**A De Novo Variant in CTLA-4 Confers Responsiveness to Abatacept in a Patient with Severe Autoimmune Features**

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Cytotoxic T lymphocyte antigen 4 (CTLA-4) suppresses immune reactions by interacting with CD80 and CD86, which are displayed by antigen presenting cells, making it a useful target for immune modulation. Haploinsufficiency of *CTLA-4* in human or knockout of the gene in mouse leads to immune dysregulation. Here we report a human patient with severe multiple autoimmune features due to a *de novo* point mutation in the ligand-binding motif of CTLA-4, which effectively abolished the essential immuno-suppressive function of the protein. Several strategies for targeting CTLA-4 are currently available, including a fusion protein of extracellular domain of CTLA-4 with IgG1 Fc region (CTLA-4-Ig) to control immune reactivity. Administration of CTLA-4-Ig agent abatacept to the patient reconstructed regulatory T (Treg) cell function and reduced inflammatory cytokine levels, finally achieving clinical improvements such as reduced diarrhea output and total independence from blood transfusions. The finding emphasizes the crucial role of CTLA-4 in maintaining immunologic self-tolerance and the potential utility of CTLA-4-Ig in controlling autoimmune disorders in human patients.

Key words: *CTLA-4*, CTLA-4-Ig, abatacept, autoimmune enteropathy, whole exome sequencing