













![](_page_1_Figure_2.jpeg)

![](_page_1_Figure_3.jpeg)

![](_page_1_Picture_4.jpeg)

![](_page_1_Figure_5.jpeg)

![](_page_2_Figure_1.jpeg)

![](_page_2_Figure_2.jpeg)

![](_page_2_Picture_3.jpeg)

![](_page_2_Figure_4.jpeg)

![](_page_2_Figure_5.jpeg)

![](_page_3_Figure_1.jpeg)

![](_page_3_Figure_2.jpeg)

![](_page_3_Picture_3.jpeg)

![](_page_3_Figure_4.jpeg)

![](_page_3_Figure_5.jpeg)

## **CME-Summary**

Please identify the one mistake: Susceptibility to fungal infections may be caused by:

- homozygous mutations in the IL17-receptor Casanova, Science 2011
- autoantibodies against IL17 and/or IL22 - dominant negative mutations in STAT1
- dominant negative mutations in STAT3
- homozygous mutations in CARD9
- mutations in Dectin-1 confer risk
- dominant-negative mutations in IL17

Meager, JExpMed 2010 Casanova, JExpMed 2010 Netea NEJM, 2011 Casanova, JExpMed 2011 Minegishi, Nature 2007 Grimbacher, NEJM 2007 Grimbacher, NEJM 2010

Netea, NEJM 2010

Casanova, Science 2011

![](_page_4_Picture_12.jpeg)

![](_page_4_Picture_13.jpeg)

## Clinical phenotype in 5 patients with autosomal-recessive CVID # Patients 2 < 2 years < 13 years IgG low IgA low IgM low ITP Arthirtis IFA Myastenia Hypotiroydism ent pneumonia Brohchiectasis Asthma Urticaria Alelrgic dermatitis Warts contagiosum Histoplasma Diarrhea Growth retardation Cerebral granuloma

Patient #	Patient 1	Patient 2	Patient 3 R1683X	Patient 4	Patient 5
Lymphocyte counts:	5v	14v	29v	19v	19v
Age at measurement CD3 (cells/µl)	900	2.073	2.350	5.716	355
CD4 (cells/µl)	(900-4.500) 685 (500-2.400)	(800-3.500) 767 (400-3.100)	1.290	1.061	(100-2-100)
CD4 CD45RA	(300-2.400) N.D	(400-2.100) 179 (230-770)*	201 (27.833) <sup>b</sup>	(300-1.400) 72 (27,833) <sup>b</sup>	N.D
CD4 CD45RO	N.D	(240-700)*	887 (167-670) <sup>b</sup> ↑	588 (167-670) <sup>b</sup>	N.D
CD8 (cells/µl)	380 (300-1.600)	1.200	1032 (200-900) ↑	4.707 (200-900) ↑	165
CD8 CD45RA	N.D	1.003 (240-710)* 1	941 (19-508) <sup>6</sup> 1	1.991 (19-508) <sup>b</sup> ↑	N.D
CD8 CD45RO	N.D	473 (10-142) <sup>b</sup> ↑	627 (15-275) <sup>b</sup> ↑	374 (15-275) <sup>6</sup> ↑	N.D
Age at measurement	5y	10y	16y	16y	19y
NK cells (cells/µl)	260	190	35 (70.1.2000 ↓	N.D.	N.D.
CD19 (cells/µl)	280	300	219	69 (200.4000 ↓	121
Switched memory B cells (CD19 <sup>+</sup> CD27 <sup>+</sup> IgM <sup>-</sup> , % of total B-cells)	0 (3.9-16.2) ↓	1 (3.85-16.5) ↓	0.8 (4·22.8) ↓	0.89 (4-22.8) ↓	N.D.

![](_page_4_Figure_16.jpeg)

![](_page_5_Figure_1.jpeg)

![](_page_5_Figure_2.jpeg)

![](_page_5_Picture_3.jpeg)

![](_page_5_Figure_4.jpeg)

![](_page_5_Figure_5.jpeg)

![](_page_5_Figure_6.jpeg)

![](_page_6_Figure_1.jpeg)

![](_page_6_Figure_2.jpeg)

![](_page_6_Figure_3.jpeg)

![](_page_6_Figure_4.jpeg)

+12657S (P1) +12657S (P2) ■R1683X (P3) +Control EBV

![](_page_6_Figure_5.jpeg)

![](_page_6_Figure_6.jpeg)

![](_page_7_Figure_1.jpeg)

![](_page_7_Picture_2.jpeg)

![](_page_7_Picture_3.jpeg)

## Summary

 $\diamond$ LRBA is a new genetic defect associated with early onset CVID

- $\diamond$  LRBA deficiency is characterized by:
  - ♦Low B and T cell activation
  - Increased susceptibility to apoptosis

  - ♦Reduced proliferation
  - ♦Reduced autophagy

## Acknowledgements niversity College London briela Lopez-Herrera nudia M Trujillo-Vargas

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MARIE CURIE ACTIONS

![](_page_7_Picture_21.jpeg)