

Lilian Lwin, Biology

Year in School: Freshman

Hometown: Columbia, MO

Faculty Mentor: Dr. Kathy L. Timms, Obstetrics, Gynecology, & Women's Health

Funding Source: National Institutes of Health

Peritoneal fluid haptoglobin from women with endometriosis differentially regulates macrophage cytokine production

Lilian Lwin, Terri Lyddon, Randy Zimmer, Breton Barrier, & Kathy Sharpe-Timms

The objective of this study was to define mechanisms by which haptoglobin from endometriotic lesions (eHp) which binds to macrophages modulates immune surveillance and inflammation in the peritoneal cavity by characterizing macrophage products regulated by eHp. To eliminate human macrophage variation, the established THP-1 monocyte cell line (1.0×10^6 cells/mL/well, 24-well plates, RPMI 1640+L-glutamine, FBS, and antibiotics) was routinely differentiated into macrophage-like cells with low dose PMA (20 ng/mL) and concurrently treated with media only (M), serum haptoglobin (sHp) or haptoglobin purified from peritoneal fluid of women without (cHp) or with (eHp) endometriosis (10 μ g/mL, 24 h). The RayBio Inflammatory Antibody Array III was used per instructions and chemiluminescence signal intensity was quantified by densitometry. Differences were evaluated by ANOVA and post hoc tests. Variation in 8 control spots per and between membranes was <9% ($P=0.661$). eHp differentially increased 8/40 substances: Eotaxin-2 (eHp>sHp, cHp, M. $P=0.002$), TNF- α (eHp>sHp, cHp, M. $P=0.045$), TNF- β (eHp>sHp, cHp, M. $P=0.043$), PDGF-BB (eHp>sHp, cHp, M. $P=0.016$), IL-6sR (eHp>cHp, M. $P<0.001$), IL-16 (eHp>sHp>cHp, M. $P=0.072$), IP-10 (eHp, sHp>cHp, M. $P=0.017$), RANTES (eHp, sHp>cHp, M. $P=0.004$) and TGF- β (eHp, sHp>M, cHp. $P=0.008$). Unexpectedly, cHp differentially decreased IL-2 (cHp<eHp, sHp, M. $P=0.001$) and MCP-1 (cHp<eHp, sHp, M. $P=0.023$). Twenty substances were similar in all treatments; the expression range was divided into quartiles: High: IL-8. Moderate: IL-1 β , MIP-1 β . Slight: IL-10, TNFsRII, TIMP-2. Minimal: ICAM, INF-gamma, I-309; IL-1 α , IL-3, IL-6, IL-11, IL-12p40, IL-12p70, IL-15, M-CSF, MIP-1 α , MIP-1 δ and TNFsRI. Nine were not detected in any treatment: Eotaxin-1, GCSF, GM-CSF, IL-4, IL-7, IL-13, IL-17, MCP-2, MIG. Differential eHp up-regulation and cHp down-regulation of macrophage inflammatory substances indicates that the function of eHp, hence the function of macrophages in women with endometriosis is skewed compared to controls. We postulate that peritoneal macrophages interaction with eHp contributes to endometriosis persistence and/or pathophysiologies.