Connecting Autoimmunity and Immunodeficiency Through Mutations of CTLA-4: A Literature Review

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Researchers consider autoimmune disorders and immunodeficiencies to be two completely unrelated conditions. However, it has been shown that patients can develop both diseases in spite of opposing etiologies. This has led researchers to examine the commonalities between autoimmunity and immunodeficiency in terms of pathogenesis, clinical manifestations, treatments and, more recently, genetics. Cytotoxic T-lymphocyte associated protein 4 (CTLA-4) is encoded by the CTLA gene and is known for its immunoregulatory role in terminating immune responses. CTLA-4 directly regulates the development of T-cells by activating T regulatory cells, but it can also affect the development of B-cells in downstream effects. However, it is unclear how CTLA-4 can induce both autoimmunity and immunodeficiency within patients. In this literature review we show that heterozygous mutations of CTLA-4 can lead to patients developing both autoimmune and immunodeficiency manifestations such as hypogammaglobulinemia, autoimmune cytopenia, lymphoproliferation, autoimmune enteropathy. Such mutations point toward commonalities in both autoimmunity and immunodeficiency, leading researchers to believe that these two diseases are more alike than different. With this newfound discovery, treatments can be developed to target the CTLA-4 gene in hopes of treating both autoimmunity and immunodeficiency in patients.