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Identify Cryptic genetic background under Thyroiditis from ICI treatments using Whole Genome Sequencing

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Portion of cancer patients undergoing treatment with immune checkpoint inhibitors (ICI) encountered with the immune-related adverse events (IRAE), which show diverse phenotypes, such as myositis, pancreatitis and thyroiditis. In our samples who are taken thyroiditis after treatment of ICI, shrinking of thyroid like autoimmune thyroiditis, a rare event, is revealed. The causal genetic factors of IRAE are reported in some papers, but IL17A is only revealed as the factor for thyroiditis so far. Until now, Whole Exome Sequencing (WES) is widely used in field of gene discovery associated with phenotype. But the importance of the functions of non-coding region in genome is on the rise, Whole Genome Sequencing (WGS) become essential, to explore this region. To find the causal genes using a signal of analysis from the coding region to one which is expended to noncoding region, WGS for thyroiditis samples(n=25) is conducted. To get the causal genes, in our analysis, we approach this cryptic genetic background under the rare disorder phenotype using monogenic model. IRF7 gene is found as the possible causal gene in our research. The gene encodes interferon regulatory factor 7, a member of the interferon regulatory transcription factor family. And the variants included in coding regions and non-coding regions of IRF7 shows possibility of gain of function. Therefore, we suggest the overexpression of IRF7 by these variants cause thyroiditis to patient with treatment of ICI.