Nelson Textbook of Pediatrics

21 EDITION

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Autosomal Dominant Hyper-IgE Syndrome
DOCK8 Deficiency

Keywords
Interferon-γ Receptors 1 and 2, IL-12 Receptor β1, and IL-12P40 Defects
IL-1R–Associated Kinase 4 Deficiency and Myeloid Differentiation Factor 88
Natural Killer Cell Deficiency
Defects in Innate Responses to Viral Infection
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Keywords

Autoimmune Lymphoproliferative Syndrome

Immune Dysregulation, Polyendocrinopathy, Enteropathy, X-Linked Syndrome

Cytotoxic T-Lymphocyte Antigen 4 (CTLA4) Deficiency

Lipopolysaccharide (Lps)-Responsive Beige-Like Anchor Protein (LRBA) Deficiency

Activated Phosphoinositide 3-Kinase (PI3K) δ Syndromes

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