lncRNAs as potential biomarkers in ER+ breast cancer macrophages in anti-PD-1 response

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INTRODUCTION

Although presenting fewer tumor infiltrating lymphocytes (TILs) than triple-negative breast cancer (TNBC), luminal (ER+) tumors have other important immune cells in the tumor microenvironment (TME) that act in response to ICIs targeting the PD-1/PD-L1 pathway in breast cancer (BC) [1].

An example of those cells populations are the tumor-associated macrophages (TAMs), comprising approximately 50% of the cells in the TME in breast cancer, and exhibiting high PD-L1 expression [2].

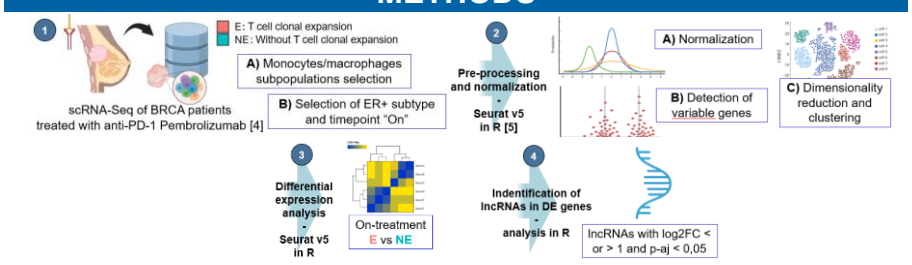
Polarized macrophage phenotypes are of immunotherapeutic relevance, with M1 being associated with an antitumor effect and M2 being associated with an immunosuppressive effect [2].

Long non-coding RNAs (lncRNAs) are a potential class of biomarker as they display a highly tissue-specific expression and are involved in various regulatory functions in cancer [3].

MAIN GOAL

Considering TAMs can affect response to anti-PD-1/anti-PD-L1 immunotherapy, we aim to investigate the potential molecular mechanisms involved in treatment effectiveness of regulating molecules such as lncRNAs in ER+ patients' responsiveness.

METHODS



RESULTS AND DISCUSSION

Figure 1. Differentially expressed lncRNAs in ER+ patients treated with Pembrolizumab (n=15) identified in a scRNA-Seq dataset, in the subset On-treatment, assessing E group (n=3) versus NE group (n = 12).

BRCA Subtype	Gene expression (p<0,05)	Cell population
		Myeloid (monocytes, macrophages)
ER+	UPREGULATED	INHBA-AS1, LINC00937, LINC01679, MUC20-OT1, USP30-AS1
	DOWNREGULATED	GAPLINC, LINC01094

Criteria: average log2FC < or > 1 and p-value adjusted < 0.05.

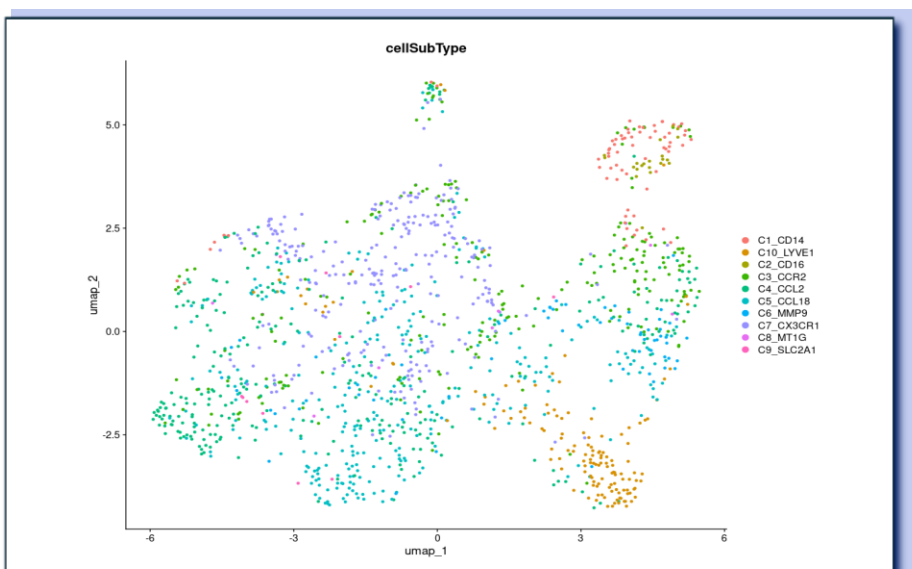


Figure 2. UMAP of myeloid subpopulation distribution in ER+ patients treated with Pembrolizumab (Bassez et al., 2021 scRNA-Seq dataset).

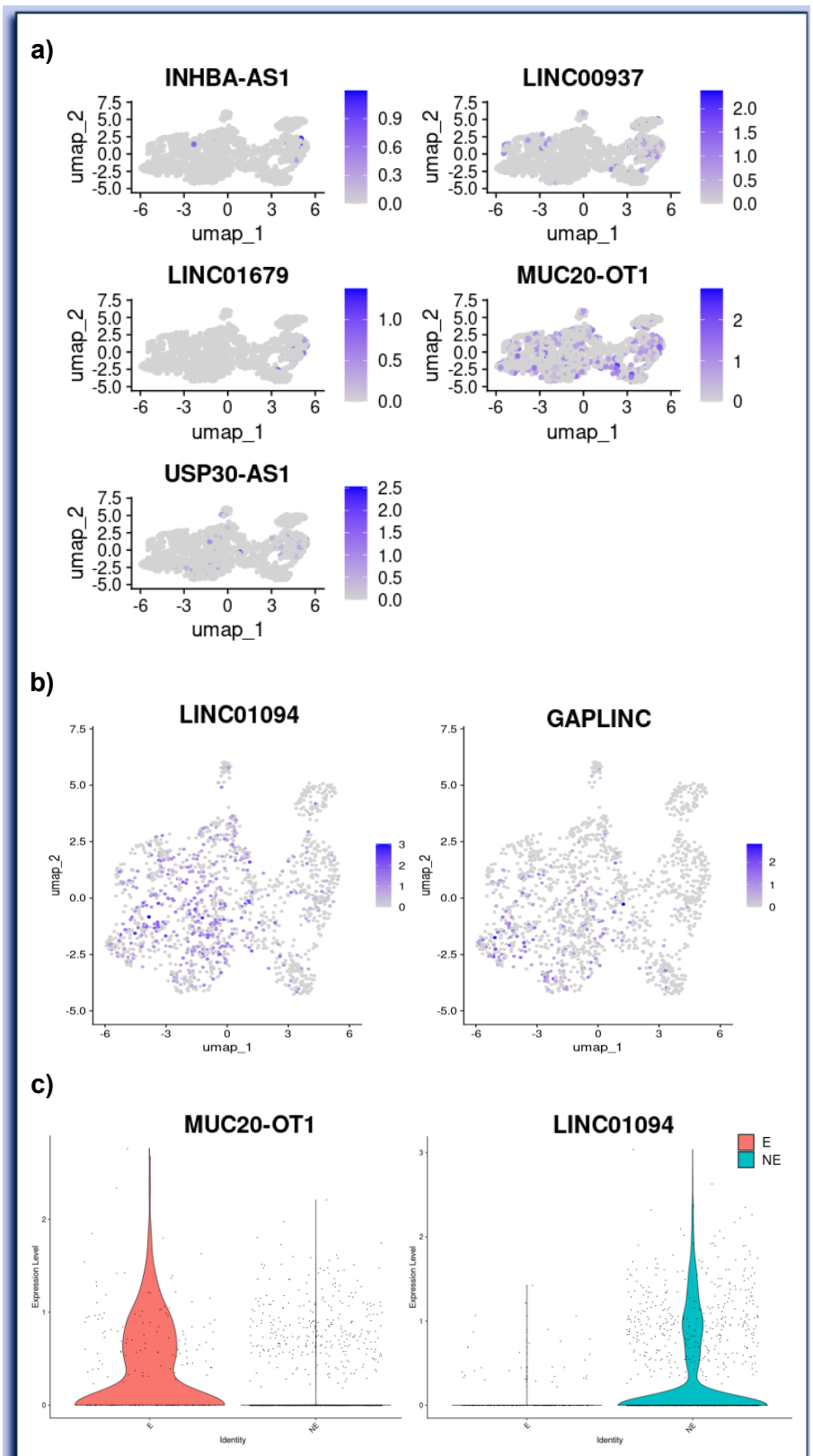


Figure 3. a) Feature plots showing the distribution of upregulated lncRNAs in myeloid subpopulations from ER+ patients; **b)** feature plots showing the distribution of downregulated lncRNAs in the same subpopulations; **c)** violin plots of the most variable lncRNAs in ER+ patients' myeloid cells, with MUC20-OT1 being more highly expressed in the 'E' group (potential responders), while LINC01094 is more highly expressed in the 'NE' group (non-responders).

CONCLUSIONS

Those findings indicate lncRNAs have a potential role associated with macrophages responsiveness to anti-PD-1 treatment in ER+ subtype of BC, suggesting that further studies of their regulatory mechanisms can highlight them as potential response biomarkers.

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AGRADECIMENTOS