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# X-linked agammaglobulinemia (XLA) as a model disease for the development of molecular diagnostic and gene therapy for primary immunodeficiency

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The X-linked agammaglobulinemia (XLA) is the one of the most common primary antibody deficiency in man. XLA is caused by mutations in the Bruton's tyrosine kinase (*BTK*) gene and *BTK* mutations are responsible for 85% of all antibody deficiencies. Current treatments with intravenous immunoglobulin (IVIG) infusion and antibiotics are effective, however they are expensive and non-curative. We investigate whether stem cell-based gene therapy using the lentiviral vectors could provide a novel treatment option for XLA. Moreover, mutation analysis have never been applied for XLA in Turkey, therefore we incorpeated *BTK* mutation analysis to improve the diagnosis of XLA.

*Btk*-/- mice engrafted with transduced cells showed correction of B-cell in bone marrow, spleen and blood. All treated mice exhibited the recovery serum immunoglobulins as well as responses to T cell-independent antigens. Moreover, transplantation into secondary *Btk*-/- recipients resulted in functional restoration of B cells and serum immunoglobulins, without any adverse effects. To validate the *BTK* mutation analysis, patients (n=14) with antibody deficiency were screened for *BTK* mutation. In seven patients, *BTK* mutations were confirmed by sequencing and all mutations have resulted in a premature stop codon and consequently lead to the absence the Btk protein. Interestingly in other seven patients, no *BTK* mutation was found indicating the high incidence of autosomal recessive agammaglobulinemia in Turkey.

In conclusion, we demonstrated in the *Btk*-/- mouse model the feasibility of stem cell-based lentiviral gene therapy for XLA. Furthermore, we also conclude that *BTK* mutation analysis provides a significant improvement for XLA diagnosis.

## Biography

Yuk Yin (Peter) Ng, studied Medical Biology at the Free University Amsterdam The Netherlands. Afterward he did his PhD at the Utrecht University, Medical Center at the department of Hematology. During his post-doc career at the Erasmus Medical Center in Rotterdam, he had the opportunity to lead studies to develop novel diagnostic tools for childhood leukemias and stem cell based gene therapy for primary immunodeficiencies . His research had been presented in national (NVGT and NvvH) and international meetings (EU-CONSERT-FP6, ESGCT and ASCGT) and published the results in well-known peer-reviewed journals.

In August 2010 he moved to Istanbul at the department of Genetics at DETAE of Istanbul University. In April 2012, he received a three-years funding by TUBITAK for is research in the development of lentiviral gene therapy for primary immunodeficiencies.

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