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Serum Albumin as an Independent Prognosis Factor in Patients with Non-Small Cell Lung Cancer by Affecting the Distribution of CD8+ T Cells
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Background: Serum albumin (ALB) as the most common biomarker for nutritional status is often closely associated with the prognosis of patients with non-small cell lung carcinoma (NSCLC). Whether the cause is related to the effects on host immune status, especially for distribution of host immune cells, remains currently unknown. Patients and Methods: Clinical data, peripheral blood (PBL), and tumor tissues were obtained from enrolled patients with primary NSCLC in the First Hospital of Jilin University. We performed flow cytometry to analyze the PBL immunocytes and quantitative immunofluorescence to detect the tumor-infiltrating CD8+ T cells. TCR repertoire analysis was examined by high-throughput sequencing of TCR β-chain. All the clinical outcomes, correlations between ALB, and immune indexes were analyzed by SPSS 17.0. Results: In the total of 211 enrolled NSCLC patients, ALB became an independent prognostic factor through multivariate Cox regression analysis (P=0.037). The median OS and PFS in patients with low ALB (N=155) vs. high ALB (N=56) were 28.2 vs. 42.2 months (P=0.0142), and 14.6 vs. 25 months (P=0.0149), respectively. Among patients with non-metastasis NSCLC (stage I-III), there was a higher incidence rate of distant metastasis in low ALB group than that in high ALB group (41.3% and 22.2%; P=0.043), in addition to a strong association with higher risk of death (P<0.01) and disease progression (P=0.037). We further found that high ALB was closely correlated with higher PBL cholesterol (r=0.4189, P<0.0001), triglyceride (r=0.2302, P=0.0008) and HDL (r=0.2849, P<0.001), resulting in more CD8+ cytotoxic T cells in PBL (P=0.007) and around the tumor (P=0.047) but not infiltrated in tumor. Furthermore, high ALB also associated with more diversity of TCR repertoire (P=0.023). Conclusions: High ALB improved the survival and reduced risk of distant metastasis in NSCLC patients by affecting the distribution of CD8+ T cells and diversity of TCR repertoire.

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Cancer and Palliative Care in Rural India (West Bengal): Experience of an NGO
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Introduction: As in any developing countries, the state of West Bengal in India has a huge burden of cancer patients in advanced stage coming from rural area where awareness regarding the usefulness of palliative care in rather poor. Objective: Our goal is to give a pain-free good quality of life in these advanced-stage cancer patients. The objective of this study is to identify the main difficulties in achieving the above goal in a rural village setting in India. Method: Advanced cancer patients in need of palliative care in various villages in rural India were selected for this study. Their symptoms and management in those rural surroundings were evaluated by an NGO (under the guidance of a senior palliative care specialist) working in that area. An attempt was made to identify the main obstacles in getting proper palliative care in a rural setting. Results: Pain and fatigue are the main symptoms affecting these patients. In most patients pain and other symptoms' control were grossly inadequate due to lack of properly trained manpower in rural India. However, regular home care visits by a group of social workers were of immense help in the last few months of life. The NGO team was well guided by a palliative care specialist. Conclusion: There is a wide gap of trained manpower in this field in rural areas of India. Dedicated groups from the rural area itself need encouragement and proper training, so that difficult symptoms can be managed locally along with necessary social and psychological support of these patients.

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IGF-Binding Protein-Mediated Sensitization of EGFR-Mutant NSCLC Cells to Osimertinib by Cancer-Associated Fibroblast
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Background: Cancer-associated fibroblasts (CAFs) are known to be able to support tumor growth, metastasis, and drug resistance. However, in resistant EGFR mutant lung cancer cells we also observed noncanonical CAF-driven sensitization to specific targeted drug treatment. Elucidation of the underlying mechanisms may identify novel biomarker or drug combination approaches. Methods: Viability of EGFR-mutant, gefitinib-resistant PC9/GR cells in coculture or in the presence of CAF conditioned medium (CM) was monitored by live-cell imaging using the Incucyte system or via CellTiterGlow (CTG, Promega), respectively. Clonogenic assays were analyzed by crystal violet staining. Gene expression differences of CAFs vs. normal activated fibroblasts (NAFs) were determined by microarrays. Secreted proteins in the CM were identified by mass spectrometry-based proteomics. Signaling changes were monitored by RTK array, phosphoproteomics, and Western blot. Loss- and gain-of-function experiments were performed using siRNA, small-molecule inhibitors, or addition of recombinant human (rh) proteins. Drug combinations were evaluated by CTG, crystal violet, and mouse xenografts. Results: Gene expression and secretome analysis of CAFs vs NAFs identified differential expression of secretory molecules, in particular IGFBP1 and 2 and IGF-binding proteins (IGFBPs), which regulate IGFR1 signaling, a pathway linked to EGFR inhibitor resistance. RTK arrays and phosphoproteomics showed enhanced inhibition of IGFR1 and ERK phosphorylation by osimertinib in the presence of CAF CM. Consistently, combination of IGFIR1 and EGFR inhibitors closely mimicked the effect of EGFR inhibition in the presence of CAF CM. CM from CAFs where IGFBPs were silenced by siRNA or treatment with IGF1 or 2 partially rescued cells from osimertinib, while rhIGFBPs conversely mimicked CM sensitizing effects. CAF CM vs. NAF CM further reduced AKT and ERK phosphorylation upon EGFR inhibition. The combination effect of EGFR and IGFIR1 inhibition has been shown in several cell lines, in vivo, as well as with several different drug combinations. Conclusion: We found CAF-mediated drug sensitization in EGFR-mutant lung cancer, which involves the IGFR1 signaling axis. IGFBPs secreted from CAFs attenuate compensatory signaling, leading to improved EGFR inhibitor efficacy. This result highlights tumor-suppressive effects of CAFs competing with their tumor-promoting effects and adds to the growing evidence that eliminating CAFs in an undifferentiated way may be detrimental to cancer therapy. Rather, we show that mechanistic understanding of these suppressive pathways can lead to improved drug combinations that mimic these effects and may delay the onset of resistance.

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Translating Lung Cancer Research into Primary Care Provider Training: An Innovative Online Course

Background: Lung cancer (LC) is the leading cause of cancer death in the U.S., and primary care provider (PCP) education is essential for reducing the country’s overall LC burden. Despite recent LC treatment...