

Dear all,

In September 2015 we published that heterozygous mutation in NFKB1 can cause an antibody deficiency (CVID):

<http://www.ncbi.nlm.nih.gov/pubmed/26279205>

Haploinsufficiency of the NFKB1 Subunit p50 in Common Variable Immunodeficiency.

Am J Hum Genet. 2015 Sep 3;97(3):389-403.

Fliegau M, Bryant VL, Frede N, Slade C, Woon ST, Lehnert K, Winzer S, Bulashevskaya A, Scerri T, Leung E, Jordan A, Keller B, de Vries E, Cao H, Yang F, Schäffer AA, Warnatz K, Browett P, Douglass J, Ameratunga RV, van der Meer JW, Grimbacher B.

Since, it became clear that mutations in NFKB 1 and NFKB2 actually account for the majority of mutations in CVID:

Using next generation sequencing, we identified 33 mutations in NFKB1 and NFKB2 in a cohort of 320 CVID patients. Ten mutations in NFKB1 are predicted to lead to expression of truncated, non-functional proteins which undergo rapid decay, thus causing p50 haploinsufficiency. Four mutations are predicted to cause constitutive nuclear localization of aberrant p50 proteins and a shortcut or a delay in canonical NF-kappaB signaling. Fourteen missense variants were identified, with yet unknown effects. In NFKB2 we identified four frame-shift mutations leading to expression of unprocessable p100 precursor, and functional p52 haploinsufficiency. A novel frame-shift mutation suggests constitutive nuclear localization of a mutant p52. The phenotypical spectrum ranged from clinically inapparent IgG subclass deficiency to severe forms of CVID with progressing pulmonary disease, inflammatory bowel disease, and rheumatoid joint disease. In summary, mutations in NFKB1 or NFKB2 are highly prevalent and could account for approximately 10% of monogenetic defects in CVID.

(This is actually part of an abstract submitted to ESID 2016 by the following set of authors: *Manfred Fliegau, Katrin Hübscher, Jessica Rojas, Natalie Frede, Klaus Warnatz, Christian Klemann, Robin Kobbe, Vassilios Lougaris, Alessandro Plebani, Oliver Bartsch, Roya Sherkat, Mikko Seppänen, Lennart Hammarstöm, Vanessa Bryant, Jo Douglass, Anna Shcherbina, Siobhan Burns, Rohan Ameratunga, Jos van der Meer, and Bodo Grimbacher*)

Therefore, we now think it is **time to publish a large case series on patients with mutations in NFKB1 and 2:**

To this end, I suggest to collect all the information of patients with mutations in NFKB1; and to share the work-load, Dr Karin Chen <karin.chen@hsc.utah.edu> from the Department of Pediatrics at the University of Utah will collect the clinical data from all NFKB2 patients.

If you are interested in a collaboration, please write to:

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Best regards,

Bodo