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Natural killer cell biology illuminated by primary immunodeficiency syndromes in humans

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Abstract

Natural killer (NK) cells are innate immune cytotoxic effector cells well known for their role in antiviral immunity and tumor immunosurveillance. In parts, this knowledge stems from rare inherited immunodeficiency disorders in humans that abrogate NK cell function leading to immune impairments, most notably associated with a high susceptibility to viral infections. Phenotypically, these disorders range from deficiencies selectively affecting NK cells to complex general immune defects that affect NK cells but also other immune cell subsets. Moreover, deficiencies may be associated with reduced NK cell numbers or rather impair specific NK cell effector functions. In recent years, genetic defects underlying the various NK cell deficiencies have been uncovered and have triggered investigative efforts to decipher the molecular mechanisms underlying these disorders. Here we review the associations between inherited human diseases and NK cell development as well as function, with a particular focus on defects in NK cell exocytosis and cytotoxicity. Furthermore we outline how reports of diverse genetic defects have shaped our understanding of NK cell biology.

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