Defective immune homeostasis mechanisms in Celiac Disease (CD), in its progression to Refractory Celiac Disease (RCD) and transformation to Enteropathy–Associated T–Cell Lymphoma (EATL type 1).

To evaluate the status of the immune regulation and homeostasis mechanisms in Celiac Disease (CD), and its progression toward Refractory Celiac Disease (RCD) and transformation to EATL type 1 focusing on FOXP3+ Tregs, ITGAX+ DCs, BTLA+ cell, PDCD1+ TFH subpopulations.

The series was comprised of 69 cases consisting on 50 samples of CD and 19 samples of EATL type 1. Protein expression was analyzed and quantified by digital image analysis. Histological compartmentalization included lamina propria, isolated lymphoid follicles and tumoral lymphoid area. In comparison to physiological conditions, CD was characterized by higher numbers of FOXP3+ Tregs and ITGAX+ DCs, but lower BTLA+ cells and PDCD1+ TFH cells. Progression from CD to RCD1, RCD2 and transformation to EATL was characterized by decreasing trends of FOXP3+ Tregs and BTLA+ cell. ITGAX+ DCs showed a similar decreasing trend from CD to RCD stages but transformation to EATL was characterized with a striking increase. The RCD progression and EATL transformation stages show a defect in inhibitory pathways of FOXP3 and BTLA. Those results pinpoint the role of immune homeostasis and tolerance in CD and in the generation of cancer.