

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



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## BACKGROUND

- 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.
- 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, and the development of B-cells
- It's unclear how CTLA-4 can induce both autoimmunity and immunodeficiency within patients.

## IMMUNODEFICIENCY AND CTLA-4

- A sharp and severe decrease in immune cells for a prolonged period of time that leads to immune dysregulation and/or increased susceptibility to infection
- Individuals diagnosed with immunodeficiency are likely to have heterozygous (+/-) mutations of CTLA-4
- These mutations are responsible T cell hyperproliferation, T regulatory cell suppression, and lymphocytic organ infiltration
- Mutations of CTLA-4 are shown to cause reduced numbers of B cells

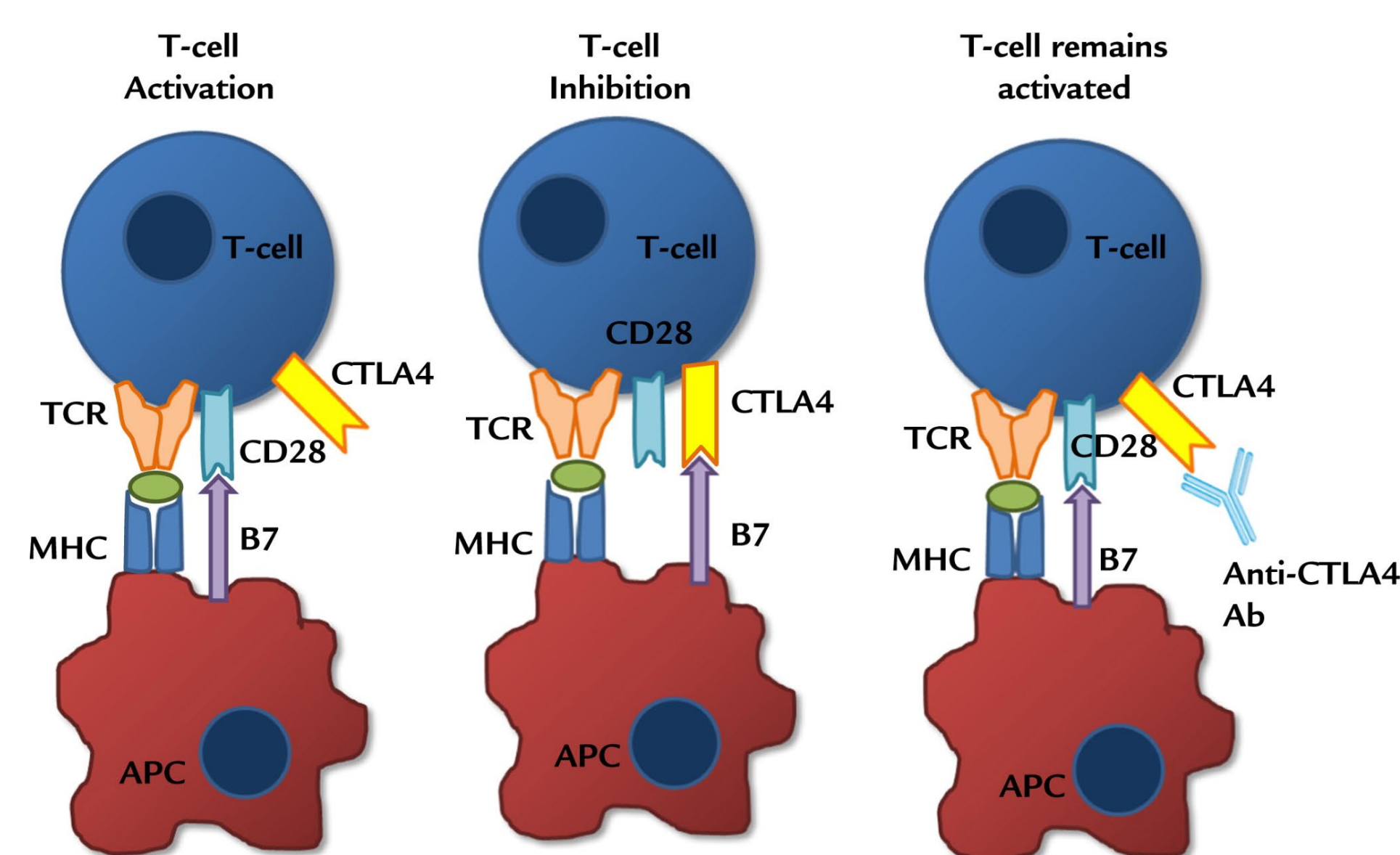
## AUTOIMMUNITY AND CTLA-4

- The immune system recognizes self antigens as pathogenic, leading to the activation of the adaptive immune system
- Leads to the production of autoantibodies that are responsible for attacking healthy tissues and organs
- A mutation of CTLA-4 was identified in patients with Crohn's Disease who also displayed autoimmune symptoms
- There are some identifiable single nucleotide polymorphisms (SNPs) of CTLA-4 found in patients with rheumatoid arthritis

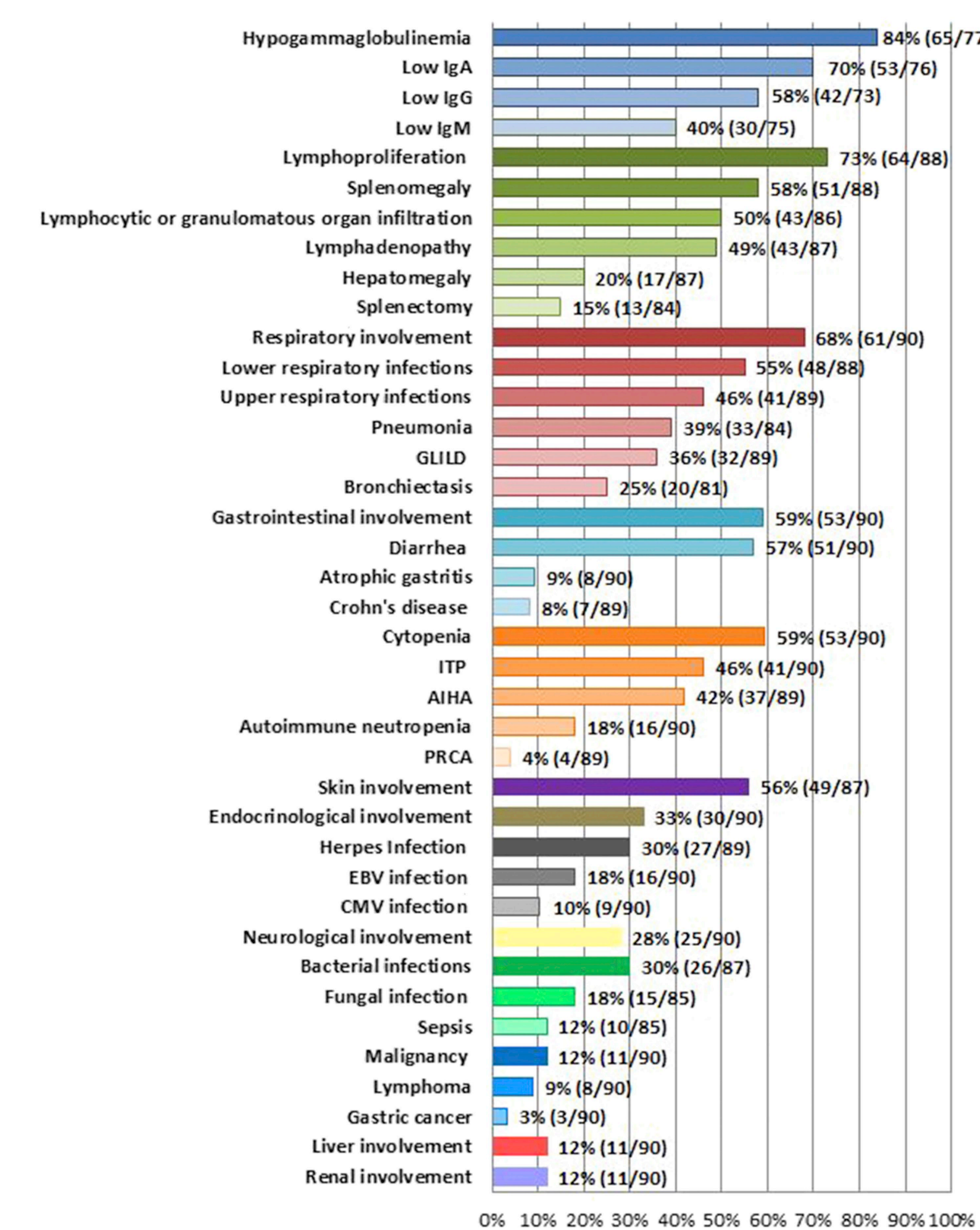
## CONCLUSIONS

- CTLA-4 plays a role in the development of both autoimmunity and immunodeficiency
- Mutations of CTLA-4 increases the chance of a patient developing both diseases
- There is no well-known treatment that can treat both an autoimmune disorder and immunodeficiency
- Immunotherapies have been developed as cancer treatments by blocking certain immune pathways such as the CTLA-4 mechanism (Ipilimumab)

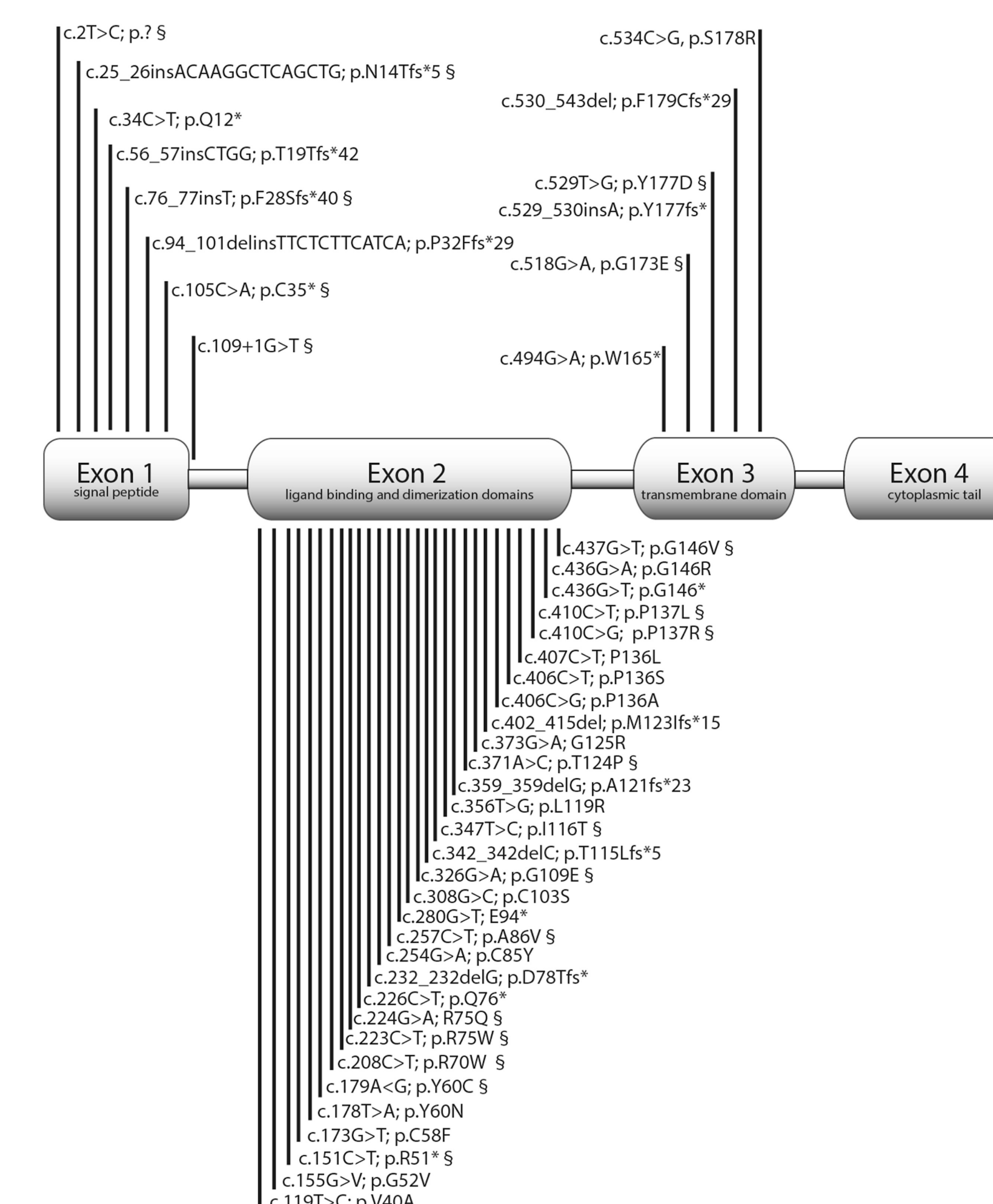
## CTLA-4 FUNCTION



**Figure 1.** CTLA-4 helps to regulate the immune response by inhibiting T cell activation and by releasing T regulatory and T follicular helper cells. (Buchbinder and McDermott 2015)



**Figure 2.** Autoimmune and immunodeficiency complications associated with CTLA-4 haploinsufficiency (Schwab et al. 2018).



**Figure 3.** Mutations of CTLA-4 are primarily found in exon 2 (Schwab et al. 2018).

## REFERENCES

