Transcriptomic mapping of integrins and inmune activation in High Grade Serous Ovarian Cancer.

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Background

- Integrins, transmembrane receptors that mediade cell-extracellular matrix and cell-cell interaction, have been linked to cancer features. A less explores function of integrins in cancer is their role in leukocyte homing and activation. Understanding their role and relationship with immune infiltrates and immune checkpoints is an area of interest in cancer research.

Methods

- The gene expression of 10 different integrins was explored in relation with ovarian cancer patient outcome using transcriptomic data (Affymetrix dataset, exploratory cohort) and the METABRIC study (validation cohort). The TIMER online tool was used to explore the association of the identified integrins and immune infiltration, and the TCGA and METABRIC studies to analyze the correlation between integrin expression and genomic signatures of immune activation.

Results

- We identified 2 individual genes which encode for integrin alfa (A) and beta (B) subunits, ITGAE and ITGA2, which predict favorable prognosis in High-Grade Serous Ovarian Cancer. Their expression positively correlated with the presence of immune infiltrates within the tumor (CD8+ cells and dendritic cells) with markers of T cell activation and antigen presentation, and with gene signatures of immune surveillance (cytotoxic T lymphocyte activation and IFN gamma signature) (Fig.1). By contrast those integrins which predicted for detrimental outcome (ITGAM, ITGA4, ITGB2, ITGAV, ITGAL and ITGAX). Their expression positively correlated with the presence of immune infiltrates within the tumor (dendritic cells, neutrophils, macrophages, CD8+ T cells and B cells) (Fig.2).

Figure Nº 1

ITGAE, ITGA2

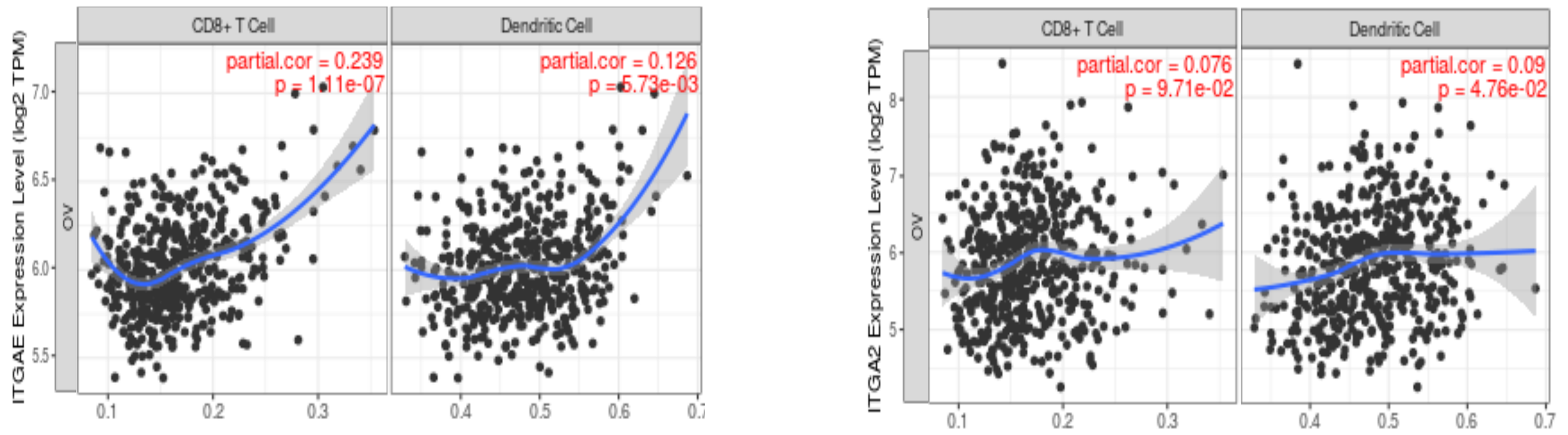
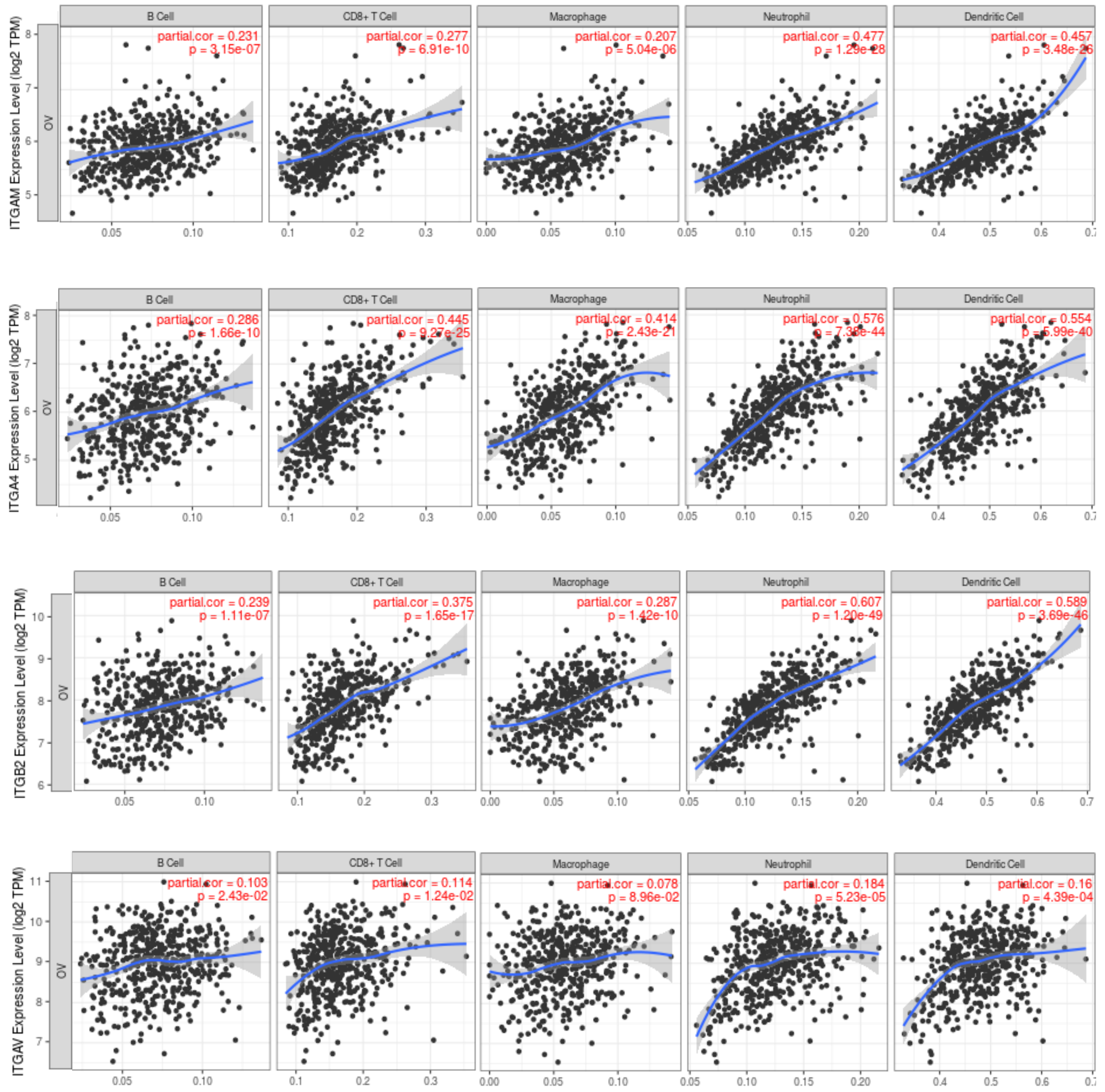
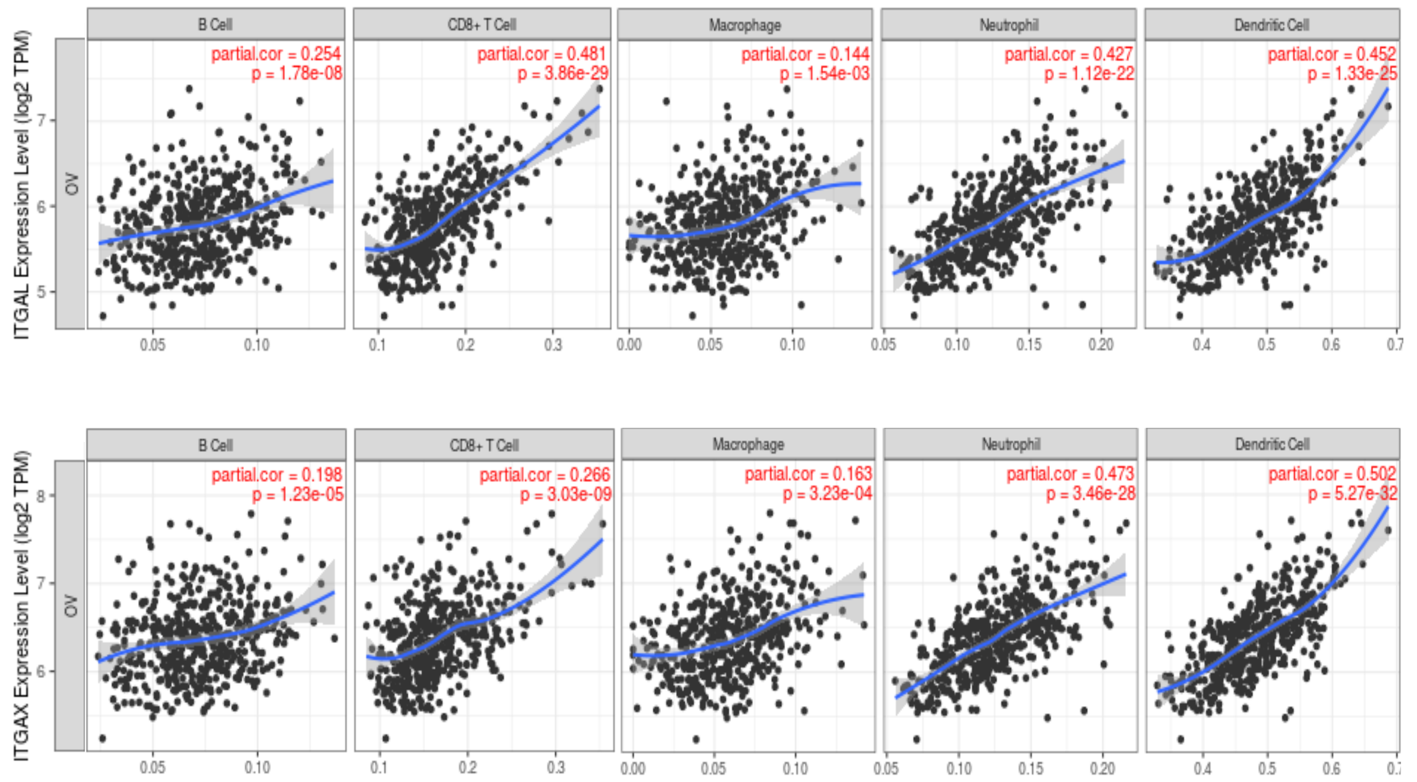


Figure Nº 2

ITGAM, ITGA4, ITGB2, ITGAV, ITGAL, ITGAX.





Conclusions

- Our analysis identifies two integrin signatures composed of 2 genes with favorable prognosis and 6 genes with poor prognosis; with potential to recognize immune infiltrated and activated high-grade serous ovarian cancer.

Bibliography

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