GLUT1 plays an important role in cancer cell glycometabolism. We aimed to investigate the correlation between EGFR mutation status and SUVmax, and a potential mechanism of decreased FDG uptake in EGFR mutants relevant to its GLUT 1 distributions. We identified 474 patients with lung adenocarcinoma（LAD）with EGFR mutation genotyping. On multivariate analysis, the decrease SUVmax of a tumor（$p < 0.001$）, sex（$p = .025$）, and smoke status（$p = .017$）were independent predictors for EGFR mutations. Immunostaining of cell lines and resected LADs revealed that predominant areas of GLUT1 expression was observed not on the cell membrane but in the cytoplasm of EGFR-mutated cells as opposed to EGFR-wild type cells. SUVmax can be a predictive marker for EGFR mutational status in LADs by a potential mechanism underlying alteration of GLUT1 distribution.

P2-20.

Programmed cell death 2 forms coinhibitory microclusters that directly attenuate T cell receptor signaling by recruiting the phosphatase SHP2

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Anti-PD-1 antibodies have made tremendous therapeutic effects on advanced or recurrent non-small cell lung cancer. The expression level of PD-1 ligand, PD-L1, in tumor tissues is commonly measured as a biomarker in the clinical setting, but not necessarily correlated with their efficacy. Some kinds of tumors are reported to express another PD-1 ligand, PD-L2, which is possible to contribute to PD-1 signaling through PD-1-PD-L2 binding, but the precise mechanisms of the PD-L2-mediated coinhibitory signaling are not completely elucidated. We invented the high-resolution imaging system combined with the antigen-presenting planar lipid-bilayer constructed by MHC-peptides, adhesion molecules and PD-L1. Using our unique strategies, we found that PD-1 colocalized at the clustering TCRs called “TCR microclusters” in the presence of PD-L1 and that SHP2 recruiting to PD-1 suppressed T cell activity by dephosphorylating the activated signaling molecules. We newly invented engineered PD-L2 incorporated lipid-planar bilayers and found that PD-1 is translocated into TCR microclusters and then accumulates at the center of the T cell-bilayer interface in the presence of PD-L2. We further confirmed the rapid and transient recruitment of SHP2, not SHP1, to PD-1 microclusters by PD-1-PD-L2 binding. Biochemical assays demonstrated that PD-L2 dephosphorylates TCR downstream signaling molecules, resulting in the reduction of IL-2 production by forming PD-1-PD-L2 microclusters. The biological function of PD-L2 itself was almost as the same as that of PD-L1, then we are now evaluating the PD-L1 vs PD-L2 competition toward PD-1 binding and the effect of PD-1/L1/L2 blocking for TCR signaling.

P2-21.

マウスを用いた子宮頸部前癌性病変の発症メカニズム解析

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ヒトパピローマウイルス（HPV）は性交渉によって感染し、近年では若年層によくみられる感染性ウィルスである。通常、HPV は免疫系によって除去されるが、持続的感染が継続すると子宮頸部上皮に子宮頸部前癌性病変（cervical intraepithelial neoplasia：CIN）を発症させる原因になる。このHPV には高リスク型や低リスク型など様々なタイプが存在し、特に高リスク型の HPV16 型や HPV18 型を持った患者の約 70％が CIN から子宮頸癌へ発展する。子宮頸癌は進行が進むと治療が困難となるが、CIN の初期段階で適切な治療を施すことで発見から 5 年間の生存率がおよそ 100% を示すことが報告されている。つまり、子宮頸癌は CIN の段階で