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Immunogenomics and Immunotherapy

演者：公益財団法人がん研究会 がんプレシジョン医療研究センター
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スコット・トーマス

日時：2019年8月22日（木）8：00～8：50

会場：第1会場（高知市文化プラザ かるぽーと 大ホール）

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The recent development of cancer immunotherapies, particularly drugs modulating the immune checkpoint molecules, clearly demonstrated the importance of host immune cells in the fight against cancer. However, the molecular mechanisms by which these new therapies kill tumor cells still remain unclear. Hence, we have been proposing the significance of the new field to characterizing the systemic and tumor immune environment including T cell and B cell repertoires by next-generation sequencers. This field has enormously helped for better understanding of the changes/alterations of our immune responses during the course of various disease conditions and treatments. The deep sequencing of T-cell receptors enabled us to capture the immune microenvironment in tumors. We have analyzed T cell changes in melanoma tumors before and after anti-PD-1 antibody treatment and found that tumors in responders exhibited a substantial increase of CD8, GZMA and perforin 1 (PRF1) expression levels as well as oligoclonal expansion of tumor-infiltrating T lymphocytes (TILs) in the tumor tissues of the responders. In one patient who showed myocarditis after one-shot of anti-PD-1 antibody treatment, we identified infiltration of clonally expanded T cell populations in the skeletal muscle, implying the very strong T cell immune response against muscular cells. Furthermore, we collected surgically-resected tumor tissues from five breast cancer and six mesothelioma patients, and characterized 3 different portions of individual tumors through somatic mutation analysis by whole exome sequencing, T cell receptor beta (TCRB) repertoire analysis of tumor-infiltrating lymphocytes (TILs), and found that tumors revealed significant correlation between the number of predicted neoantigens and the diversity of TILs ($P = 0.0009$), suggesting that certain TILs might recognize the cancer-specific antigens including neoantigens derived from non-synonymous somatic mutations of cancer cells. This kind of immunogenomics analysis is extremely important to uncover the changes in immune microenvironment during the cancer treatment and may improve the clinical outcome of immunotherapy including development of TCR-engineered T cell therapy.

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