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MYSM1 deficiency - genotoxic stress-associated bone marrow failure and developmental aberrations.

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Bone marrow (BM), a semi-solid tissue within the spongy or cancellous portions of our bones, is the primary site of blood cell reproduction in humans. Approximately one trillion cells per day arise in a healthy human bone marrow. In some patients, due to the inherited genetic defects, BM fails to produce sufficient blood cell(s). These diseases which comprise a very heterogeneous group of disorders are called “Inherited bone marrow failure syndromes (IBMFS). So far, about 50 genes have been discovered to be involved in pathogenesis of BMF syndromes. However, there are still many patients suffering from IBMFS but with unknown genetic cause.

Through systematic basic and clinical investigations of the genome of two kids with IBMFS, performed in the laboratory of Prof. Christoph Klein at the Dr. von Hauner Childrens Hospital (LMU) in Munich, The group, which is part of the Primary Immundeficiency Network PID-NET, were able to discover a rare genetic defect in a gene called MYSM1. The patients, two siblings with Arab background, manifested with progressive BMFS, defects in immune system (immunodeficiency) and developmental aberrations. Moreover, comprehensive laboratory studies revealed that the cell from MYSM1-deficient patients having some molecular defects such as increased sensitivity to genotoxic stresses (for instance UV light) and increase reactive oxygen species (ROS) production.

Considering both clinical and laboratory findings, the kids underwent successful bone marrow transplantation at Dr. von Hauner Childrens Hospital . The results of this research projects have been published as an original paper in Journal of Allergy and Clinical Immunology in 2017.

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