine. In addition, patients with a MCD clinical experience has confirmed measles can be mitigated, studies have shown that measles virus infection in Treg cells number increase, IL - 10 expression increase high, thus speculated that measles virus infection in remission of MCD associated with IL - 10 continuous high expression, reverse phase proved T cell dysfunction related to MCD egg white urine continues. CD80 expression are Abatacept is CTLA - 4 - IgG1, as CD80 antagonism agent clinically used to treat patients with MCD, urine CD80 molecule in the treatment of obviously dropped to disappear within 24 hours, at the same time accompanied by proteinuria rapid decline in 72 hours, the treatment effect is only lasted for 11 days, when proteinuria relapse again, continue to offer Abatacept treatment still has achieved good results, further confirmed CTLA 4 in patients with MCD to adjust the action of CD80.

Clinical Application of CD80

The relationship between FSGS and MCD has always been the focus of debate among scholars. Some scholars believe that these two pathological types are two stages of a disease, and some scholars believe that it is a completely different disease. The researchers looked for more evidence to confirm their relationship. The comparison of CD80 in FSGS and MCD was not satisfactory, urinalysis. Ga such rin, such as\textsuperscript{[11, 12]} many times found CD80 expression in MCD episode in the urine of patients and patients with FSGS episodes have significant statistical difference, patients with FSGS episode MCD patients and other patients with glomerular diseases CD80 increases obviously high in his urine. Large single-center clinical control studies showed that CD80 could be used as a suitable diagnostic marker to distinguish MCD and FSGS\textsuperscript{[14]}. The truncation value was 328.98ng/g, with a sensitivity of 81.1% and specificity of 94.4%. The expression level of CD80 in urine was difficult to accurately identify patients with MCD or tip type and NOS type FSGS. Kidney pathology: the glomeruli of the patients with FSGS did not express CD80, and the glomerular CD80 in some FSGS patients was also positive.

IgA nephropathy, lupus nephritis and diabetic nephropathy are common chronic diseases in China. The cause of kidney disease. It was found that CD80 was also expressed in renal pathology of IgA nephropathy and lupus nephritis, mainly expressed in renal tubular epithelial cells. In the pathological study of diabetic nephropathy, the result of the contradiction was obtained. At present, the researches on CD80 and MCD are mostly confined to children, and there are few studies on adult MCD, and the study on the functional changes of CD80 related foot cells and the pathogenesis of proteinuria is not yet advanced. Whether CD80 can be applied in clinical differentiation of FSGS and MCD requires further multi-center clinical studies, and
the pathogenesis of the disease is discussed, which leads to new strategies for the diagnosis and treatment of FSGS and MCD in the future.

References


