

Early transient suppression of immune checkpoint proteins T-cell immunoglobulin mucin-3 and programmed cell death-1 in peripheral blood lymphocytes after blastocyst transfer is associated with successful implantation

ZHANG, Tao, ZHU, Wenyue, ZHAO, Yiwei, CHEUNG, Wing Ching, LIU, Yingyu, CHEN, Xiaoyan, DU, Yan, LEUNG, Kam Tong, CHAN, Yiu Leung, WANG, Chi Chiu, LAIRD, Susan <<http://orcid.org/0000-0003-4020-9020>> and LI, Tin Chiu

Available from Sheffield Hallam University Research Archive (SHURA) at:

<http://shura.shu.ac.uk/26006/>

This document is the author deposited version. You are advised to consult the publisher's version if you wish to cite from it.

Published version

ZHANG, Tao, ZHU, Wenyue, ZHAO, Yiwei, CHEUNG, Wing Ching, LIU, Yingyu, CHEN, Xiaoyan, DU, Yan, LEUNG, Kam Tong, CHAN, Yiu Leung, WANG, Chi Chiu, LAIRD, Susan and LI, Tin Chiu (2020). Early transient suppression of immune checkpoint proteins T-cell immunoglobulin mucin-3 and programmed cell death-1 in peripheral blood lymphocytes after blastocyst transfer is associated with successful implantation. *Fertility and Sterility*, 114 (2), 426-435.

Copyright and re-use policy

See <http://shura.shu.ac.uk/information.html>

Table 1. Demographic characteristics of women included in the study (n=51)

Parameters	Pregnant (n=33)	Non-pregnant (n=18)	P value
Age (years)	34.9±3.2	37.3±1.8	0.007
Body mass index (kg/m²)	23.5±3.9	22.8±2.7	0.484
Duration of infertility (years)	4.5±3.7	4.8±2.9	0.231
Type of infertility			
Primary	16 (48.5)	10 (55.6)	0.771
Secondary	17 (51.5)	8 (44.4)	
Infertility diagnosis			
Tubal factor	9 (27.2)	4 (22.2)	
Male factor	17 (51.5)	8 (44.4)	
Ovulation disorder	2 (6.1)	2 (11.1)	
Endometriosis	2 (6.1)	1 (5.6)	
Multiple factors	1 (3.0)	1 (5.6)	
Unexplained	2 (6.1)	2 (11.1)	
Baseline FSH (IU/l)	6.7 (5.9~10)	6.5 (4.9~13.3)	0.953
Endometrial thickness (mm) at time of hCG trigger	10.6±2.5	10.1±1.5	0.368
Number of embryos transferred			
1	32 (96.9)	15 (83.3)	0.083
2	1 (3.1)	3 (16.7)	
Cycle type			
Fresh	3 (9.1)	2 (11.1)	0.817

Frozen	30 (90.9)	16 (88.9)	
natural	20 (66.7)	7 (43.8)	0.063
HRT	10 (33.3)	9 (56.2)	

Data are presented with mean \pm SD for parametric data, median (range) for non-parametric data and number (%) for categorical variables.

FSH = follicle-stimulating hormone; hCG = human chorionic gonadotropin; HRT = hormone replacement treatment.

Table 2. The changing levels of lymphocyte subsets, Tim-3 and PD-1 expression in lymphocyte subsets after ET

Immune cells	NK cells			T cells			NK-like T cells	Tim-3 ⁺ NK cells			Tim-3 ⁺ T cells			Tim-3 ⁺ NK-like T cells	PD-1 ⁺ NK cells	PD-1 ⁺ T cells			PD-1 ⁺ NK-like T cells	
	total NK cells	CD56 ^{dim} NK cells	CD56 ^{bright} NK cells	CD3 ⁺ CD56 ⁻ T cells	CD8 ⁺ T cells	CD4 ⁺ T cells		Total Tim-3 ⁺ NK cells	Tim-3 ⁺ CD56 ^{dim} NK cells	Tim-3 ⁺ CD56 ^{bright} NK cells	Tim-3 ⁺ CD3 ⁺ CD56 ⁻ T cells	Tim-3 ⁺ CD8 ⁺ T cells	Tim-3 ⁺ CD4 ⁺ T cells			PD-1 ⁺ CD3 ⁺ CD56 ⁻ T cells	PD-1 ⁺ CD8 ⁺ T cells	PD-1 ⁺ CD4 ⁺ T cells		
Pregnant	D0	14.51 \pm 0.87	94.42 \pm 2.21	4.56 \pm 0.46	57.40 \pm 1.98	35.65 \pm 1.42	56.85 \pm 1.29	6.20 \pm 0.71	34.82 \pm 2.03	35.91 \pm 2.50	25.58 \pm 1.79	3.37 \pm 0.32	4.14 \pm 0.36	2.91 \pm 0.29	3.96 \pm 0.51	ND	26.83 \pm 1.11	26.53 \pm 1.36	26.88 \pm 1.15	31.11 \pm 1.68
	D3	14.92 \pm 1.13	94.31 \pm 2.17	4.70 \pm 0.38	55.98 \pm 1.67	36.62 \pm 1.34	56.16 \pm 1.29	6.18 \pm 0.59	28.59 \pm 2.75*	28.76 \pm 2.46*	23.51 \pm 2.33	2.35 \pm 0.33*	2.92 \pm 0.33*	1.80 \pm 0.26*	2.37 \pm 0.28*	ND	25.18 \pm 1.18*	25.61 \pm 1.61	25.18 \pm 1.20*	29.50 \pm 1.59
	D6	12.84 \pm 1.01	93.76 \pm 2.97	4.98 \pm 0.43	57.72 \pm 2.05	35.40 \pm 1.41	57.76 \pm 1.32	5.64 \pm 0.56	30.62 \pm 1.81*	30.89 \pm 1.98*	25.54 \pm 2.40	2.49 \pm 0.25*	3.32 \pm 0.34*	1.78 \pm 0.18*	2.85 \pm 0.39*	ND	24.60 \pm 1.12*	24.04 \pm 1.52*	25.00 \pm 1.14*	29.52 \pm 1.55
	D9	13.69 \pm 0.93	94.62 \pm 2.93	4.48 \pm 0.34	56.51 \pm 2.12	35.28 \pm 1.44	57.25 \pm 1.41	6.31 \pm 0.71	41.72 \pm 2.06*	42.33 \pm 2.67*	32.39 \pm 2.54*	2.89 \pm 0.22	3.52 \pm 0.25	2.57 \pm 0.19	4.14 \pm 0.43	ND	26.04 \pm 1.21	25.79 \pm 1.49	26.12 \pm 1.00	30.08 \pm 1.61
Non-pregnant	D0	14.01 \pm 0.89	93.66 \pm 2.02	5.31 \pm 0.55	60.43 \pm 1.25	37.66 \pm 1.98	56.34 \pm 2.07	6.44 \pm 0.63	34.01 \pm 1.89	34.49 \pm 1.97	22.02 \pm 1.67	3.08 \pm 0.43	3.68 \pm 0.48	2.82 \pm 0.37	3.15 \pm 0.53	ND	26.03 \pm 1.37	25.88 \pm 1.17	26.11 \pm 1.58	27.56 \pm 2.44
	D3	13.41 \pm 0.86	94.11 \pm 1.99	5.27 \pm 0.53	60.22 \pm 1.39	36.39 \pm 1.88	58.22 \pm 3.66	6.53 \pm 0.74	37.08 \pm 3.32	37.53 \pm 2.84	25.65 \pm 2.64	3.64 \pm 0.55	4.18 \pm 0.58	3.46 \pm 0.46	3.93 \pm 0.68	ND	26.77 \pm 1.17	26.05 \pm 1.11	27.12 \pm 1.64	28.96 \pm 2.34
	D6	13.47 \pm 0.88	94.28 \pm 2.18	5.45 \pm 0.65	60.73 \pm 1.58	36.11 \pm 1.71	58.21 \pm 2.15	6.23 \pm 0.62	37.01 \pm 2.62	37.68 \pm 2.26	24.57 \pm 1.89	3.97 \pm 0.53	4.19 \pm 0.46	3.65 \pm 0.51	4.19 \pm 0.49	ND	26.76 \pm 1.19	26.52 \pm 1.32	26.64 \pm 1.65	29.34 \pm 2.43
	D9	14.59 \pm 1.07	94.61 \pm 2.23	4.95 \pm 0.51	58.39 \pm 3.23	36.69 \pm 1.83	57.46 \pm 3.66	6.60 \pm 0.63	41.83 \pm 3.63*	42.17 \pm 3.24*	28.11 \pm 3.20*	3.16 \pm 0.45	3.25 \pm 0.45	2.99 \pm 0.41	3.11 \pm 0.57	ND	25.65 \pm 1.18	25.42 \pm 1.23	25.86 \pm 1.57	28.48 \pm 2.36

The results were expressed as the mean value \pm standard error of the mean (SEM) (%). ND stands for not detectable. * $P < 0.05$ when compared with D0.

