Table S3. The summary of CD161's role in different types of cancers and its potential molecular.

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| --- | --- | --- | --- | --- | --- |
| Cancer types | Subject | Methods | Prognostic significance | Possible mechanisms | Reference |
| Breast cancer | Tissue/ cancer cells | mRNA | Positive | KLRB1/CD161 suppresses the proliferation, invasive and migrative abilities. KLRB1/CD161 enhance the anti-cancer immunity. | Huang G, et al [1] and He JR,et.[2] |
| Oral squamous cell carcinoma | Tissue | IHC/ immunofluorescence | Positive | CD161/LLT1 influences the OSCC tumor immune microenvironment. | Hu X, et al. [3] |
| HPV-Driven Oropharyngeal Cancer | Tissue | Single-cell RNA-seq | Positive | KLRB1(CD161) boost the anti-tumor immune responses. | Wei Y, et al.[4] and Cha J, et al[5] |
| Pancreatic cancer | Tissue | Immunofluorescence  staining | Positive | Promote cytokine secretion, and enhance anti-tumor immunity | Chen Q,et al.[6] |
| Lung cancer | Tissue/  cancer cells | mRNA | Positive | KLRB1 regulates lung adenocarcinoma cell proliferation and metastasis through the MAPK/ERK pathway. Down-regulation of KLRB1 is associated with increased cell growth, metastasis, poor prognosis, as well as a dysfunctional immune microenvironment. | Xu S, et al.[7] and Chen JL,et al.[8] |
| Gliomas | Tissue/  cancer cells | Single-cell RNA-seq/Co-Culture | Negative | KLRB1 inhibits the T cell- mediated immune response. | Mathewson ND, et al [9] and Wang Di, et al. [10] |
| Hematological malignancies | tumor cells and T-cells | CD161 mAb | Negative | A high-affinity CD161 mAb enhanced key aspects of T-cell function, including cytotoxicity, cytokine production, and proliferation in hematological malignancies. | Alvarez Calderon F, et al.[11] |
| Breast cancer | Tissue | Single-cell RNA-seq | Negative | CD161 compromises T-cell cytotoxicity, inhibiting calcium influx in CTLs, leading to chemoresistance and poor outcomes. | Lao L, et al.[12] |

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