

## ***Supplemental material***

### **Glomerular filtration barrier dysfunction in a self-limiting, RNA virus-induced glomerulopathy resembles findings in idiopathic nephrotic syndromes**

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*Tables*

**Table S1:** Baseline characteristics of healthy controls in comparison to hantavirus patients

|                              | Hantavirus patients<br>(n=26) | Healthy controls<br>(n=18) | p-value |
|------------------------------|-------------------------------|----------------------------|---------|
|                              | Median (Range)                | Median (Range)             |         |
| Age [years]                  | 36.5 (18-62)                  | 35.5 (18-63)               | 0.694   |
| Sex [male/female]            | 19/7                          | 13/5                       | 0.963   |
| <b>Laboratory parameters</b> |                               |                            |         |
| Serum creatinine max [mg/dl] | 5.1 (1.93-18.02)              | 0.78 (0.52-1.10)           | <0.0001 |
| Serum urea max [mg/dl]       | 88.5 (38.0-221.0)             | 29.0 (19.0-44.0)           | <0.0001 |
| Serum albumin min [g/l]      | 35.4 (22.7-42.4)              | n.a.                       |         |
| CRP max [mg/l]               | 59.5 (4.2-151.3)              | n.a.                       |         |
| Hemoglobin min [g/l]         | 12.3 (10.1-14.5)              | 15.1 (12.4-16.80)          | <0.0001 |
| Hematocrit min [l/l]         | 0.35 (0.30-0.44)              | 0.44 (0.37-0.48)           | <0.0001 |
| Platelets min [G/l]          | 126.5 (21.0-291.0)            | 228.5 (158.0-401.0)        | <0.0001 |
| Leukocytes max [G/l]         | 10.1 (5.0-14.5)               | 6.41 (4.18-9.78)           | <0.0001 |
| ACR max [mg/gCr]             | 1,592.9 (13.8-29,759.2)       | 5.3 (2.2-13.4)             | <0.0001 |
| PCR max [mg/gCr]             | 2,930.6 (42.2-50,219.7)       | 43.7 (19.1-89.9)           | <0.0001 |

ACR = albumin-to-creatinine ratio, CRP = C-reactive protein, gCr = gram creatinine, max = maximum, min = minimum, n.a. = not available, PCR = protein-to-creatinine ratio.

**Table S2:** Clinical symptoms of 26 patients with acute hantavirus infection

| Clinical symptoms      | All patients<br>(n=26) | Moderate PCR<br>(n=13) | Severe PCR<br>(n=13) | p-value |
|------------------------|------------------------|------------------------|----------------------|---------|
|                        | Patients (%)           | Patients (%)           | Patients (%)         |         |
| Fever                  | 23 (88.5)              | 11 (84.6)              | 12 (92.3)            | 0.539   |
| Flank pain / Back pain | 22 (84.6)              | 11 (84.6)              | 11 (84.6)            | 0.588   |
| Abdominal pain         | 16 (61.5)              | 7 (53.8)               | 9 (69.2)             | 0.271   |
| Headache               | 24 (92.3)              | 12 (92.3)              | 12 (92.3)            | 0.327   |
| Nausea                 | 21 (80.8)              | 10 (76.9)              | 11 (84.6)            | 0.619   |
| Vomiting               | 18 (69.2)              | 9 (69.2)               | 9 (69.2)             | >0.999  |
| Diarrhea               | 4 (15.4)               | 1 (7.7)                | 3 (23.1)             | 0.277   |
| Blurred vision         | 13 (50.0)              | 8 (61.5)               | 5 (38.5)             | 0.239   |

PCR = protein-to-creatinine ratio.

**Table S3:** Foot process width in three patients with acute hantavirus infection and one healthy control

| Statistical parameters | Control | Hantavirus patient I | Hantavirus patient II | Hantavirus patient III |
|------------------------|---------|----------------------|-----------------------|------------------------|
| N                      | 117     | 132                  | 122                   | 126                    |
| Mean [nm]              | 516.8   | 488.5                | 442.2                 | 446.4                  |
| SD [nm]                | 353.3   | 347.6                | 279.1                 | 304.8                  |
| Min [nm]               | 84.2    | 125.2                | 109.9                 | 79.8                   |
| Max [nm]               | 1,885.5 | 2,064.2              | 1,998.3               | 2,301.0                |

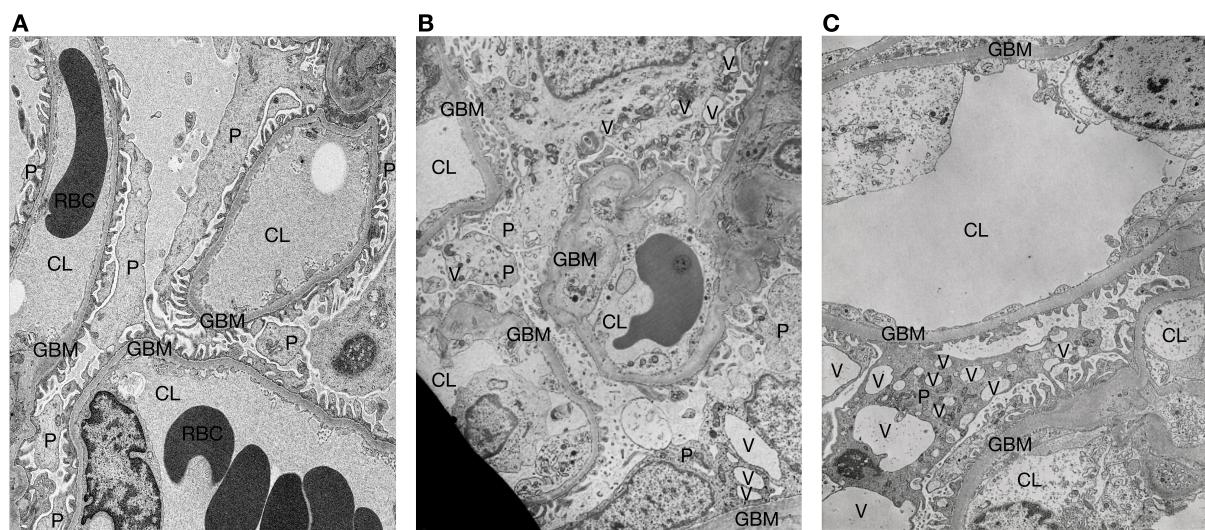
Max = maximum, min = minimum, SD = standard deviation, N = number of measurements performed.

**Table S4:** Serum suPAR correlation analyses

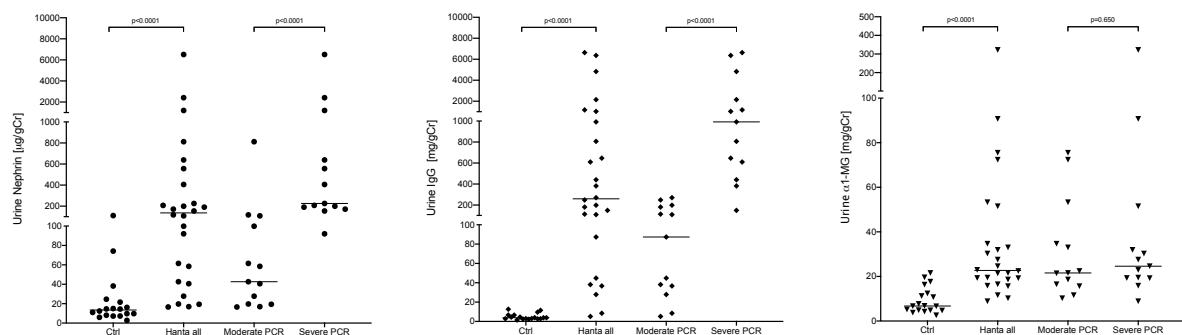
| Renal parameters | suPAR [pg/mL] on admission |              |
|------------------|----------------------------|--------------|
|                  | r                          | p-value      |
| PCR [mg/gCr]     |                            |              |
| Adm (n=26)       | 0.41                       | <b>0.038</b> |
| 24h (n=24)       | 0.42                       | <b>0.043</b> |
| 48h (n=25)       | 0.41                       | <b>0.042</b> |
| Max (n=26)       | 0.44                       | <b>0.023</b> |
| ACR [mg/gCr]     |                            |              |
| Adm (n=26)       | 0.50                       | <b>0.009</b> |
| 24h (n=24)       | 0.40                       | 0.056        |
| 48h (n=25)       | 0.28                       | 0.192        |
| Max (n=26)       | 0.53                       | <b>0.005</b> |
| IgG [mg/L]       |                            |              |
| Adm (n=26)       | 0.51                       | <b>0.008</b> |
| 24h (n=24)       | 0.39                       | 0.061        |
| 48h (n=21)       | 0.49                       | <b>0.026</b> |
| SCr [mg/dL]      |                            |              |
| Adm (n=26)       | 0.13                       | 0.515        |
| 24h (n=24)       | 0.31                       | 0.127        |
| 48h (n=21)       | 0.29                       | 0.170        |
| Max (n=26)       | 0.30                       | 0.143        |
| Nephrin [ng/mL]  |                            |              |
| Adm (n=26)       | 0.45                       | <b>0.021</b> |
| 24h (n=24)       | 0.36                       | 0.095        |
| 48h (n=21)       | 0.31                       | 0.177        |

ACR = albumin-to-creatinine ratio, Adm = day of admission, IgG = immunoglobulin G, PCR = protein-to-creatinine ratio, SCr = serum creatinine, suPAR = soluble urokinase plasminogen activator receptor.

## Figures



**Figure S1:** Exemplary electron microscopy pictures of podocyte vacuolization in patients with acute hantavirus infection. **A** healthy control (living kidney donation), **B/C** patients with acute hantavirus infection CL = capillary lumen, GBM = glomerular basement membrane, P = podocyte, V = vacuole.



**Figure S2:** Admission levels of urinary nephrin, immunoglobulin G (IgG),  $\alpha$ -1 microglobulin ( $\alpha$ 1-MG) normalized to urinary creatinine excretion and in relation to the extent of total proteinuria (protein-to-creatinine ratio, PCR) in patients with acute hantavirus infection (n=26) and age and gender-matched, healthy controls (n=18).