Mutations in IL1RN in bone and skin inflammation

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Autoinflammatory diseases are a group of disorders characterized by seemingly unprovoked inflammation in the absence of high-titer autoantibodies or antigen-specific T cells. They include familial Mediterranean fever; the tumor necrosis factor receptor–associated periodic syndrome; the hyper-IgD syndrome; a syndrome of pyogenic arthritis, pyoderma gangrenosum and acne; the cryopyrin-associated periodic syndromes; chronic recurrent multifocal osteomyelitis and others. A new autoinflammatory syndrome of skin and bone caused by recessive mutations in IL1RN, the gene encoding the interleukin-1–receptor antagonist, has been recently described and has been named deficiency of the interleukin-1-receptor antagonist, or DIRA.

Three unrelated patients with symptoms suggestive of DIRA were referred to our laboratory. The three patients had skin and bone inflammation since birth manifested as pustulosis and chronic recurrent multifocal osteomyelitis. The course of the disease was progressive with chronic sequelae. Two patients were from Brazil and the third is from Palestine. We identified a novel homozygous inframe deletion of 15 bases (c.213-228delAGATGTGGTACCCA T ; p.72-77delDVVPI) in the two unrelated patients from Brazil. In the Palestinian patient, a homozygous nonsense mutation (c.160C>T; p.Q54X) was identified. This mutation has been described before in a family from Lebanon, which probably reflects on a founder effect in Middle Eastern populations.