

## Materials and methods

*Study groups and sampling time points* (Supplementary Figure 1):

All bolus injections were given over 20 seconds.

Group 7: Time points for obtaining blood samples for 1/3 bolus three times RMP treatment group (three consecutive bolus injections 7.5 min apart, each injection of  $2.02 \times 10^{10}$  RMPs / kg, i.v.) were 0 (pre-dose), 15, 30 and 45 minutes post-first dose.

Group 8: Time points for obtaining blood samples for RMP dose infused over thirty minutes group (one bolus injection of one-third of the total dose was followed, after a break of 40 seconds, by an infusion of two-thirds of the total dose administered over the remaining 29 minutes; total dose =  $6.07 \times 10^{10}$  RMPs / kg, i.v.) were 0 (pre-dose), 15, 30, and 45 minutes post-first dose.

Group 9: Time points for obtaining blood samples for 4 times the single dose group (one bolus injection of one-tenth of the total dose administered was followed, after a break of 40 seconds, by an infusion of nine-tenths of the total dose administered over the remaining 59 minutes; total dose =  $2.43 \times 10^{11}$  RMPs / kg, i.v.) were 0 (pre-dose), 15, 30, 45, 60, and 75 minutes post-first dose.

## Results

Number of RMPs injected:

Total number of RMPs administered to group 7-8 were  $6.07 \times 10^{10}$  RMPs / kg. Group 9 received RMPs dose of  $2.43 \times 10^{11}$  RMPs / kg (Supplementary Figure 1).

#### The effect of RMP-treatment on physiological parameters

To determine potential side-effect / toxicity of RMP injection to animals, we monitored physiological parameters such as mean arterial blood pressure, blood gases (pH, pCO<sub>2</sub>, and pO<sub>2</sub>), body and head temperature, and hematocrit at baseline and after RMP injection for different in vivo experiments (Supplementary Figure 2-6). We did not observe any adverse effects of RMP injection. However, we did observe a minor but significant drop in blood pH ( $7.43 \pm 0.02$  at 45 min post-RMP injection vs  $7.47 \pm 0.00$  at baseline) and body temperature ( $36.95 \pm 0.05$  °C at 45 min post-RMP injection vs  $37.30 \pm 0.08$  °C at baseline) for animals belonging to group 8 (Supplementary Figure 3). A minor but significant increase in blood pO<sub>2</sub> ( $139 \pm 7$  mmHg at 45 min post-RMP injection vs  $115 \pm 4$  mmHg at baseline) was also noted for animals belonging to group 8 (Supplementary Figure 3). We also observed a significant drop in hematocrit values over time for animals belonging to group 7 (Supplementary Figure 2), group 8 (Supplementary Figure 3), and group 9 (Supplementary Figure 4), potentially due to frequent blood withdrawal for the parameter studied. In general, we did not observe any toxic side-effect (drop in blood pressure or pO<sub>2</sub>, or increase in pCO<sub>2</sub> post-injection) of RMP therapy to rats.

## **Figure legends:**

### **Supplementary Figure 1**

Schematic representation of experimental protocol with dosing and sampling time points.

### **Supplementary Figure 2**

Physiological parameters A) mean arterial blood pressure, B) blood pH, C) blood pCO<sub>2</sub>, D) blood pO<sub>2</sub>, E) body temperature, F) head temperature, G) hematocrit, and H) body weight for animals used in the study using 1/3 bolus three times regimen. \*\*\* p<0.001 compared to base line.

### **Supplementary Figure 3**

Physiological parameters A) mean arterial blood pressure, B) blood pH, C) blood pCO<sub>2</sub>, D) blood pO<sub>2</sub>, E) body temperature, F) head temperature, G) hematocrit, and H) body weight for animals used in the study using infuse first bolus dose over 30 min regimen. \* p<0.05 and \*\* p<0.01 compared to base line.

### **Supplementary Figure 4**

Physiological parameters A) mean arterial blood pressure, B) blood pH, C) blood pCO<sub>2</sub>, D) blood pO<sub>2</sub>, E) body temperature, F) head temperature, G) hematocrit, and H) body weight for animals used in the study using four times the single dose infused over 60 min regimen. \*\* p<0.01, and \*\*\* p<0.001 compared to base line.

### **Supplementary Figure 5**

Physiological parameters A) mean arterial blood pressure, B) blood pH, C) blood pCO<sub>2</sub>, D) blood pO<sub>2</sub>, E) body temperature, F) head temperature, G) hematocrit, and H) body weight for animals used in thromboembolism study using four times the single dose infused over 60 min regimen.

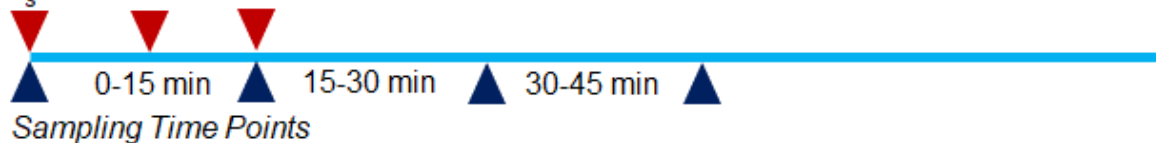
### **Supplementary Figure 6**

Physiological parameters A) mean arterial blood pressure, B) blood pH, C) blood pCO<sub>2</sub>, D) blood pO<sub>2</sub>, E) body temperature, F) head temperature, G) hematocrit, and H) body weight for animals used in biodistribution study using a single bolus regimen.

## Supplementary Figure 1

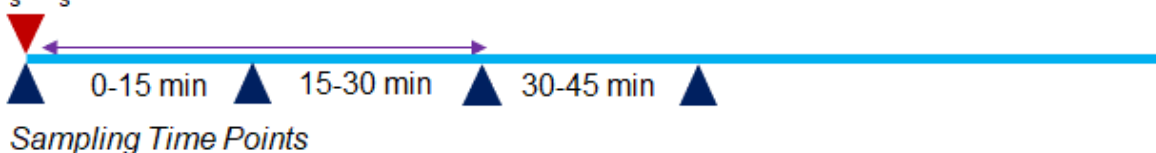
### Group 1: 1/3 bolus three times RMP treatment

$$(\frac{1}{3} \times 3) = 6.07 \times 10^{10} \text{ RMPs / kg}$$



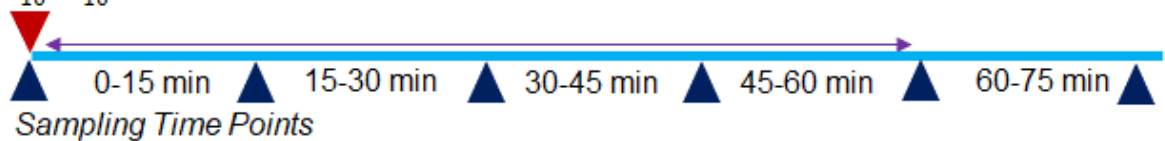
### Group 2: RMP dose infused over thirty minutes

$$(\frac{1}{3} + \frac{2}{3}) = 6.07 \times 10^{10} \text{ RMPs / kg}$$

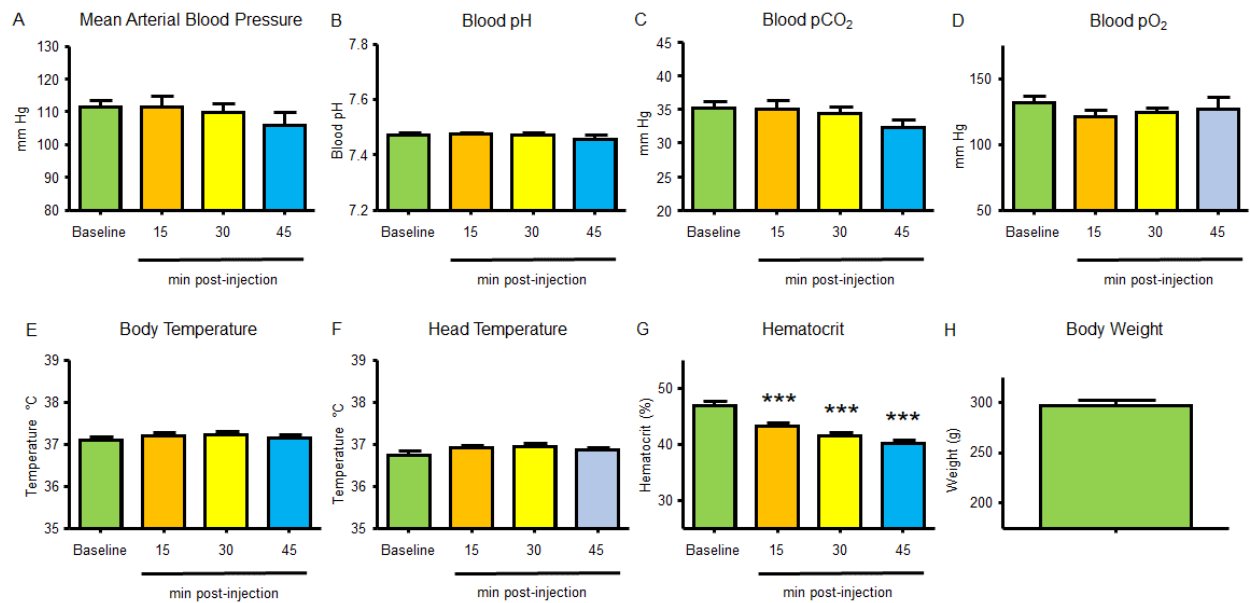


### Group 3: 4 times RMP dose infused over sixty minutes

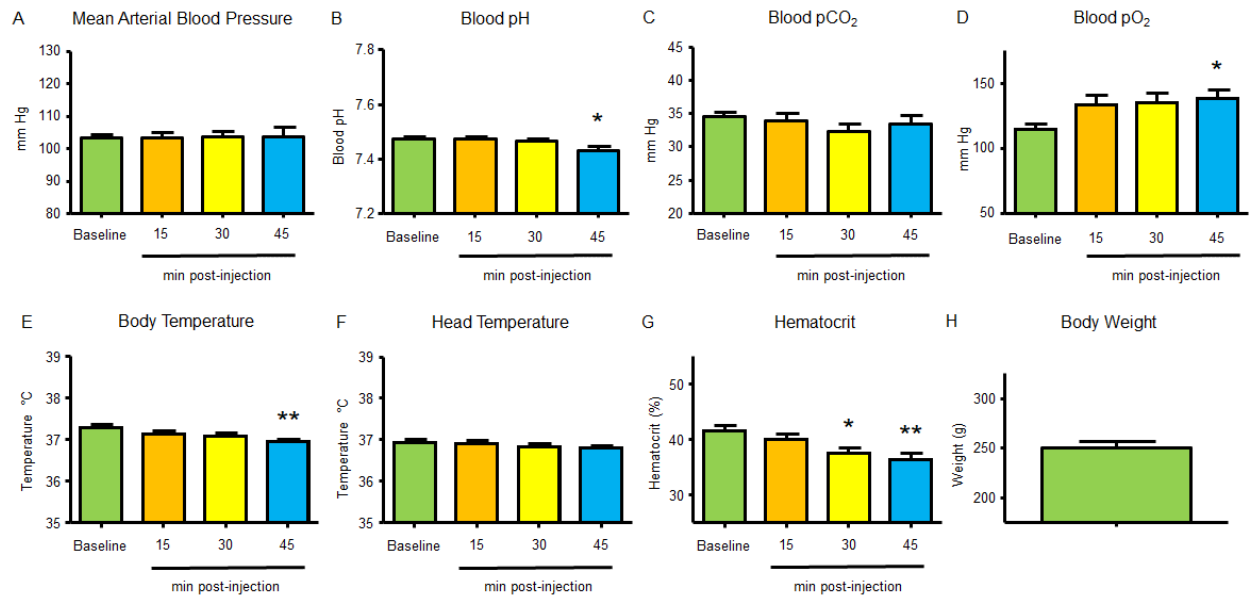
$$(\frac{1}{10} + \frac{9}{10}) = 2.43 \times 10^{11} \text{ RMPs / kg}$$



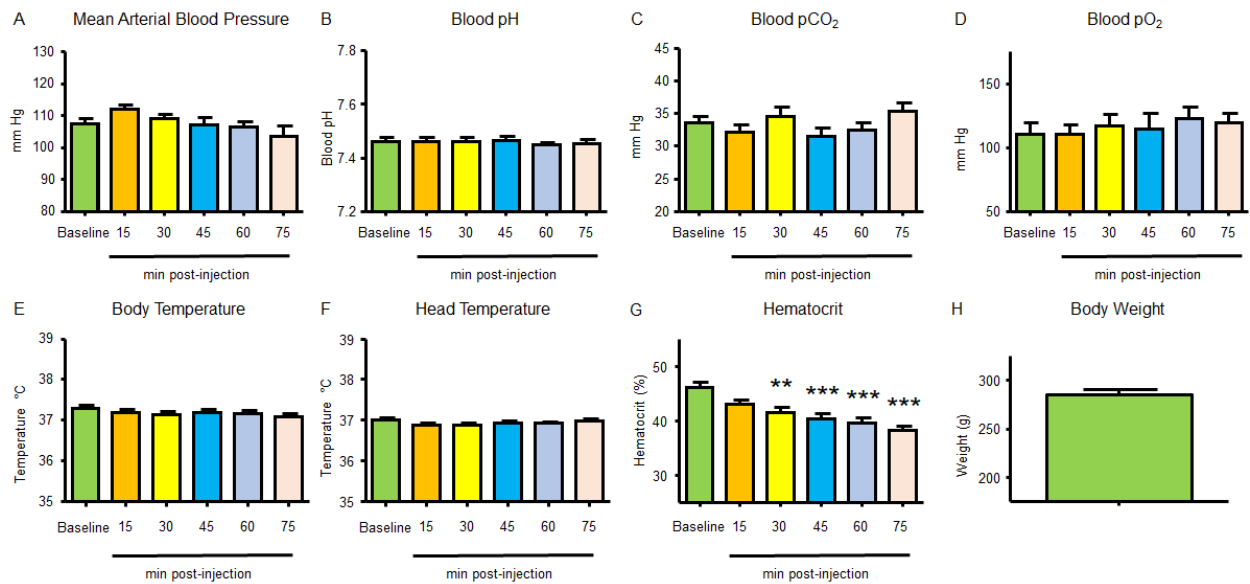
Supplementary Figure 2



Supplementary Figure 3

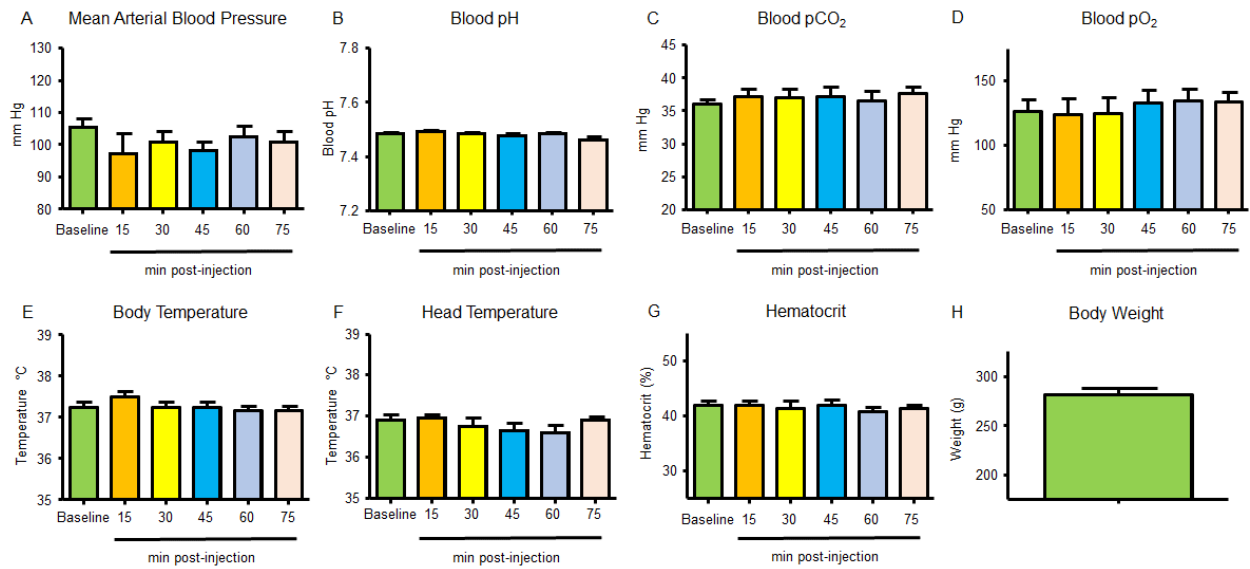


Supplementary Figure 4





Supplementary Figure 5



Supplementary Figure 6

