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Comparative analysis of papillary and anaplastic thyroid cancer using single-cell transcriptomics

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The mutational landscape of PTC and ATC has been demonstrated so far, but the complex interactions between immune cells and tumor cells in the TME and the transformation process from PTC to ATC are poorly understood. To characterize the properties and mechanisms inducing PTC and ATC, we profiled 25,276 and 17,001 single-cell transcriptomes from four patients with PTC and three patients with ATC. We discovered CD4+ cytotoxic T lymphocytes secrete more cytotoxic substances in TME of PTC than ATC and are therefore more capable of eradicating established tumor cells in PTC. TREM2+ Tumor Associated Macrophages (TAMs), SPP1+ TAMs and myofibroblast Cancer Associated Fibroblasts(myCAFs) suppresses the immune system and promote tumor growth and invasion in the TME of ATC. Furthermore, we identified pathways that allow ATC to become more malignant than PTC and to escape the control of the immune system. Moreover, we detected chromosomes with sample-specific copy number alterations in ATC and elucidated that ATC is homogeneous, whereas PTC is heterogeneous. Developmental trajectory analysis also revealed a transformation from follicular cells through PTC to ATC. Taken together, our study delineated the architecture of TME and highlighted biological process that transform PTC to malignant ATC.