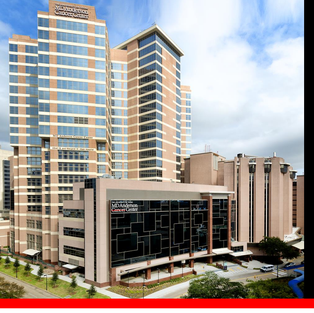

CCR7 Immune Cell Receptor Expression in Inflammatory Breast Cancer

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Introduction

Inflammatory breast cancer (IBC) is a rare form of breast cancer that is characterized by breast skin changes, such as changes in skin color, and breast swelling caused by invasion of tumor emboli into lymphatic vessels. CCR7 is an immune cell receptor known to be upregulated in IBC tumor cells that is involved in immune cell movement into lymphatics.

Our objective is to understand the prevalence of CCR7 in IBC tissues and identify its association with the presence or absence of estrogen receptors (ER) in order to understand its role in IBC proliferation and potential novel therapies.

Materials/Methods

A human tissue microarray (TMA) of 36 primary breast tissue biopsies from IBC patients underwent immunohistochemical staining for CCR7.

The stained TMA was converted to an e-slide and analyzed for percent of positive stain per sample using Aperio ImageScope software. Positivity values reflected total CCR7 presence throughout the sample, including tumor and stromal stain.

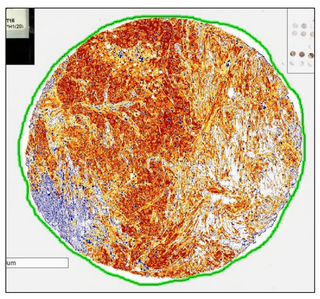

Figure 1. Example of ImageScope analysis on an 84% positive sample. Red indicates a CCR7-positive area; blue is negative.

In order to differentiate between positive tumor and positive stroma, the TMA was then reviewed by an expert pathologist, where tissue cores containing tumor cells (24 out of 36 samples) were evaluated for:

- CCR7 positivity
- Staining pattern
- Percent tumor stained
- Intensity

Results were interpreted alongside ER status.

Results – Aperio ImageScope

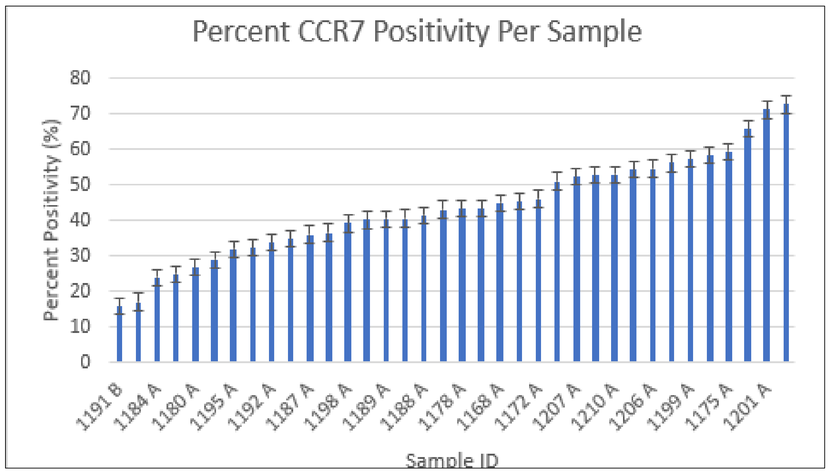

Figure 2. Graph of percent CCR7 positivity. All samples expressed CCR7 positivity in the stroma or tumor (Median = 44%). However, the software did not discriminate between tumor cells and stromal cells, so many samples expressing CCR7 did not actually contain positive tumor cells (See Figures 3A and 3B for examples of false positives).

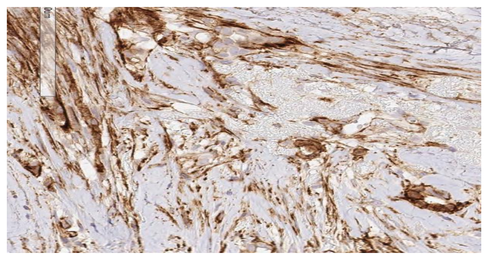

Figure 3A. Positive Stroma. No tumor is present, making this a false positive.

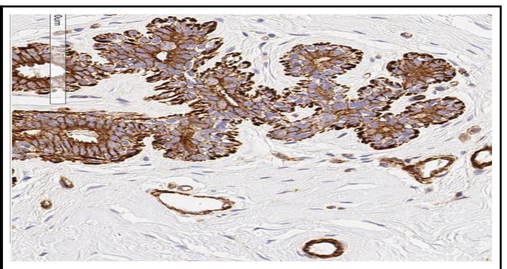

Figure 3B. Positive Mammary Ducts. No tumor is present, making this a false positive.

Results - Pathology

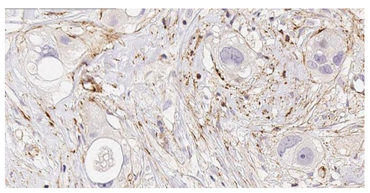

Figure 4A. Negative tumor. Tumor cells are present, but do not stain positive for CCR7.

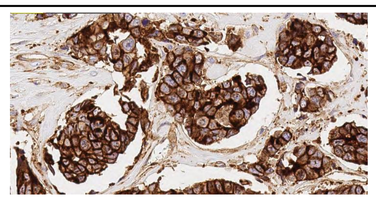

Figure 4B. Tumor cells are CCR7 positive with complete membranous pattern, 3+ intensity, and 100% stain.

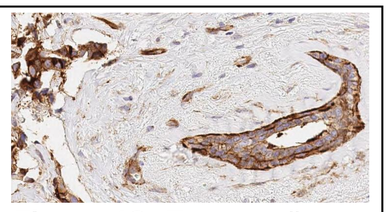

Figure 4C. Tumor cells are CCR7 positive with incomplete membranous pattern, 3+ intensity, and 100% stain.

Pathology Data

CCR7 Positivity		Percent Tumor Stained	
POS	23	100%	14
NEG	1	90%	2
Pattern		80%	4
		50%	2
Complete Membranous	15	10%	1
Incomplete Membranous	8		
Intensity		**ER Status**	
2+	2	ER+	9
3+	21	ER-	8
		Unknown	6

Table 1. CCR7 pathology results and ER status data for all tumor-containing samples. 23 samples had CCR7 tumor positivity, of which 65% had complete membranous pattern, 91% had 3+ intensity, and 61% had 100% tumor stain. Approximately half of the samples with known ER data were ER positive.

Next Steps

CCR7 was highly expressed in 96% of tumor-containing samples, including both ER+ and ER- subtypes. Thus, it can be further studied for future personalized IBC treatments. Additionally, since all samples lacking tumors still exhibited CCR7 positivity in the stroma, the effect of stromal CCR7 on IBC development must be further explored.

Further analysis includes obtaining data for the samples of unknown ER status in this study, as well as HER2 data. Future repeated studies should include patients for whom we have medical images for comparison with CCR7 pathology, as CCR7 may influence IBC clinical presentation.

Conclusions

Since CCR7 is present in nearly all cases of IBC, including both ER+ and ER- subtypes, it should be further studied as a target for future personalized IBC treatments.

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