Abstract: The renal glomerulus is composed of three types of glomerular cells (mesangial cell (MC), endothelial cell and podocyte) and extracellular matrix (ECM) consisting of the glomerular basement membrane (GBM) and mesangial matrix. It constitutes a highly specialized microcirculation in which the permeability characteristics of the capillary wall allow its unique filtration function. The proliferation of MCs, an increase of mesangial ECM and detachment podocyte from GBM are key biological features of progressive glomerulonephritis (GN), leading to glomerular scarring and dysfunction. Thus, the study of the molecular and cellular mechanisms responsible for pathological glomerular alterations may help to elucidate the pathogenesis of progressive glomerular diseases. A growing body of evidence indicates that β1 integrin family (β1 integrins), that mainly mediates cell adhesion to ECM, controls cell behaviors such as cell migration, proliferation, apoptosis and ECM assembly. In addition, a correlation between glomerular expression of β1 integrins and their ligand ECM components is observed in various human and experimental GN, suggesting that altered β1 integrins-mediated cell behaviors may contribute to the progression of GN. It is now becoming apparent that the expression of glomerular β1 integrins is not only critical for maintaining the glomerular capillary permeability but it modulates cell signaling pathways regulating the cell phenotypes involved in the progression of glomerular diseases. J. Med. Invest. 51: 1-13, February, 2004

Keywords: β1 integrins, Glomerulosclerosis, Focal adhesion kinase (FAK), Transforming growth factor-β (TGF-β), Platelet-derived growth factor (PDGF), Mitogen activated protein kinase (MAPK)
Function and structure of β₁ integrins

Role of β₁ integrins in glomerular injury

<table>
<thead>
<tr>
<th>α₁β₁</th>
<th>α₂β₁</th>
<th>α₃β₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>α₁β₁</td>
<td>α₂β₁</td>
<td>α₃β₁</td>
</tr>
</tbody>
</table>

In vitro and in vivo analyses indicate that β₁ integrins play a crucial role in glomerular injury. The interaction between α₁β₁, α₂β₁, and α₃β₁ integrins and their ligands is essential for the development and progression of glomerulosclerosis.

S. Kagami et al. β₁ integrins and glomerulosclerosis
Renal perfusion with either anti-α1 Ab or control IgG1

SD rats

0 3 7 days

Injection of anti-Thy-1 antibody (Ab)

Histological evaluation

normal + control IgG1 + anti-α1 Ab
Role of β1 integrins in MC-induced ECM assembly

In vitro studies have shown that the αβ integrins play a significant role in the formation of extracellular matrix (ECM) in mesangial cells (MCs). Specifically, it has been demonstrated that the αβ integrins are involved in the assembly of ECM in MCs, which is critical for the development of glomerulosclerosis. The interaction between αβ integrins and ECM plays a crucial role in the pathogenesis of glomerulosclerosis. In vitro studies have shown that the αβ integrins are involved in the assembly of ECM in MCs, which is critical for the development of glomerulosclerosis. The interaction between αβ integrins and ECM plays a crucial role in the pathogenesis of glomerulosclerosis.
β integrins-mediated signaling pathways regulate cell proliferation, survival and ECM remodeling by MCs
S. Kagami et al. β integrins and glomerulosclerosis

αβ1 integrins and glomerulosclerosis

A

<table>
<thead>
<tr>
<th>Control</th>
<th>S(5)</th>
<th>AS(1)</th>
<th>AS(5)</th>
</tr>
</thead>
</table>

% Initial diameter

B

Control | S(5) | AS(1) | AS(5)

* *


A

Cell adhesion
(630nm)

Control | S | AS


Cell migration
(Cells per field)

Control | S | AS

B

Control | S | AS

Total-ERK1
Total-ERK2

Phospho-ERK1
Phospho-ERK2

The Journal of Medical Investigation Vol. 51 February 2004

\[ \text{Cell adhesion (630nm)} \]

\[ \text{Cell migration (Cells per field)} \]

\[ \text{Control | S | AS} \]

\[ \text{Total-ERK1 | Total-ERK2} \]

\[ \text{Phospho-ERK1 | Phospho-ERK2} \]
Migration, Proliferation, Apoptosis, ECM assembly

et al. 1 integrins and glomerulosclerosis

S. Kagami et al. β1 integrins and glomerulosclerosis
in vivo
The Journal of Medical Investigation  Vol. 51  February 2004