Influence of genetic variations in TLR4 and TIRAP/Mal

On the course of sepsis and pneumonia and cytokine release:

An observational study in three cohorts

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Supplemental material

Table S1 Reasons for ICU admissions in the different patient cohorts

Type of surgery / Reason for admission	*[No (%) of patients]*
Group I (n=375)	
Upper-GI resection	123 (27.6)
Colorectal resection	105 (30.4)
[a]*Other abdominal*	78 (22.1)
Thoracic	27 (7.7)
Limb and others	42 (12.5)
Group II (n=159)	
Brain hemorrhage	26 (43.9)
Multiple injuries	26 (29.3)
Respiratory failure	68 (14.6)
Postoperative support	27 (2.4)
Other	12 (9.8)
Group III (n=415)	
CABG	242 (58.1)
Valve repair	41 (9.9)
Combined	54 (13.0)
[b]*Other*	78 (18.8)
ECC	375 (90.4)

[a]Other abdominal operations: pancreas-, liver- and multiple visceral organ resection. [b]Other procedures: Aortic replacement, peripheral vascular procedure or thoracic procedure. CABG = Coronary artery bypass grafting, ECC = extracorporal circulation, GI = gastro-intestinal

Table S2 Characteristics of the different patient groups:

Characteristic	Group I (n=375)	Group II (n=159)	Group III (n=415)	Controls (n=176)
Age, (years, mean ± SD)	61.8 ± 12.6	59.6 ± 18.6	66.5 ± 12.2	30.8 ± 3.7
Male/female	238 / 137	119 / 40	305 / 110	152 / 24
Co-existing diseases [No (%) of patients]				
Arterial hypertension	157 (41.9)	16 (10.1)	279 (67.2)	- -
Myocardial disease	129 (34.4)	31 (19.5)	401 (96.6)	- -
Diabetes	77 (20.5)	23 (14.5)	132 (31.8)	- -
Lung pathology	69 (18.4)	3 (1.9)	41 (9.9)	- -
Renal pathology	25 (6.7)	2 (1.3)	57 (13.7)	- -

SD = standard deviation

Table S3. Detailed clinical characteristics of 375 postoperative patients (Group I):

	Wild-type Control (n=240)	Any mutant TLR4 (n=41)	Homozygous mutant TIRAP (n=10)	Heterozygous mutant TIRAP (n=75)	Any mutant TIRAP/TLR4 (n=9)
Age (years, mean ± SD)	61.4 ± 13.5	64.0 ± 10.6	58.5 ± 15.0	61.7 ± 10.6	68.6 ± 7.4
Male/female	154/86	18/23	7/3	54/21	5/4
ASA	2.8 ± 0.7	2.8 ± 0.8	2.6 ± 0.7	2.8 ± 0.6	3.1 ± 0.3
Co-existing diseases [No (%) of patients]					
Arterial hypertension	100 (41.7)	19 (46.3)	3 (30.0)	29 (38.7)	6 (66.6)
Myocardial disease	89 (37.1)	11 (26.8)	1 (10.0)	25 (33.3)	3 (33.3)
Diabetes	40 (16.7)	11 (26.8)	3 (30.0)	19 (25.3)	4 (44.4)
Lung pathology	51 (21.3)	4 (9.8)	1 (10.0)	8 (13.3)	5 (55.5)
Renal pathology	15 (6.3)	3 (7.3)	1 (10.0)	5 (6.7)	1 (11.1)
Type of surgery / [No (%) of patients]					
[a]Upper-GI resection	72 (30.0)	18 (43.9)	2 (20.0)	27 (36.0)	4 (44.4)
Colorectal resection	67 (27.9)	12 (29.3)	3 (30.0)	21 (28.0)	2 (22.2)
[b]Other abdominal	53 (22.2)	6 (14.6)	4 (40.0)	13 (15.3)	2 (22.2)
Thoracic	19 (7.9)	1 (2.4)	1 (10.0)	6 (8.0)	- -
Limb and others	29 (12.1)	4 (9.8)	- -	8 (10.7)	1 (11.1)
Infections / [No (%)]	**(n=135)**	**(n=18)**	**(n=9)**	**(n=34)**	**(n=7)**
Pneumonia	54 (40.0)	7 (38.9)	4 (44.4)	17 (50.0)	2 (25.0)
Peritonitis	22 (16.3)	4 (22.2)	3 (33.3)	6 (17.6)	4 (50.0)
Abscess	40 (29.6)	5 (27.8)	1 (11.1)	8 (23.5)	- -
[c]Other	19 (14.1)	2 (11.1)	1 (11.1)	3 (8.8)	1 (12.5)

[a]Upper-GI resection: Esophageal resection, Gastrectomy. [b]Other abdominal surgery: pancreas-, liver- and multiple visceral organ resection. Percentage of infections relates to the number of total infections in a genotype group. [c]Other infections: Urinary tract, catheter related, skin/soft tissue. ASA = American Society of Anesthesiologists, GI = gastro-intestinal, SD = standard deviation

Table S4. Detailed clinical characteristics of 159 patients with ventilator-associated pneumonia (VAP) and sepsis (Group II)

	Wild-type Control (n=106)	Any mutant TLR4 (n=9)	Heterozygous TIRAP (n=40)	Any mutant TIRAP/TLR4 (n=3)
Age (years, mean ± SD)	60.7 ± 18.4	62.9 ± 18.3	56.2 ± 19.4	57.0 ± 19.9
Male/female	80/26	7/2	29/12	3/0
CPIS (mean ± SD)	7.68 ± 1.08	8.00 ± 1.19	7.75 ± 1.48	8.75 ± 1.70
SAPS II score (mean ± SD)	39.0 ± 14.4	38.4 ± 12.4	38.4 ± 13.6	28.0 ± 4.0
White blood cells (/nl, mean ± SD)	13.6 ± 7.3	11.5 ± 4.2	12.7 ± 4.9	15.3 ± 4.6
[a]pO_2/FiO_2 (mean ± SD)	228.7 ± 121.1	223.9 ± 82.7	217.9 ± 101.3	246.1 ± 70.3
Reason for ICU admission [No (%) of patients]				
Brain haemorrhage	14 (13.2)	2 (22.2)	6 (14.6)	- -
Multiple injuries	17 (16.1)	2 (22.2)	9 (21.9)	- -
Respiratory failure	47 (44.3)	5 (55.5)	13 (36.6)	1 (33.3)
Postoperative support	18 (16.9)	--	5 (12.2)	- -
Other	10 (9.4)	--	7 (17.1)	2 (66.7)
Mortality [No (%) of patients]				
	29 (27.4)	2 (22.2)	14 (34.1)	0 (0)

[a]pO_2/FiO_2 ratios as an index of the oxygenation. CPIS = clinical pulmonary infection score. SAPS = Simplified Acute Physiology Score, SD = standard deviation, TLR4 = Toll-like receptor 4, TIRAP = [TIR] – associated protein, VAP = ventilator associated pneumonia

Table S5. Detailed clinical characteristics of 54 matched patients (Group III) following elective cardiac surgery.

Characteristic	*Wild-type Control (n=18)*	*Any mutant TLR 4 (n=18)*	*TIRAP[hom] (n=5)*	*Any mutant TIRAP/TLR4 (n=13)*
Age (years, mean ± SD)	68.5 ± 9.3	70.0 ± 9.7	67.8 ± 8.8	69.1 ± 9.2
Male/female	13/5	13/5	4/1	9/4
ASA class (mean ± SD)	3.3 ± 0.5	3.1 ± 0.3	3.2 ± 0.4	3.2 ± 0.4
Procedures [No (%) of patients]				
CABG	14 (77.8)	15 (83.3)	4 (80.0)	12 (92.3)
Valve repair	1 (5.6)	0 (0.0)	0 (0.0)	0 (0.0)
[a]*Combined*	2 (11.2)	2 (11.2)	1 (20.0)	1 (7.7)
[b]*Other*	1 (5.6)	1 (5.6)	0 (0.0)	0 (0.0)
Mortality [No (%) of patients]				
	1 (5.6)	0 (0.0)	1 (20.0)	1 (7.7)

[a]Combined = CABG + Valve repair. [b]Other = Miscellaneous procedures on extracorporal circulation. ASA = American Society of Anesthesiologists, CABG = Coronary artery bypass grafting, SD = standard deviation.