Clinical assessment of MUC1 protein expression in FFPE tissue: Development and validation of an immunohistochemistry assay as a predictive assay for response to MUC1 vaccines

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Introduction
MUC1 (MUC1, Mucin 1, epithelial mucin), a transmembrane glycoprotein that is expressed on the apical membranes of epithelial cells of many tissues including breast, prostate, lung, pancreas, thyroid, ovary, stomach, and intestine, is tumor cells. MUC1 is over-expressed in a range of malignant tumors, including ovarian, breast, lung, and pancreatic cancers. Overexpression is reported in breast and ovarian cancers, where MUC1 is internalized and concentrated in cytoplasmic foci (Johnson et al. 1994; Cullinane et al. 1996). MUC1 has been shown to be associated with increased malignancy and chemoresistance (Tanaka et al. 2008; Zhao et al. 2011; Ito et al. 2015). Several applications are currently being pursued for targeting MUC1 in cancer therapy, mostly focused on vaccines targeting MUC1 antigens. We have developed an immunohistochemistry (IHC) assay to measure MUC1 protein expression in FFPE tissues, and further validate evaluation of MUC1 expression as a potential biomarker for MUC1 targeted therapies.

Materials and Methods
IHC assays were developed using the Ventana Benchmark. The MUC1 antibody was obtained from Ventana Medical Systems. The assay was validated using a recommended protocol supplied by the vendor using a combination of cell line products and formalin-fixed paraffin-embedded (FFPE) human tissue specimens purchased from ILSbio and BioServe. A breast cancer tissue array containing 16 matched adjacent normal and tumor tissue was purchased from BioChain Institute. Tumor positive specimens were scored based on expression of MUC1 in normal breast tissue of at least 20% of tumor cells (Ito et al. 2015). In addition, distribution of staining (apical, membranous, cytoplasmic and combination staining patterns) was noted.

Conclusions
We have developed a robust assay for MUC1 that clearly distinguishes MUC1 expression in normal versus tumor tissue, as well as demonstrates distinct MUC1 expression patterns in a variety of tumor tissues. We are currently using this assay to explore the utility of MUC1 protein expression as a biomarker for ONT-082, a novel oncolytic cancer vaccine that is currently in clinical trials.

References
Tanaka Y et al. Mol Cancer Ther 7:2316-2324, 2008

Figure 1: Expression of MUC1 in normal tissues
Several normal FFPE tissues were evaluated for MUC1 expression. As shown in Figure 1, we did not observe staining of MUC1 in benign male, skin, prostate and placenta sections for the right in the picture.

Figure 2: MUC1 staining patterns in tumor tissues

Table 1. MUC1 IHC data from 16 FFPE tissues

Table 2. MUC1 IHC data from matched breast cancer and adjacent normal tissues

Figure 3: Evaluation of MUC1 staining in a set of matched breast cancer and adjacent normal tissues

Figure 4: Evaluation of MUC1 staining in a set of matched breast cancer and adjacent normal tissues

Figure 5: Graphical representation of MUC1 staining patterns
S5: Frequency of staining patterns in 16 FFPE tissues evaluated
S6: Frequency of staining patterns in 16 duplicate matched breast cancer and adjacent normal FFPE tissues evaluated

Figure 6: A summary of the MUC1 staining patterns obtained for the FFPE tissues is presented in Figure 5.

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