The Chinese Oncology Society (COS) of Taiwan

中華民國癌症醫學會

Taiwan Pioneered in Implementing Medical Oncology Training Program in Asia

- Medical Oncology Training Program (1987~ 1990) in Taiwan

Prof. Paul P. Carbone

Prof. Jacqueline Whang-Peng

The Chinese Oncology Society (COS) of Taiwan

- The leading association of medical oncologists and cancer researchers in Taiwan:
  - 1980: founded by Prof. Ta-Cheng Tung, a basic researcher and a professor of biochemistry.
  - 1990~ : overseeing medical oncology training program and issuing certification of medical oncology board in Taiwan.
- Currently, there are 359 board-certified medical oncologists, and 1081 active members.

The Chinese Oncology Society (COS) of Taiwan

Prof. Yun Yen
President (2015-2017)

Prof. James C. Yang
Chair of Academic Committee

Taiwan Joint Cancer Conference (TJCC)

2016 Annual Meeting in Taipei

- **Date:** May 14 (Sat)~ May 15 (Sun), 2016
- **Venue:** International Conference Center, National Taiwan University Hospital, Taipei, Taiwan
- **Theme:** Precision Cancer Medicine




Dynamic changes of CD127 (IL-7 receptor alpha chain) expressing CD8+ effector memory and terminal effector subsets in head and neck squamous cell carcinoma

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Disclosure

- Hsiang-Fong Kao: no conflicts to disclosure

Head and Neck Squamous Cell Carcinoma

- Head and neck squamous cell carcinoma (HNSCC) in Taiwan
  - The 6th common cancer in Taiwan. 7,000 new HNSCC patients annually
  - The most common location of HNSCC: oral cavity
  - The etiology of HNSCC in Taiwan are betel nut chewing, cigarette smoking, and alcohol drinking [1]
  - Most patients are diagnosed at advanced stage.

- Treatment for HNSCC [2]
  - Local definitive treatment (surgery, CCRT, or RT)
  - Adjuvant CCRT/RT in high risk patients
  - Recurrent or metastatic HNSCC
    - Platinum-based chemotherapy
    - overall survival: less than 10 months

1. Hsu, W. L., et al. Int J Cancer 2014;135(6): 1480-1486.
2. Argiris, A., et al, The Lancet 2008;371:1695-1709

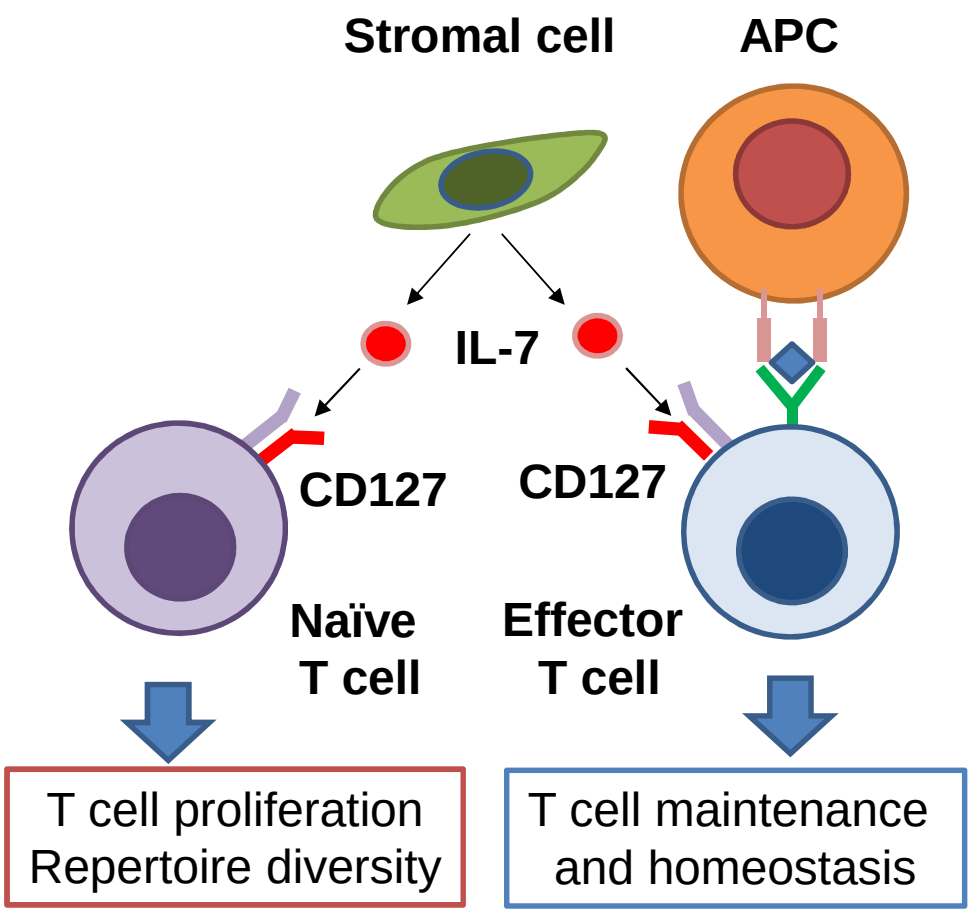
Immunotherapy for HNSCC

- Immune reaction and HNSCC
  - For immunocompromising host having head and neck cancer, the prognosis is worse. [1-2]
  - High CD8+ and PD-1+ TILs are favorable prognostic factors for HPV+ oropharyngeal cancer [3-4]
  - Infiltrating CD8+ TILs are associated with small tumors, early stage, and less LN metastases [5]

- Immune checkpoint inhibitor for HNSCC patients
  - Pembrolizumab: PD-L1+ HNSCC: ORR: 25% [6]
  - MEDI4736: HNSCC: ORR: 14% [7]

1. Schoenfeld JD Cancer Immunol Res 2015 3;12
2. Deeb R et al, Laryngoscope 2012;122:1566–9
3. Ward MJ et al, Br J Cancer 2014;110:489–500
4. Badoual C et al, Cancer Res 2013;73:128–38
5. Cho Y-A et al, Oral Oncol 2011;47:1148–53
6. Seiwert T et al, ASCO 2014 (suppl; abstr 6011)
7. Segal NH et al. ASCO 2014 (suppl; abstr 3002).

The role of IL-7 and CD127 in cancer



- IL-7 is a cytokine for: [1]
  - T cell development
  - maintaining of mature T cells
  - T cell proliferation and increasing T cell repertoire
- CD127: alpha subunit of IL-7 receptor [2-6]
  - decreased in the peripheral blood of cancer patients
  - correlated with cancer stage.
- The role of IL-7 and CD127 in tumor infiltrating lymphocyte is not well understood.

1. Mackall CL et al, Nat Rev Immunol 2011;11:330
2. Lee J-J,... and Chia JS, PLoS ONE 2014,9(1): e85521
3. Drennan S et al, Immunology. 2013;140(3):335
4. Lim KP et al, PLoS ONE 9(8): e103975
5. Vudattu NK et al, Int J Cancer. 2007;121:1512
6. Sharma S et al, Front Immunol. 2015;6:49.

Hypothesis

- The expression of CD127 in different subsets of T cells is not homogenous, with different T cell function phenotype
  - Aim 1: To define the frequency of CD127 in different subsets of T cells (CD45RA, CCR7)
  - Aim 2: to assess the functional phenotype of CD127 expressing cells
  - Aim 3: to clarify the correlation of CD127 expression and different subsets of T cell exhaustion (PD-1, TIM-3)

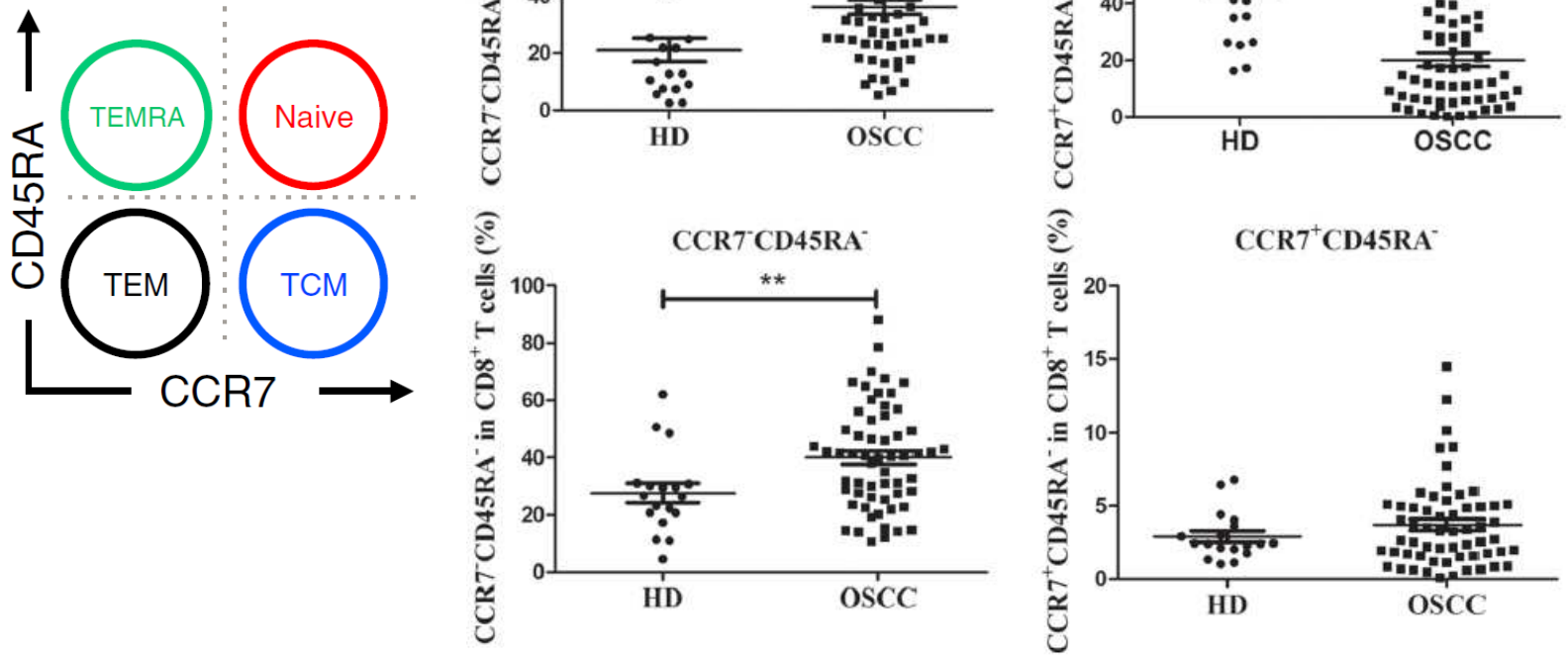
Study design and key methods

- Newly diagnosed HNSCC patients
- Tumor and blood were collected during operation

- Isolation of tumor infiltrating lymphocyte: Fragmented method with Ficoll or Percoll gradient method
- PBMC: Ficoll gradient

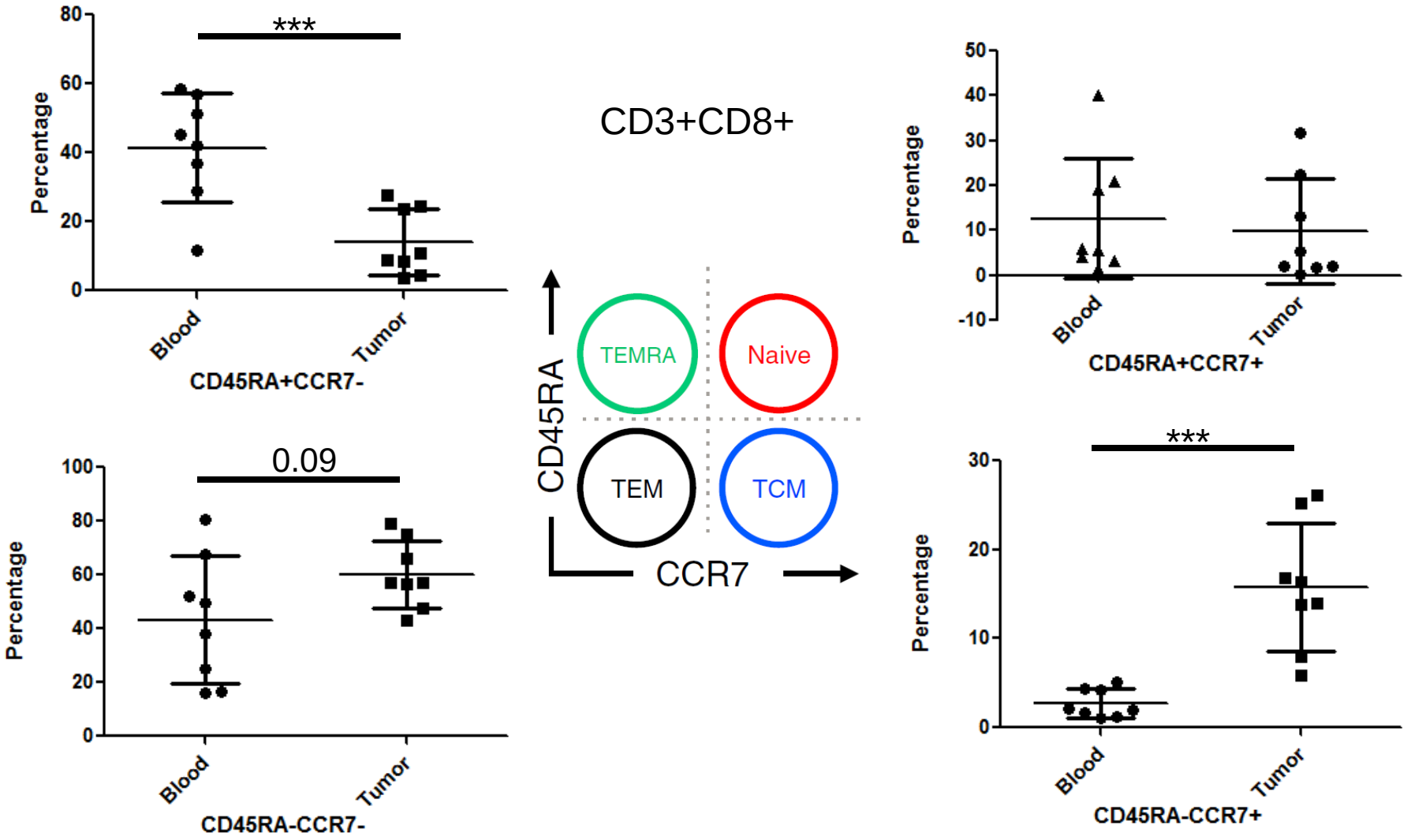
- Flow cytometry:
  - BD Fortessa
  - FlowJo
  - CD3:UCHT1, CD4:RPA-T4, CD8:SK1
  - CD45RA: HI100, CCR7: G043H7
  - CD127:eBioRDR5, PD-1:EH12-2H7, TIM3:CD366

OSCC patients had less naïve T cells and more effector memory T cells in the peripheral blood

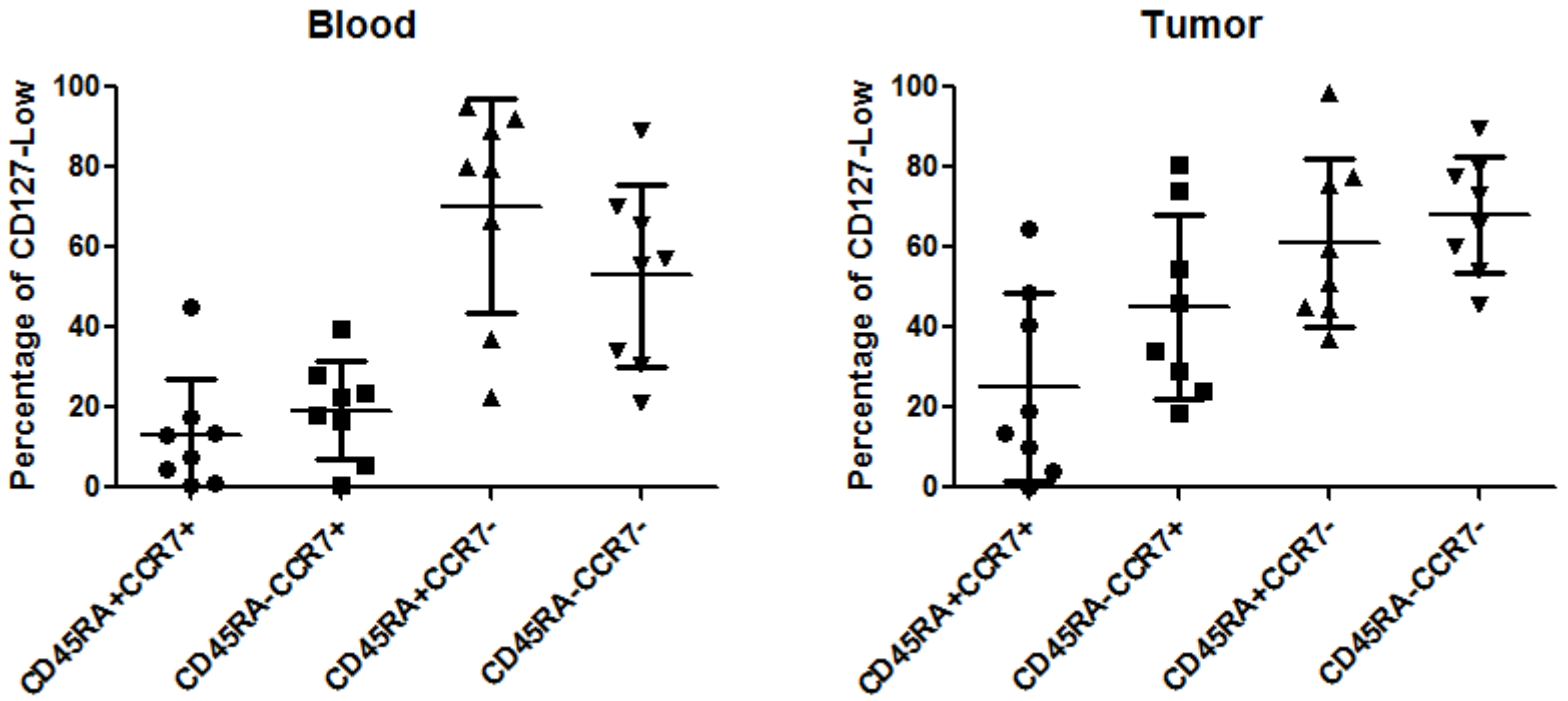


Lee J-J,... and Chia JS, PLoS ONE 2014,9(1): e85521.

Different CD8+ T cell compartmentalization in TIL and blood

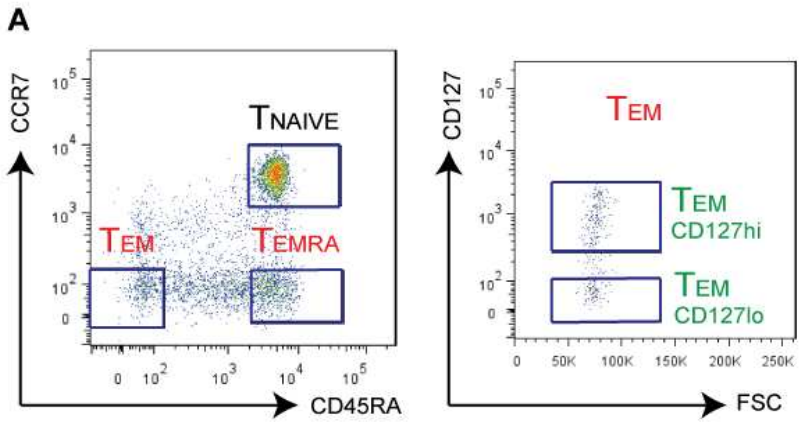


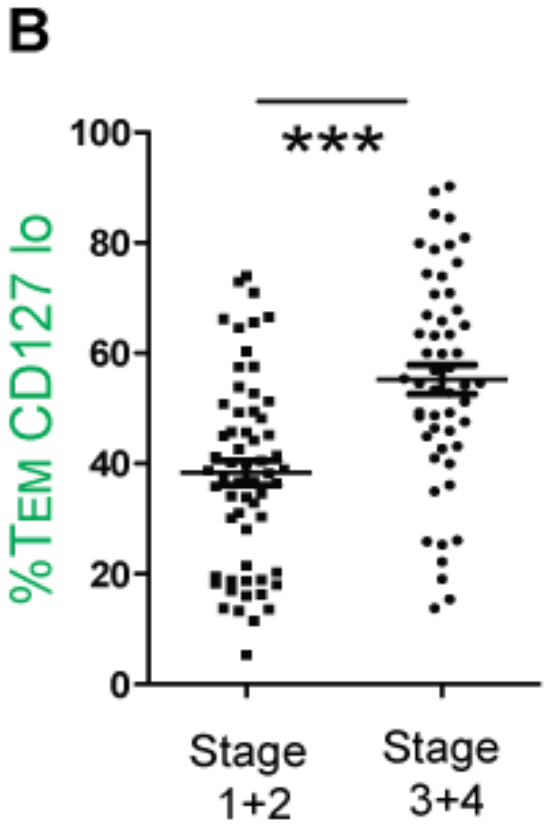
CD127^{low} in different subsets of CD8+ T cells



CD127-low: comparing with FMO control

Peripheral blood immunophenotyping of oral cancer patients is related to cancer stage





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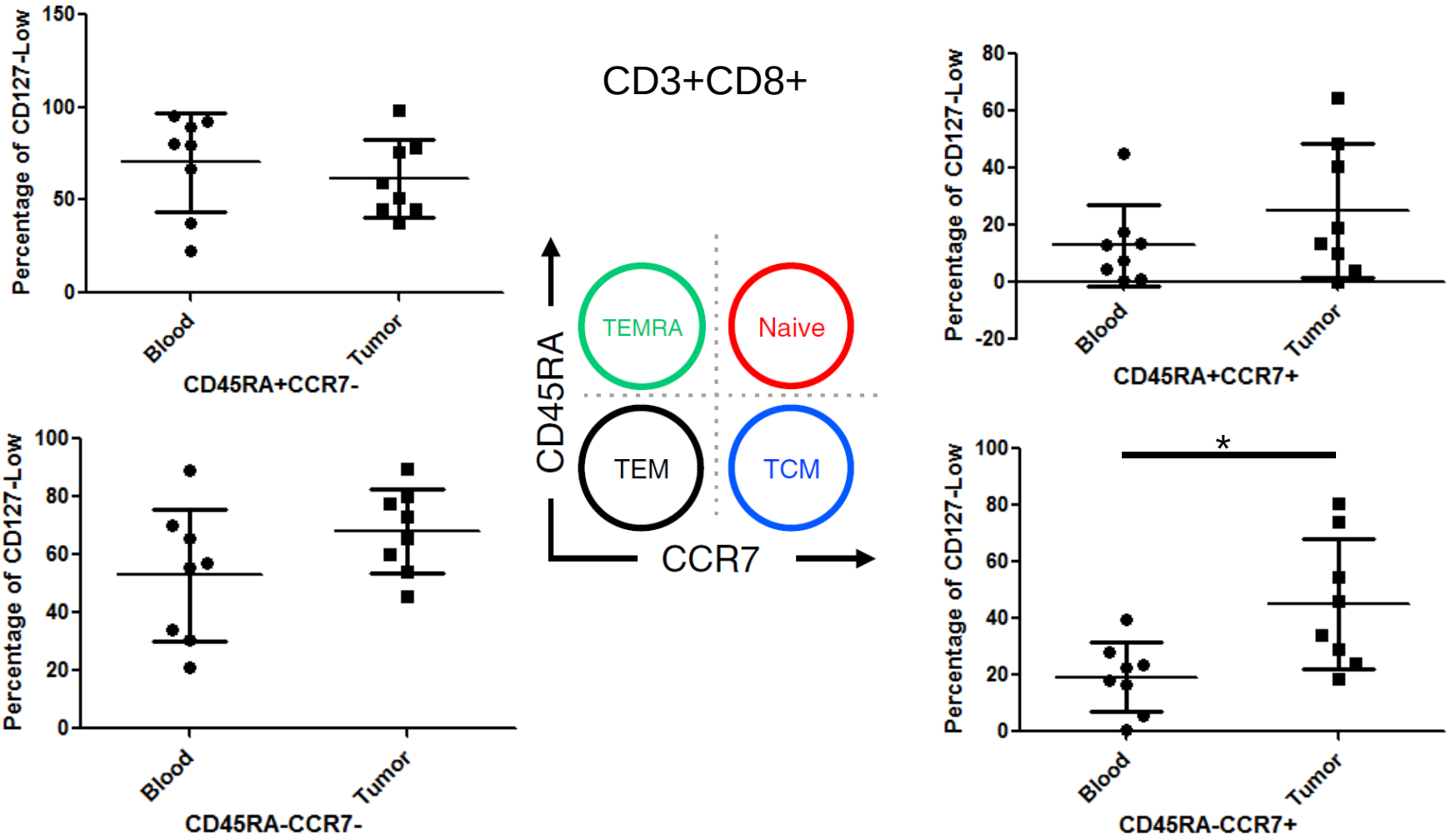
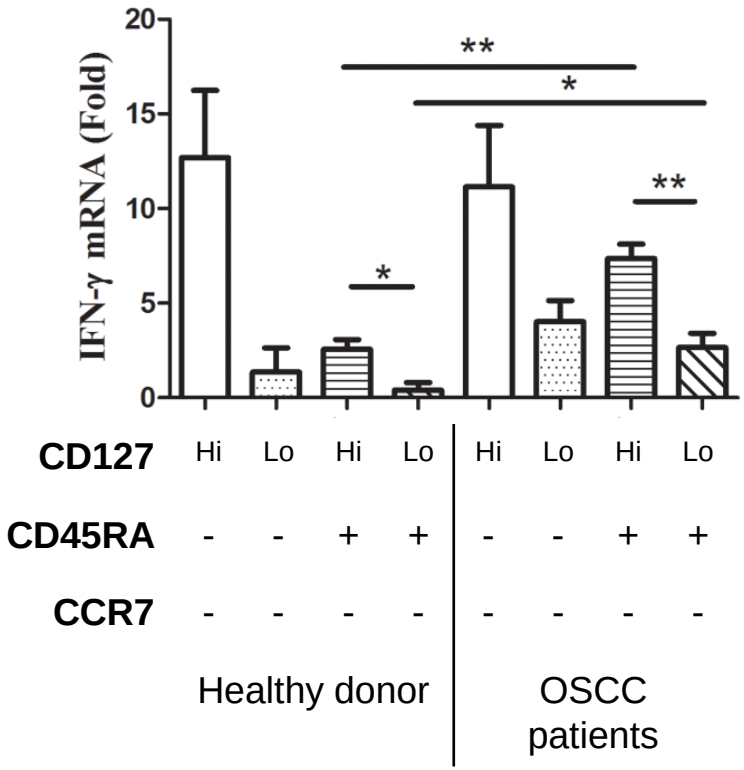
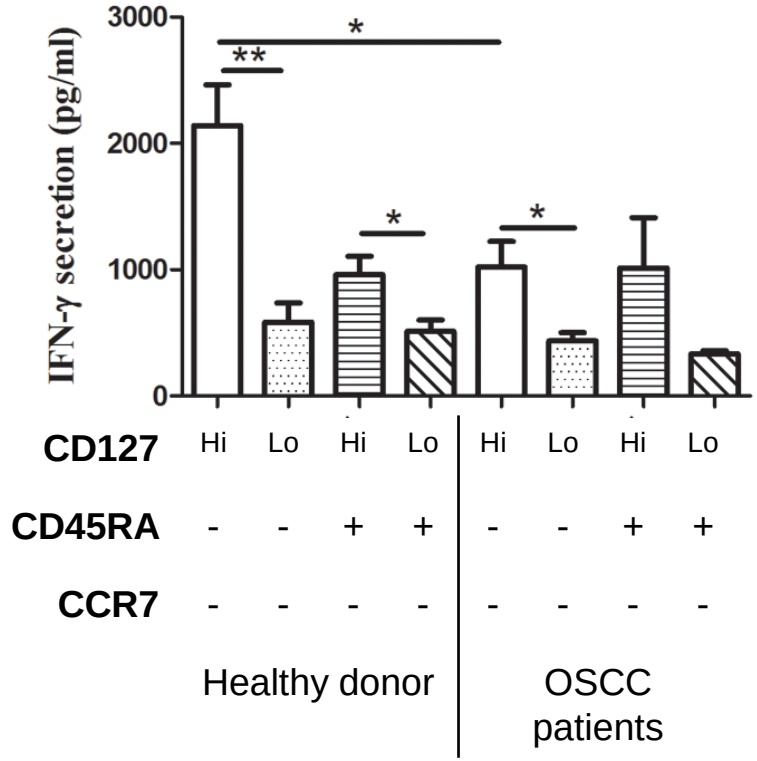
CD127^{low} in different subsets of CD8+ T cells



CD127^{low} effector memory T cells has less productivity of IFN-γ





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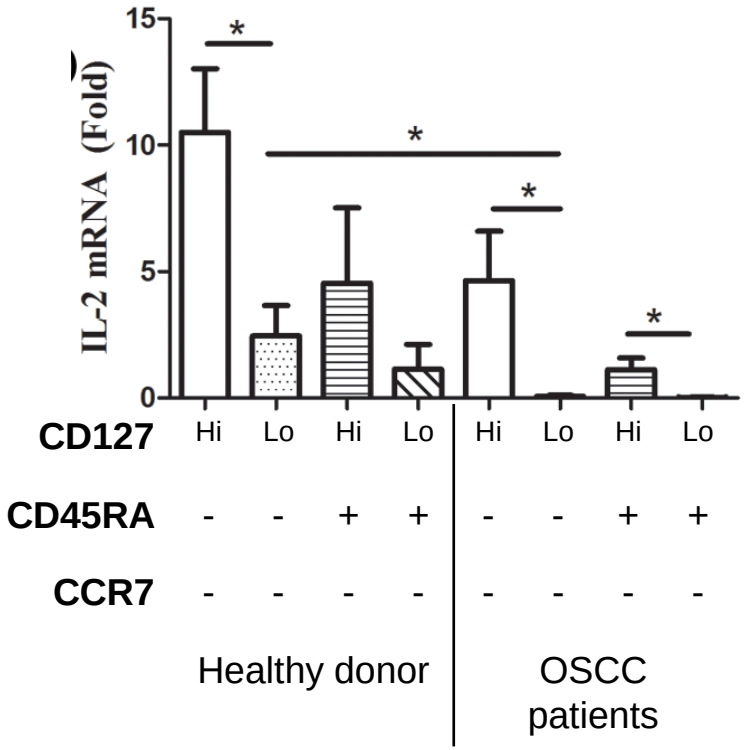
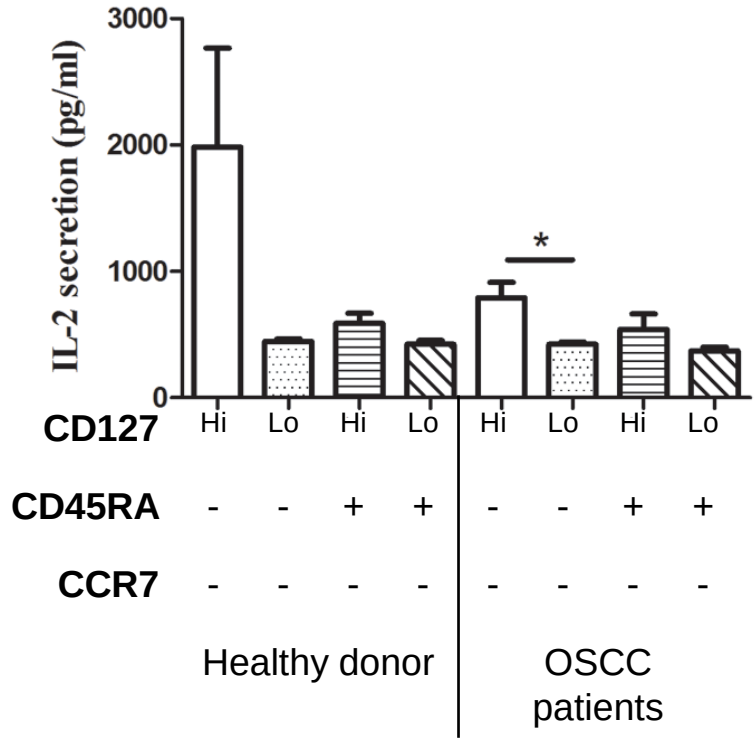
CD127^{low} effector memory T cells has less productivity of IL-2





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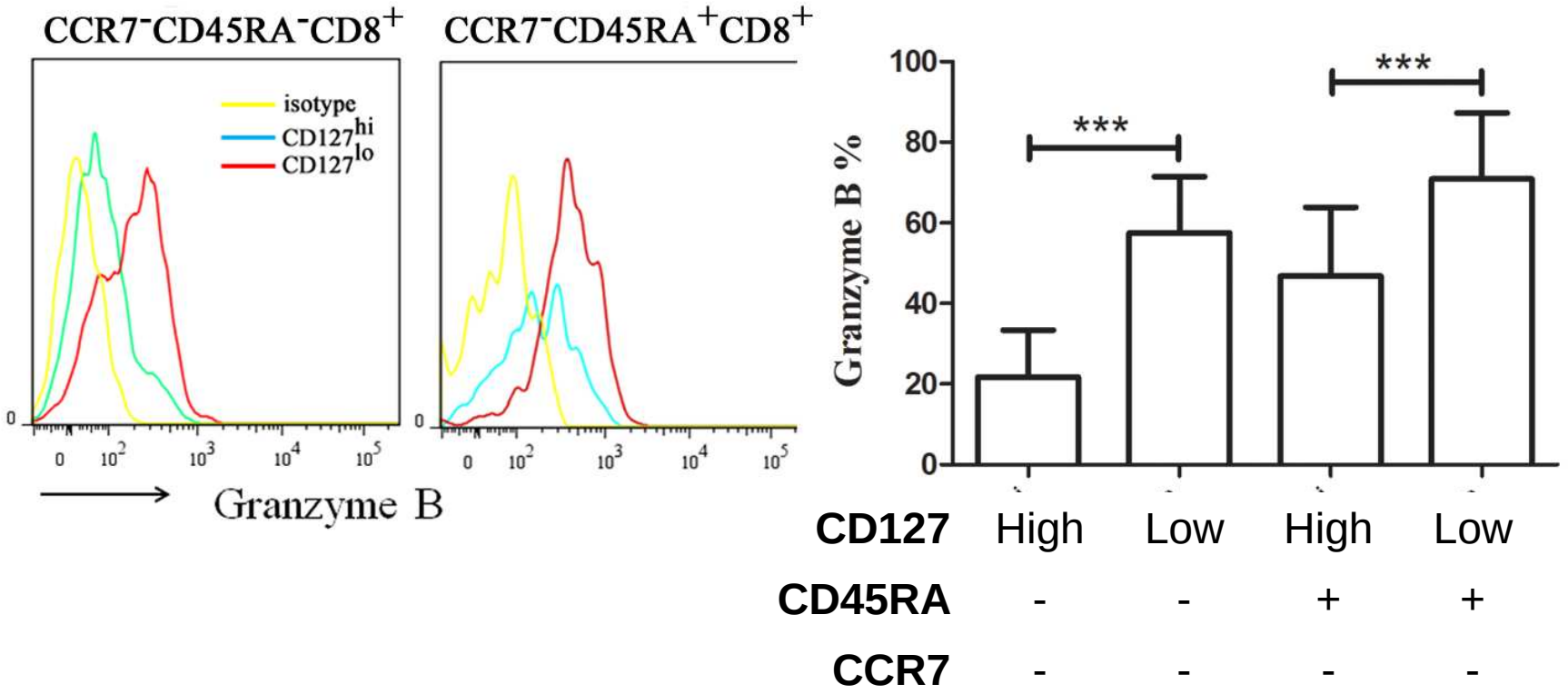
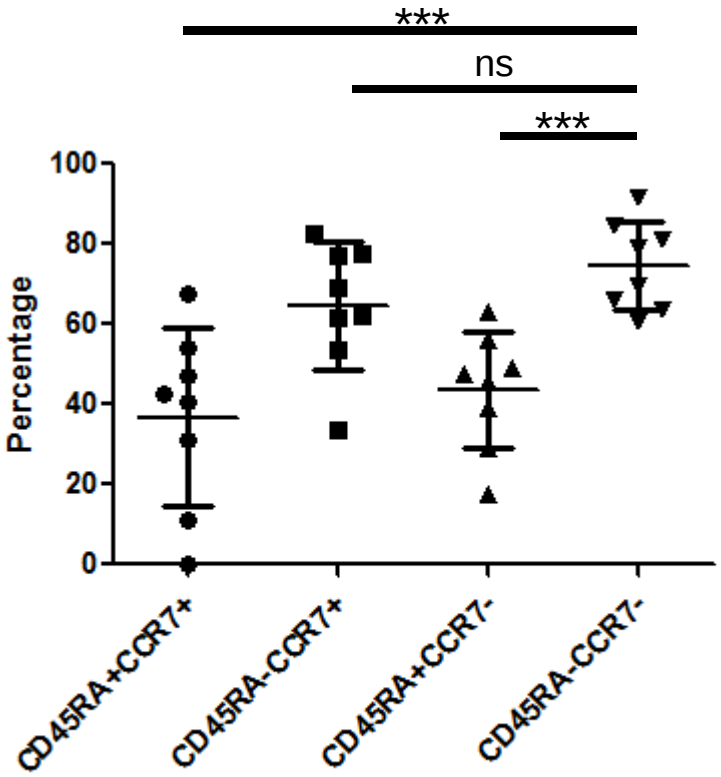
CD127^{low} effector memory cells exhibit high granzyme B production



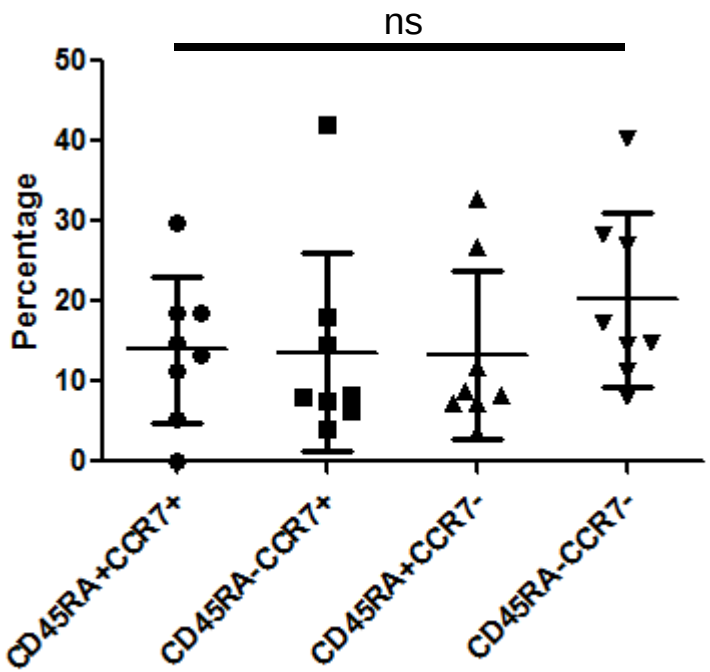
* Peripheral blood in HNSCC patients

Lee J-J,... and Chia JS, PLoS ONE 2014,9(1): e85521.

PD-1 and TIM-3 expression in different subsets of tumor infiltrating lymphocytes

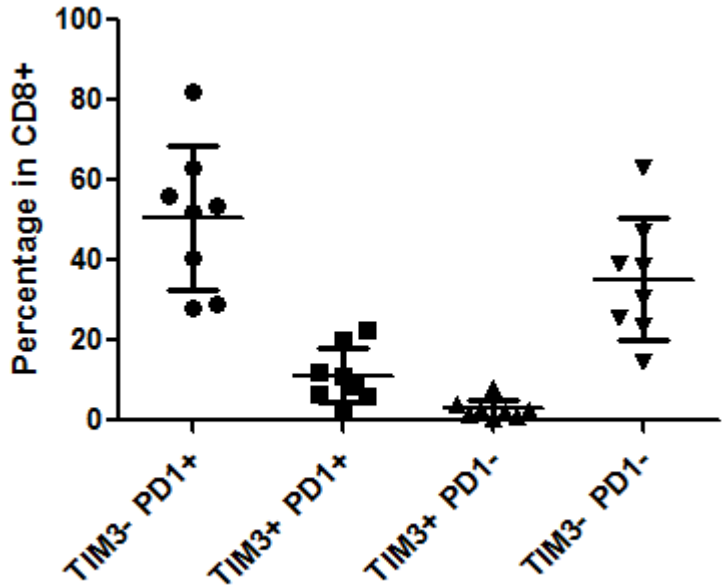


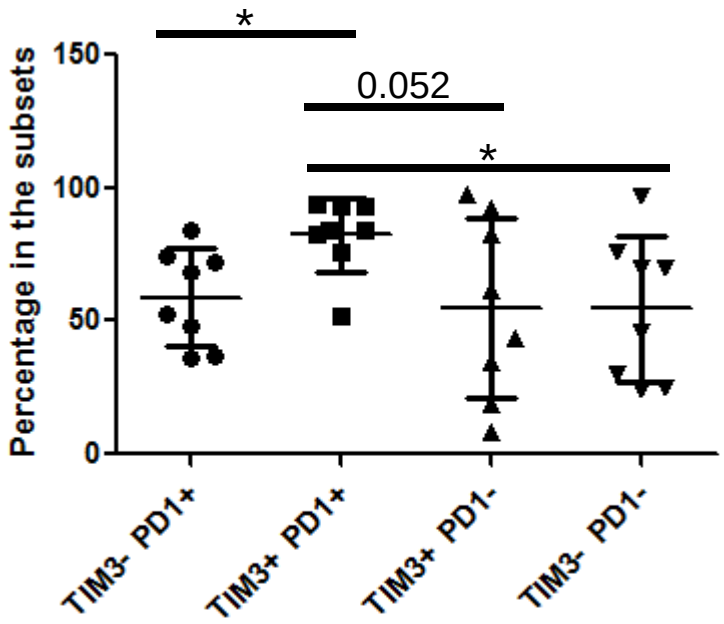
PD-1



TIM-3

The PD-1^{+}TIM-3^{+} subsets had a higher frequency of CD127^{low} lymphocytes in tumors



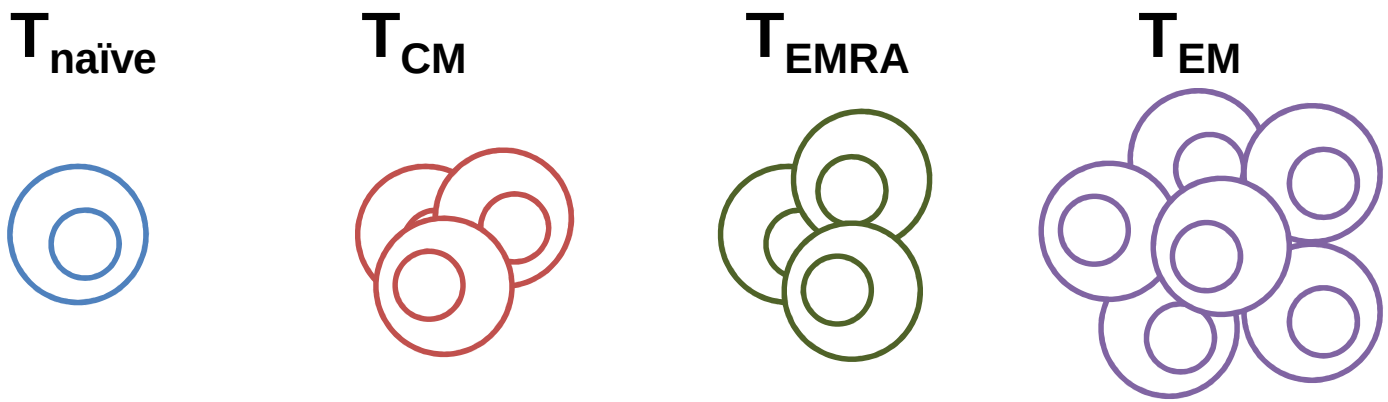


Conclusion

- The frequency of $CD127^{low}$ in effector T cell is correlated with clinical stage of HNSCC
- Tumor infiltrating lymphocyte
  - The frequency of T_{CM} and T_{EM} is higher in TIL than in blood
  - The CD127 expression decreased as the T cell matured.
- Function of $CD127^{low}$ effector T cells
  - less production of IL-2 and IFN-γ.
  - More productivity of granzyme B
- $CD127^{low}$ in different subsets of checkpoint expression
  - The frequency of $CD127^{low}$ is higher in $PD\text{-}1^{+}TIM\text{-}3^{+}$ $CD8^{+}$ T cells

Future Perspectives

The role of IL-7/CD127 in cancer immunotherapy



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