Symposium 7: Genetics

Title: **Investigational gene analysis for primary immunodeficiency diseases**

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Whole exome sequencing (WES) is an effective tool for elucidation of genetic defects in patients with primary immunodeficiency diseases (PIDs). Diagnosis for most of PIDs is made based on typical clinical presentation and laboratory data, followed by protein expression analysis when applicable, and is finally confirmed by gene sequencing. WES has currently been used for dissecting the etiology of undiagnosed cases.

We carried out WES for 79 cases with PIDs from 2012 to 2015, and for 97 cases in 2016 and 2017 with 128 family members as a reference. Identified known genes include *TRNT*1 in B cell deficiency and periodic fever, *ICOS* in CVID, *NCF2* in sarcoidosis, *HOIL1* in CVID with myoclonic seizures, *TNFAIP2* in SLE, and *IKZF1* in B cell deficiency. We present novel responsible genes for PIDs identified in our laboratory in this session. iPS technology and knock-in mice model have been used as an important tool to elucidate molecular pathogenesis of these disorders.

About 70% of the samples were left undiagnosed after WES; and detection of large deletion or splice anomaly with the aid of software is sometimes useful to reach a diagnosis . Regional and international collaboration is critically important to obtain complete picture of, and to find suitable treatment for, the patients with a novel gene defect.