Evolution of intra-tumoral and peripheral pro-tumorigenic response during primary cytoreductive surgery for ovarian cancer

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Disclosures

• I have no financial relationships with ACCME defined ineligible companies to report.

• I will not be discussing any unlabeled or investigational uses of any pharmaceutical products or medical devices.

• The views expressed in this presentation are of the author and do not reflect the official policies of the Department of the Army, the Department of Defense, or the U.S. Government.
Background

- Cytoreductive surgery remains a crucial component of upfront management of advanced-stage ovarian cancer
- Surgical stress facilitates tumor growth and metastases via paracrine and neuroendocrine response

Surgery-induced cytokine response
Surgery-induced catecholamine release
General anesthesia
Systemic opioids

These factors all lead to suppression of Cell-Mediated Immunity (CMI)
Objective

• Investigate the evolution of intra-tumoral and peripheral stress response in patients undergoing primary cytoreductive surgery for advanced stage high grade serous ovarian cancer.
Experimental set-up

- 0h: Laparotomy
- 4h: intraop
- 24h: postop

Serum collection
Tumor and normal peritoneum collection
Observed transcriptomic changes due to laparotomy

0h = at laparotomy
4h = 4 hours post laparotomy
Differential gene expression of tumor tissue

**Volcano plot**

87 DE genes FC 2 pvalue 0.05

- NS
- Log₂ FC
- P
- P and log₂ FC

**KEGG GSEA**

- JAK–STAT signaling pathway
- NOD–like receptor signaling pathway
- Chemokine signaling pathway
- Kaposi sarcoma–associated herpesvirus infection
- Transcriptional misregulation in cancer
- Lipid and atherosclerosis
- Human T–cell leukemia virus 1 infection
- Cytokine–cytokine receptor interaction
- MAPK signaling pathway
- PI3K–Akt signaling pathway

Adjusted P–value

Normalized enrichment score
Laparotomy induces changes in cytokines

Increase in cytokine:
- IL-6 concentration
- IL-8 concentration
- VEGF-A concentration
- IL-10 concentration

Decrease in cytokine:
- IL-1B concentration
- IFNγ concentration
- TNFα concentration
- LAP-1 concentration
Increased IL-6 in peripheral blood and at transcriptomic level

Volcano plot
87 DE genes FC 2 pvalue 0.05
Conclusions

• Laparotomy induces pro-tumorigenic changes in tumors at the transcriptomic level and in the peripheral blood
  • Upregulation of common oncogenic signaling pathways
  • Increase of pro-inflammatory cytokines such as IL-6 in peripheral blood

• Generates rationale for targeting of perioperative inflammatory response to alleviate the post-operative immune dysfunction

• Focused plenary session V, On the Horizon: Emerging Therapeutics – will be presenting murine model results addressing this hypothesis
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