CHANGES IN MONOCYTE FUNCTION IN RESPONSE TO ACUTE EXERCISE IN BREAST CANCER SURVIVORS

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ABSTRACT

BACKGROUND: The effects of acute exercise on immunity following breast cancer therapy are not well understood. **PURPOSE:** To determine the response of monocyte function following acute exercise in breast cancer survivors. **METHODS:** 9 breast cancer survivors [Age: 58±8y, BMI: 27.9±6.7] completed a cardiopulmonary exercise test (CPET). In a subsequent trial, 45 minutes of intermittent cycling at 60% of CPET peak wattage was performed. Blood was taken at rest, immediately post (0h), and 1h post-exercise. Phagocytosis and oxidative burst were assessed following *E.coli* exposure. Toll-like receptor 2 (TLR2) and 4 (TLR4) expression was determined on $CD14^+CD16^-$ and $CD14^+CD16^+$ monocytes. All assays were analyzed using flow cytometry and are presented as mean fluorescence intensity (MFI) ± SD. **RESULTS:** Phagocytosis increased by 13.4% 1 hour after completion of exercise (0h: 3257±772, 1h: 3692±824, p=0.035), while oxidative burst was unchanged. TLR2 expression progressively decreased from rest on both subsets of monocytes (rest: 345±48, 0h: 317±69, 1h: 283±41, all p<0.01). TLR4 expression on $CD16^-$ monocytes decreased by 12.5% from rest to 1 hour post-exercise (rest: 98±14, 1h: 86±11, p=0.009), while TLR4 expression on $CD16^+$ monocytes decreased across all time points (rest: 142±20, 0h: 134±16, 1h: 125±17, all p<0.05). **CONCLUSIONS:** In breast cancer survivors, monocyte phagocytic capacity of bacteria increased following acute exercise, while expression of TLR2 and TLR4 was progressively reduced. The reduction of TLR2 and TLR4 on monocytes may represent an anti-inflammatory response of acute exercise which promotes enhanced elimination of bacteria. Supported by the Breast Cancer Research Foundation of New York.

INTRODUCTION

- In the United States, breast cancer is the most common cancer found in women – 1 in 8 U.S. women will be diagnosed with invasive breast cancer in their lifetime.
- While more women are surviving breast cancer due to increasingly effective treatments, these survivors are facing chronic immunosuppression caused by chemotherapy and radiation treatments.
- The acute effects of exercise on cancer survivors' immunity and immune function are not well understood, including but not limited to, the function of monocytes following an acute bout of exercise.
- Monocytes, a type of leukocyte, respond to inflammation signals in bodily tissues and effect immune responses.
- These immune cells utilize a process called phagocytosis, in which bacteria is ingested and then killed intracellularly through oxidative burst.
- TLR2 and TLR4, proteins expressed on certain subsets of monocytes, have been linked to pro-inflammatory cytokine signaling and are potentially linked to promoting cancer growth.
- Evaluating these processes can help explain how monocyte function is impacted by an acute bout of exercise.
- **Purpose: To determine the response of monocyte function following acute exercise in breast cancer survivors.**

METHODS

Participants: 9 female breast cancer survivors volunteered to participate in this study (Table 1).

Table 1. Participant Characteristics (n=9)	
Age (y)	58 ± 7
Height (cm)	164.9 ± 4.7
Weight (kg)	75.4 ± 15.3
BMI	27.9 ± 6.7
Body Fat (%)	41 ± 5.8

Procedures:

- Following a familiarization visit, participants completed a cardiopulmonary exercise test (CPET) on a stationary cycle ergometer.
- In a subsequent visit, participants performed 45 minutes of intermittent cycling at 60% of their peak wattage (determined by their CPET). Venous blood samples were taken at rest, immediately post-exercise (0hr), and 1hr post-exercise (1hr).
- Phagocytosis and oxidative burst were assessed in whole blood following exposure to *E.coli*. Flow cytometry was used to analyze concentration and mean fluorescence intensity of both processes.

Procedures Continued:

- Monocytes were stained with markers to identify $CD14^+CD16^-$ and $CD14^+CD16^+$ cells and flow cytometry was used to assess these markers, as well as the mean fluorescence intensity of TLR2 and TLR4 expression.
- NO control group was used for this study.

Statistical Analysis: All data were analyzed with SPSS Version 25 using one-way within subjects ANOVAs. Data are presented as mean ± standard deviation and statistical significance was set at $p < 0.05$.

RESULTS

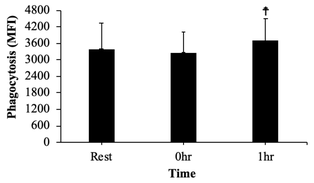

Figure 1. Monocyte phagocytosis significantly increased by 13.4% from 0hr to 1hr following acute exercise ($p = 0.035$).

† Indicates significance, $p < 0.05$ vs. 0hr.

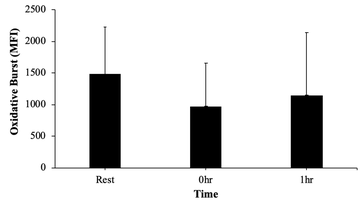

Figure 2. Monocyte oxidative burst remained unchanged across all three timepoints ($p > 0.05$).

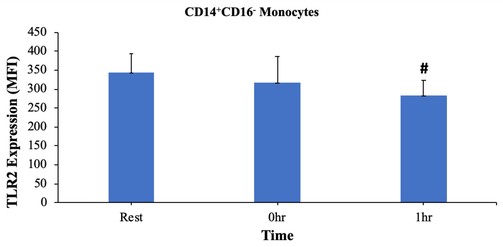

Figure 3. TLR2 expression on $CD14^+CD16^-$ monocytes significantly decreased from rest to 1hr ($p = 0.005$).

# Indicates significance, $p < 0.05$ vs. rest.

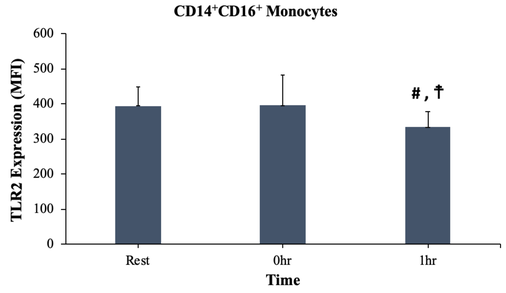

Figure 4. TLR2 expression on $CD14^+CD16^+$ monocytes significantly decreased from rest to 1hr ($p = 0.003$). TLR2 expression decreased from 0hr to 1hr ($p = 0.018$).

# Indicates significance, $p < 0.05$ vs. rest.
† Indicates significance, $p < 0.05$ vs. 0hr.

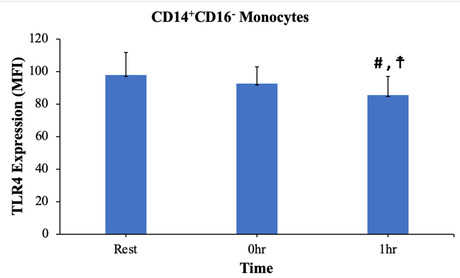

Figure 5. TLR4 expression on $CD14^+CD16^-$ monocytes significantly decreased from rest to 1hr ($p = 0.009$). TLR4 expression decreased from 0hr to 1hr ($p = 0.004$).

# Indicates significance, $p < 0.05$ vs. rest.
† Indicates significance, $p < 0.05$ vs. 0hr.

- TLR2 expression on $CD14^+CD16^-$ monocytes decreased by 18.0% from rest to 1hr.
- TLR2 expression on $CD14^+CD16^+$ monocytes decreased by 15.5% from 0hr to 1hr and by 15.4% from rest to 1hr.

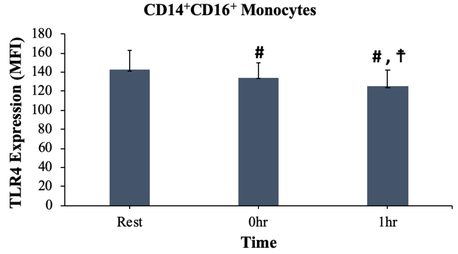

Figure 6. TLR4 expression on $CD14^+CD16^+$ monocytes significantly decreased across all timepoints: rest to 0hr ($p = 0.026$); rest to 1hr ($p = 0.003$); and 0hr to 1hr ($p = 0.016$).

# Indicates significance, $p < 0.05$ vs. rest.
† Indicates significance, $p < 0.05$ vs. 0hr.

- TLR4 expression on $CD14^+CD16^-$ monocytes decreased by 7.7% from 0hr to 1hr and by 12.5% from rest to 1hr.
- TLR4 expression on $CD14^+CD16^+$ monocytes decreased by 5.6% from rest to 0hr, by 7.1% from 0hr to 1hr, and by 12.3% from rest to 1hr.

CONCLUSIONS

- In breast cancer survivors, monocyte phagocytic capacity of bacteria increased following acute exercise, while expression of TLR2 and TLR4 was progressively reduced.
- Increased phagocytosis may demonstrate an improved ability of monocytes to defend against bacteria, however, no change in oxidative burst may attenuate this effect.
- The reduction of TLR2 and TLR4 expression on monocytes may represent an anti-inflammatory response of acute exercise which promotes enhanced elimination of bacteria.

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