New insights in genetic defect allow prevention of fatal illnesses in children

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A team of scientists led by prof. Adrian Liston (VIB–KU Leuven) and prof. Isabelle Meyts (UZ Leuven – KU Leuven) were able to characterize a new genetic immunodeficiency resulting from a mutation in a gene named STAT2. This mutation causes patients to be extremely vulnerable to normally mild childhood illnesses such as rotavirus and enterovirus. Prof. Liston's comprehensive analysis of the genetic defect allows clinicians to provide children with the proper therapies before illnesses prove fatal. The findings of the research have been published in the *Journal of Allergy and Clinical Immunology*.

Recent advancements in technologies and tools now make it possible for researchers to identify extremely subtle defects of the human immune system. In the past, many patients with "hidden" immunodeficiencies, or defects that were not obvious from the outset, often become extremely ill or die before their genetic disorders are diagnosed. Prof. Liston and his lab were able to identify a gene mutation causing an immunodeficiency that can be fatal during childhood, enabling children to be diagnosed, monitored and preemptively treated for the disorder.

Immunodeficiency disorders are not rare

Ranging from disorders as severe as the well-known "bubble boy" to nearly impossible-to-detect 'hidden' defects, immunodeficiencies are more common than scientists previously thought. Immunologists and geneticists have only just begun to scratch the surface when it comes to defining these latter types of immune disorders, which can be specific

enough to make sufferers highly susceptible to just one or two types of diseases.

Prof. Adrian Liston (VIB-KU Leuven): "I wouldn't be surprised if, when we finally do complete the identification of all genetic immunodeficiencies, we discover that up to 1 in 100 children are affected. The 'hidden' ones are especially insidious, because they do not present as obviously as other genetic immune disorders. In our study, one of the patients did unfortunately die before a diagnosis could be made. The other patient is alive and well, and now that she has been diagnosed, she is being carefully watched. We can do something about most immunodeficiencies – if only we can identify them."

Severe common illnesses may signal immune disorder

Prof. Meyts, lead clinician for the patients, stresses the importance of assessing the severity of childhood illnesses on the part of parents, suggesting that parents look for helpful information online and raise the possibility of a potential genetic immunodeficiency with a pediatrician.

Prof. Isabelle Meyts (UZ Leuven – KU Leuven): "When an otherwise healthy child experiences extremely severe infection with a common pathogen, like influenza or the chickenpox virus, or whenever a child is particularly vulnerable to infection with a single pathogen, an underlying defect in the immune system is likely. Likewise, a family history of a child succumbing to infection should alert the family and the clinician. Identifying the causative gene defect allows for genetic counseling of the family and for preventive measures to be taken."

Unraveling 'hidden' immunodeficiencies

The potential future avenues for this research are numerous and extremely relevant to current medicine. Prof. Liston's lab has developed

a unique immune phenotyping platform and gene discovery program that can help identify previously unknown immune system defects and inflammatory diseases, leading to novel new treatments that can be administered in a timely way.

Prof. Adrian Liston: "We seek to identify every possible cause of genetic immunodeficiency so that every child displaying warning signs can be tested and treated before it is too late."

More information: Leen Moens et al. A novel kindred with inherited STAT2 deficiency and severe viral illness, *Journal of Allergy and Clinical Immunology* (2017). DOI: 10.1016/j.jaci.2016.10.033

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