Using Machine Learning to Characterize Lung Cancer Microenvironment and the Development of a Model to Predict the Presence of Similar Microenvironment in Other Cancers

#476

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Introduction

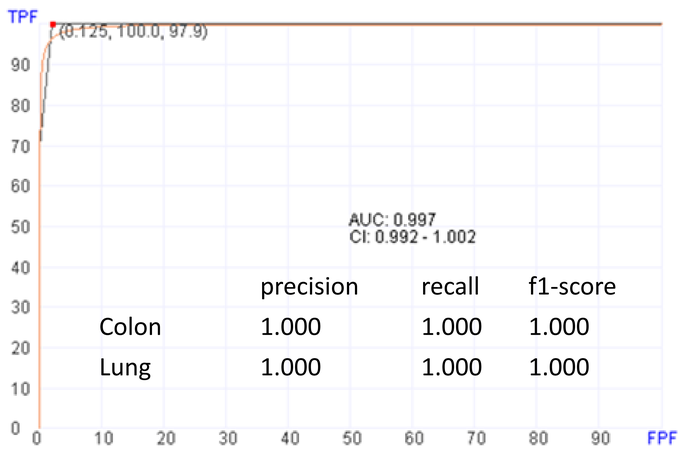
Poor response to immune checkpoint inhibitors (ICI) in colorectal cancer (CRC) is believed to be due to lack of immune suppressive tumor microenvironment (TME). In contrast, lung cancer TME is believed to be significantly more immunologically active and responsible for the relative success of ICI in lung cancer. We evaluated the TME in lung cancer and CRC using 43 immune biomarkers quantified using RNA sequencing and developed a model to classify TME into immunologically active (similar to lung cancer) vs inactive (similar to colorectal). These 43 immune biomarkers included B- and T-cell markers, cytokines and chemokines. .

Methods and Materials

RNA was extracted from FFPE samples from 707 patients with lung cancer, 227 patients with CRC, 131 patients with breast cancer, 111 patients with ovarian cancer, and 72 patients with pancreatic cancer. The expression levels of the 42 immunological markers were quantified using next generation sequencing (NGS) as a part of larger targeted RNA sequencing panel of 1408 genes. Using a machine learning algorithm, we first selected the relative genes that distinguish between two classes using two criteria: performance of each gene with K-fold cross-validation (K=12) and second based on stability measure using statistical significance tests. The selected genes were then used to predict one class from the other using random forest classifier. Samples were divided to training set (67%) and testing set (33%).

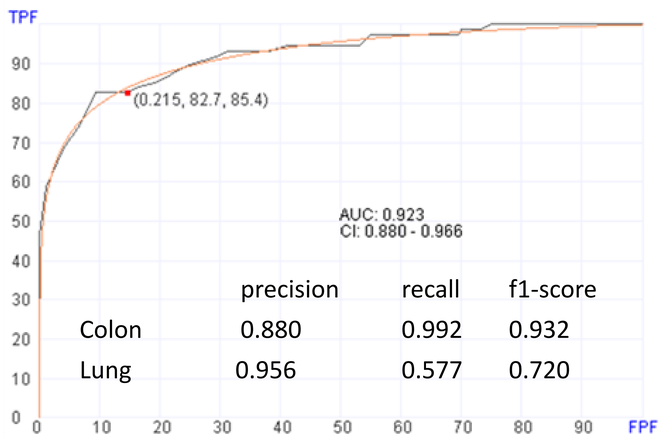
Distinguishing immunologically active from inactive TME using the expression of 20 immune biomarkers

Training (626 Samples)



	precision	recall	f1-score
Colon	1.000	1.000	1.000
Lung	1.000	1.000	1.000

Testing (308 samples)



	precision	recall	f1-score
Colon	0.880	0.992	0.932
Lung	0.956	0.577	0.720

Cytokine-cytokine receptors pathway : IL1R, IL21R, ILRAP, IL7R, CCL2, IL2RA, and IL1B.

Hematopoietic pathway: FCGBP, IL21R, CD19, IL2RA, CD8A, CD22, and IL1B

B-cell receptors pathway: CD74, CD79A, CD19, CD79, and CD22

Conclusions

-Lung cancer tumor microenvironment (TME) is significantly different from that of CRC.

-Immunologically active TME like lung cancer detected in 23 of 131 (18%) breast cancer, 13 of 111 (12%) ovarian cancers and 17 of 72 (24%) pancreatic cancers.

-Only 20 immune biomarkers are adequate to distinguish between the active and inactive TME.

-CD274 (PD-L1) T-cells (CD8A) are important but B-cells appear to play significant role in distinguishing between immunologically active and inactive TME.

CD74	Gamma Chain Of Class II Antigens
FCGBP	Fc Gamma Binding Protein
IL1R1	Interleukin 1 Receptor Type 1
CD44	GP90 Lymphocyte Homing/Adhesion Receptor
CD274	PD-L1
FCGR2B	Fc Gamma Receptor IIb
IL21R	Interleukin 21 Receptor
IL1RAP	Interleukin 1 Receptor Accessory Protein
IL7R	Interleukin 7 Receptor
CD79A	CD79a Molecule
CCL2	C-C Motif Chemokine Ligand 2
CYFIP2	Cytoplasmic FMR1 Interacting Protein 2
CD19	CD19 Molecule
IL2RA	Interleukin 2 Receptor Subunit Alpha
CD8A	CD8a Molecule
CD79B	CD79b Molecule
ID1	Inhibitor Of DNA Binding 1
CD22	CD22 Molecule
FZD10	Frizzled Class Receptor 10
IL1B	Interleukin 1 Beta