A Cellular Study of Inflammatory Responses in Women with Polycystic Ovary Syndrome as: "An In vitro Model of Anti Breast Tumor Response" Anti-Breast Tumor Response

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Abstract

Background: Although Polycystic Ovary syndrome (PCOS) is a common endocrine disorder among women of reproductive age; is unclear whether PCOS increases the risk of subsequent development of, Gynecologic cancers namely breast cancer. The present study we aimed to compare the antitumoral ability of peripheral blood mononuclear cells (PBMCs) of women with PCOS with that of healthy controls using the co-culture system between effector cells and target tumor cell lines. Materials & Methods: PBMCs were isolated from 25 women with PCOS and 25 non hirsute eumenorrheic healthy controls by density gradient centrifugation ficoll. Breast tumor cell lines (MDA-468, MCF-7) were incubated as the two target cells and were cultured adjacent to PBMCs in the transwell co-culture system. Proliferation rate of the effectors cells evaluated by BrdU cell proliferation assay after 48 and 72 hours and T CD3+ lymphocytes were assessed using flow cytometry. TNF-α cytokine production was evaluated in cell culture supernatant by sandwich ELISA technique. Results: After 48 hours incubation with MDA-468 and MCF-7, the mean proliferation score of PBMCs was significantly higher in women with PCOS compared to that of healthy controls (921.04; P=0.021 vs 287.6; P=0.002, respectively). In PCOS women, after 72 hours of incubation, TNF-α concentration was significantly reduced compared to 48-hour cultures (921.04 ± 271.4 pg/dl vs 545.6 ± 151.1 pg/dl at 48 h and 72 h intervals respectively, P<0.05); it was increased in healthy controls. There was no significant difference in CD3+ CD8+ cells between the PCOS group and healthy controls. Conclusion: The ability of PBMCs to produce of TNF-α in women with PCOS decreased gradually; as a result of which they may lack the ability required to form an in vitro efficient antitumor response to breast tumor cell lines. It is assumed that threshold activation of mononuclear cells is reduced in women with PCOS and a low-grade inflammatory condition may provide a positive background for arising myeloid derived suppressor cells (MDSCs).

Full-text

However, the manuscript can be downloaded and accessed as a PDF.

Figures
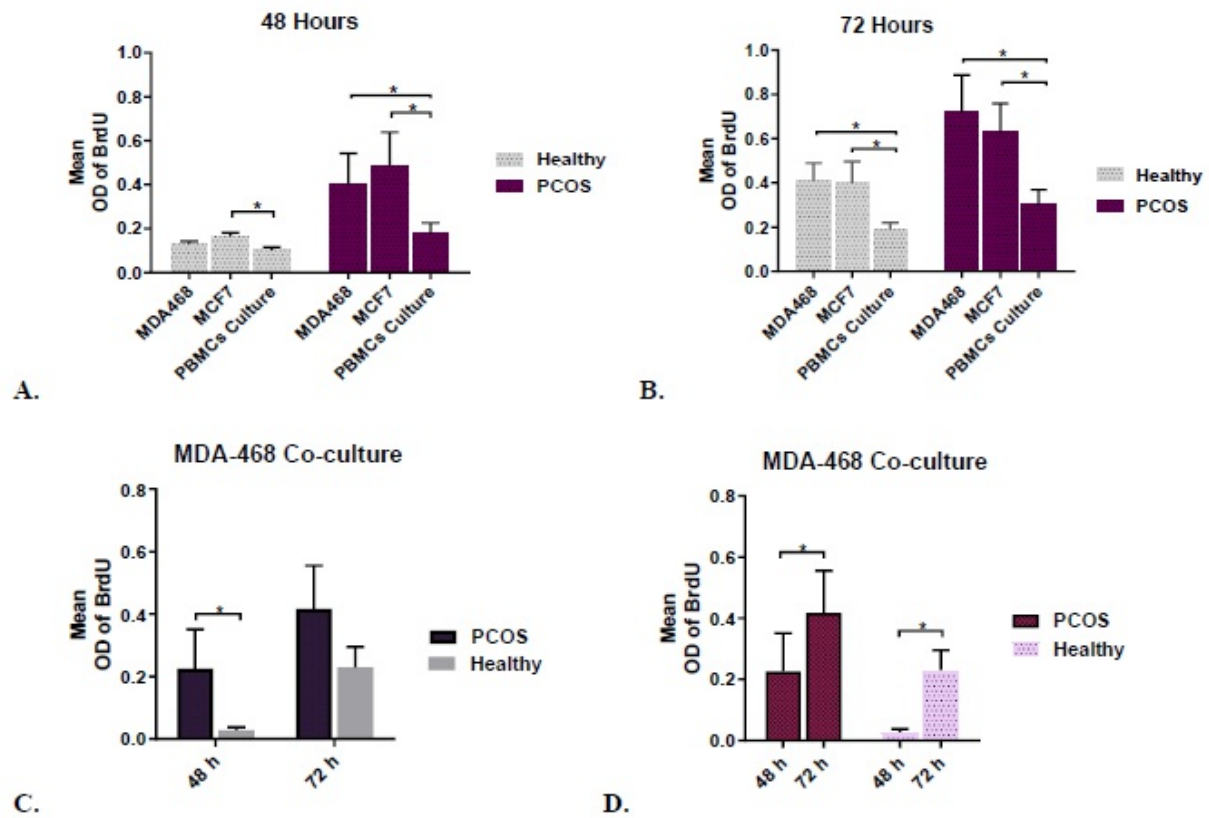
Figure 1

Comparison of mean lymphocyte proliferation score in PCOS and healthy groups. The mean lymphocyte proliferation of MD-468 and MCF-7 cell lines co-culture is compared with PBMCs culture in 48 h (A) and 72 h (B). C: Comparison mean lymphocyte proliferation score in PCOS and healthy groups, and D: Comparison mean lymphocyte proliferation at two time intervals (48 and 72 h) during co-culture with the MDA-468 cell line.
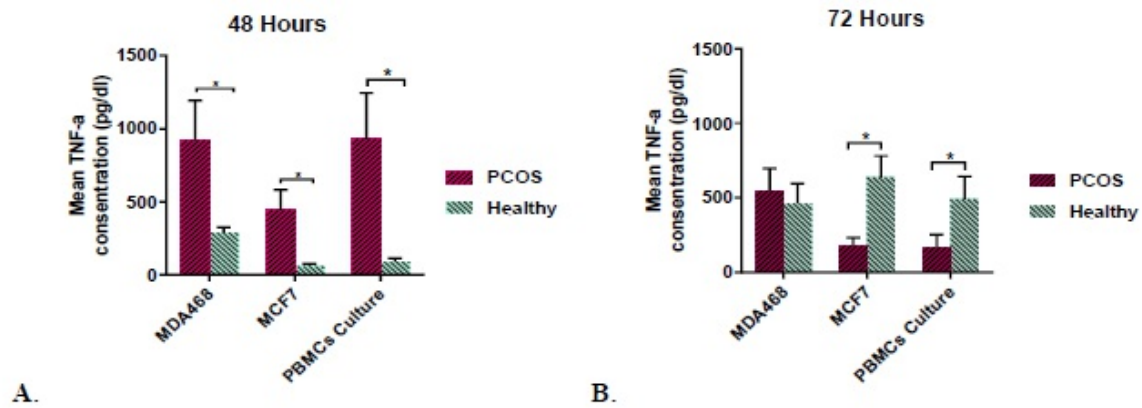
Figure 2

Comparison of mean TNF-α concentration in PCOS and healthy groups The mean TNF-α

concentration in supernatant of MD-468 and MCF-7 cell lines co-culture is compared with

PBMCs culture in 48 h (A) and 72 h (B).
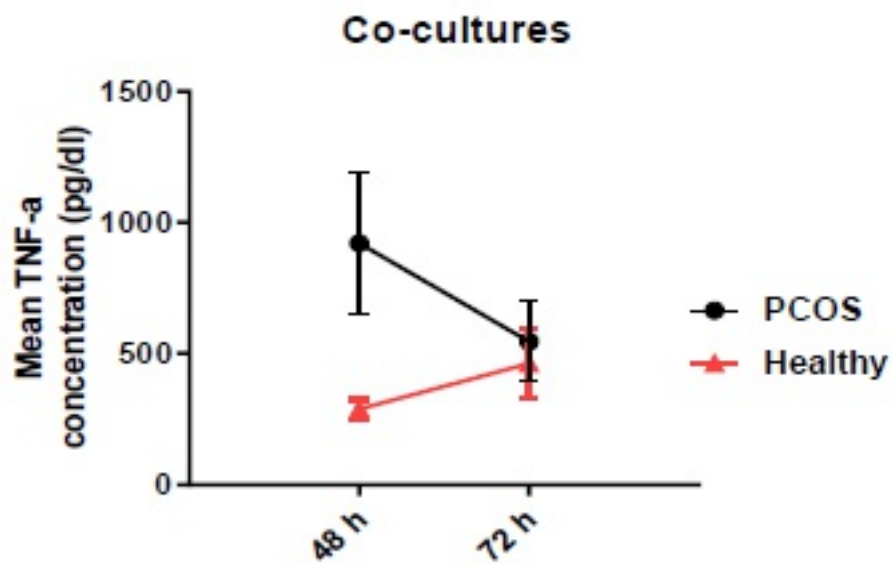
Figure 3

Comparison of mean TNF-α level at two time intervals of 48 and 72 h following co-culture

with MDA-468 tumor cell line.
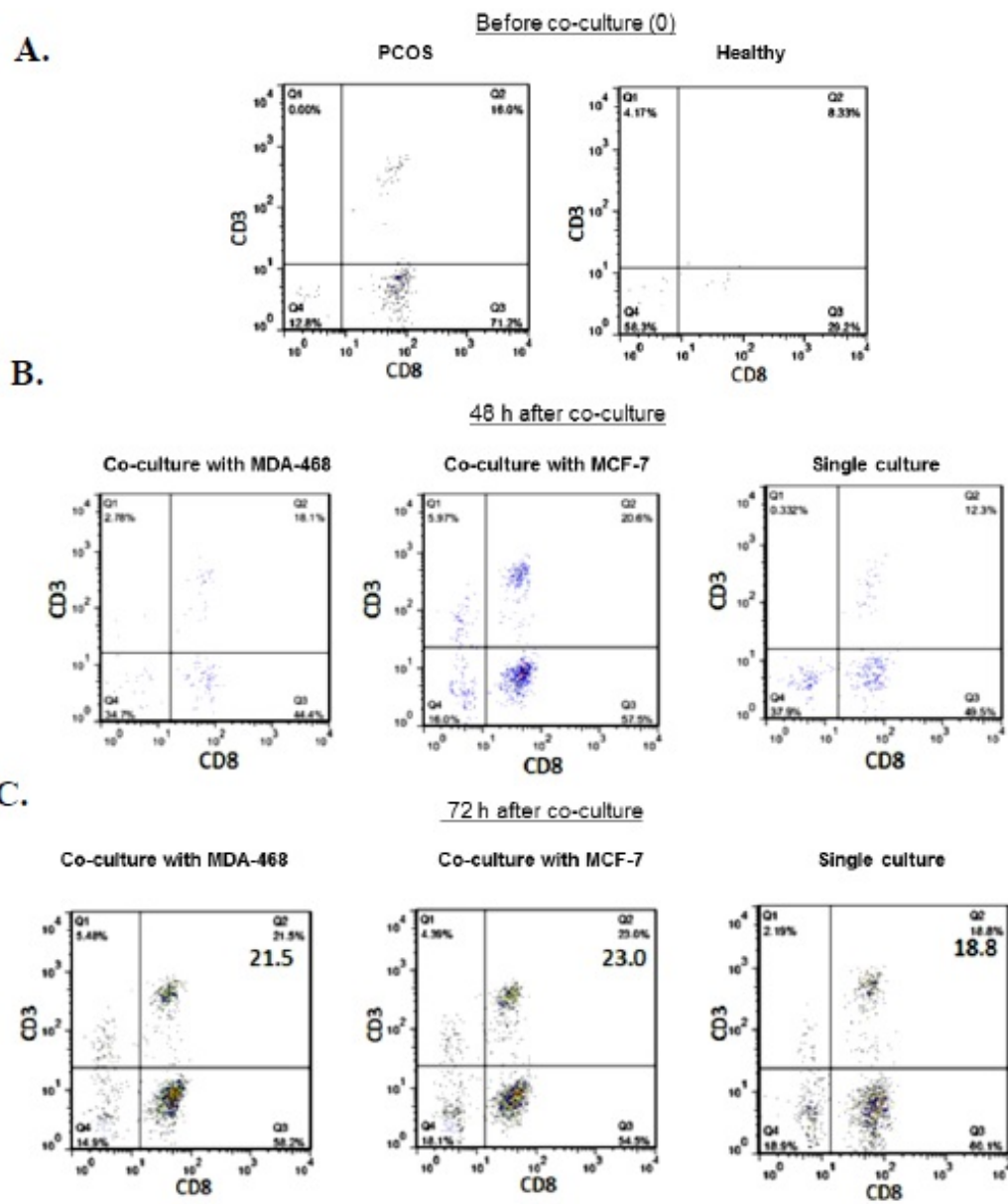
Figure 4

Flow cytometry diagrams associated with evaluating the percentage of T CD3+ CD8+

lymphocytes in three intervals, before co-culture, 48 h (B) and 72 h (C) culture in PCOS

group.

A. B.
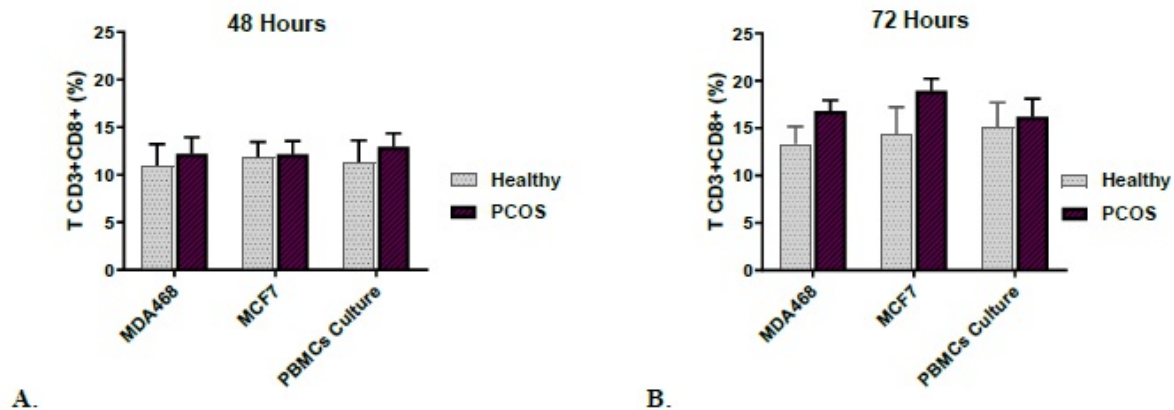
Figure 5

Comparison of mean percentage of TCD3+ CD8+ cytotoxic cells in PCOS and healthy groups

Following co-culture with both tumor cell lines and PBMCs culture, the percentage of these

cytotoxic cells showed no statistically significant difference between the two healthy and

PCOS groups in 48 h (A) and 72 h (B) intervals.
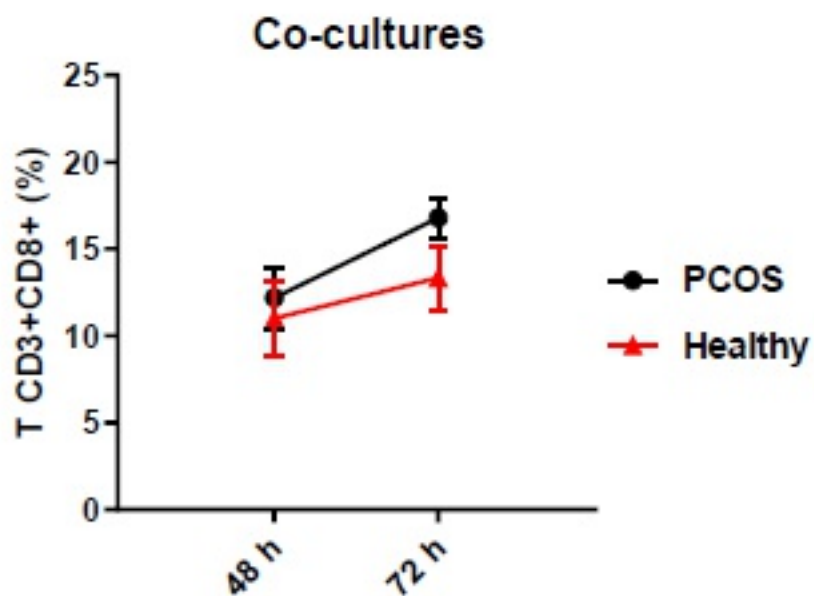
Figure 6

Comparison of mean percentage of TCD3+ CD8+ cytotoxic cells in two intervals of 48 and

72 h following co-culture with the tumor cell lines.