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Introduction:

Ovarian Cancer (OC) remains a leading gynecological cancer with high mortality. Therapeutic intervention is difficult due to advanced disease and complex metastasis at diagnosis. Tumor debulking remains the primary intervention, however residual tumor often remains undetected within the peritoneal cavity due to absence of intraoperative tumor-detection methods. Radiotheranostics is a rapidly growing modality in treating similar metastatic disease, yet inadequate radiobiological studies hinder establishing new standard of care treatments. Therefore, novel methods of intraperitoneal (IP) tumor detection are necessary.

Methods

Our lab has established a peptide-based OC targeted methodology, successfully implemented in rodents, ready for translational studies in Large Animals (LA). However, robust LA models of OC are absent from the field. We propose a method for LA models of human OC using excised human OC xenografted into immunocompetent models. LA models are comparable to human models of metastatic disease in many facets, thus findings will further efforts in earlier detection and provide a model of metastatic IP disease. Establishing our animal model has been completed in steps, validating the progression for subsequent study and now, use of extracted human tissue. First, characterization of targeted moieties of human OC cells was conducted in small animal models (SA). SKOV-3 Luciferase+ OC cells (SKOV-3) were injected into SA peritoneal cavities. Tumor burden was monitored for four weeks using In Vivo Imaging System Bioluminescence (IVIS-BLI) followed by image guided surgical excision. Specimens were fixed in formalin after ex-vivo incubation in artificial IP solution at 0-, 1-, 2-, and 4-hour post-excision times. Tumor stability was measured through histo-analysis expression of OC antigens Claudin 3 and 4, and folate receptor.

Results

Tumors were found to show increasing growth throughout the 4 weeks and positive OC surgical extraction occurred in 100% (9/9) mice who received SKOV-3 IP injection. Histological analysis confirmed the integrity of tumor targeting moieties in all time frames with Claudin 3 showing the greatest viability. Subsequently, tumors were grown in SA models, xenografted into larger SA models, then excised and analyzed at 1- and 2- hour time points. Results of this study were inconclusive.

Conclusion

Currently, pending IRB approval, extracted human OC tissue will be xenografted into LA models and analyzed for tissue viability. We hypothesize there may be a time-sensitive window for study after excision of metastatic OC. This window has been established as at least 4 hours in ex-vivo studies. In-vivo SA xenograft results could mean this time window is less than previously expected, heavily influenced by recipient immune system, or other factors. With human to LA (pig) xenograft studies, we aim to characterize these influences. Such studies will allow for in-vitro OC antigen specific radioisotope labeled detection and eventual pharmacotherapy.