	P1	P2	
Lymphocytes (/mm <sup>3</sup> )	2587	1250	
T cells			
CD3 <sup>+</sup> (%)	75	73	(56-84)
CD4 <sup>+</sup> (%)	43	33	(31-52)
CD31 <sup>+</sup> CD45RA <sup>+</sup> /CD4 <sup>+</sup> (%)	44	29	(43-55)
CD45RA <sup>+</sup> /CD4 <sup>+</sup> (%)	57	43	(58-70)
CD8 <sup>+</sup> (%)	23	25	(18-35)
CCR7 <sup>+</sup> CD45RA <sup>+</sup> /CD8 <sup>+</sup> (%)	42	46	(52-68)
CCR7 <sup>+</sup> CD45RA <sup>-</sup> /CD8 <sup>+</sup> (%)	4	4	(3-4)
CCR7 <sup>-</sup> CD45RA <sup>-</sup> /CD8 <sup>+</sup> (%)	46	42	(11-20)
CCR7 <sup>-</sup> CDR45RA <sup>+</sup> /CD8 <sup>+</sup> (%)	8	8	(16-28)
B cells			
CD19 <sup>+</sup> (/mm <sup>3</sup> )	336	188	(193-628)
CD19 <sup>+</sup> (%)	13	15	(4.8-24.3)
IgD <sup>+</sup> CD27 <sup>-</sup> /CD19 <sup>+</sup> (%)	90	97	(58.5-87.4)
IgD <sup>+</sup> CD27 <sup>+</sup> /CD19 <sup>+</sup> (%)	7	2.7	(2.6-21.1)
IgD <sup>-</sup> CD27 <sup>+</sup> /CD19 <sup>+</sup> (%)	2	0.3	(4-21.2)
CD21 <sup>+</sup> (%)	0	0	
CD24 <sup>++</sup> CD38 <sup>++</sup> /CD19 <sup>+</sup> (%)	5	6	
CD24 <sup>-</sup> CD38 <sup>++</sup> (%)	0.1	0.5	
NK cells (%)	12	9	(3-22)
Immunoglobulin levels			
IgG (g/l)	7.36	4.8	(7-16)
IgG1 (g/l)	4.05	2.6	(4-11)
IgG2 (g/l)	1.6	0.85	(0.50-5)
IgG3 (g/l)	0.98	1.21	(0.17 - 0.70)
IgG4 (g/l)	0.07	0.09	(0.002 - 1.400)
IgA (g/l)	1.91	1.25	(0.7-4)
IgM (g/l)	2.11	0.44	(0.4-2.4)
Specific antibodies			
Blood group and	Normal	Deemaarad	
allohemagglutinin	Normai	Decreased	
Tetanus toxoid	Low to	Low to	
	normal*	normal*	
Diphtheria toxoid	Low	Low	
EBV	Negative at 7 y	Isolated positive IgG anti-VCA	

## Table E1 – Most recent immunological analysis of P1 and P2.Unless otherwisementioned, analyses were performed at 14 years of age for P1 and 11 years of age for P2

\* Antibody titers against the tetanus and diphtheria toxoids have been followed since the age of seven years for P1 and the age of five years for P2.

## **Figure legends**

**Figure E1** – (A) Pedigree of the family. (B) Chromatograms for the study of the *CR2* gene in the two patients, their parents and a healthy control. (C) Structure of the CD21 propeptide (1092 amino acids (aa)) with reported mutations associated with CD21 deficiency (including those reported here). CD21 is composed of a signal peptide (SP), an extracellular domain consisting of 15 to 16 complement control protein (CCP) domains, a transmembrane domain (Trans) and a short cytoplasmic tail (Cytop). (D) Flow cytometric analysis of CD21 expression (clone B-ly4, BD Biosciences®) on CD19<sup>+</sup> cells from the two patients, their father (III.1) and a healthy control (HC). (E) Follow-up of IgG to tetanus and diphtheria toxoids in P1 and P2. Booster vaccinations are depicted with an arrow. Dotted lined represent protective IgG titers to tetanus and diphtheria toxoids (respectively 0.6 UI/ml and 1.2 UI/ml).

**Figure E2** - Adenoid tissue sections from P1 stained with hematoxylin-phloxin-saffron (HPS) and processed for anti-CD10 (clone 56C6), anti-CD23 (clone 1B12) or anti-CD21 (clone 2G9, all antibodies from Novocastra®) immunohistochemistry. The inset shows a CD21-positive external control. Immunohistochemistry showed the germinal centers to have a normal architecture, with CD10-positive centrofollicular cells associated with a CD23-positive network of follicular dendritic cells. The lymphoid tissue showed a normal physiological distribution of B and T cells with CD20 and CD3 staining, no viral EBV-LMP1 protein and the presence of polytypic plasmocytes labeled with anti- $\kappa$  and anti- $\lambda$  light-chain antibodies (data not shown).



**CD21** 

Age (years)

