**Steps to reproduce Figure 5 of main manuscript.**

**Construct the HNSCC model from the model equations given in the filename ‘HNSCC\_model\_equation’.**

**For Figure 5(a)**

1. Set the value of barrier building CAF proportion (alpha) =0.005
2. Load the parameter set for given alpha and from the document ‘HNSCC\_parameters’. Store it in a vector P.
3. Set P(14)=10
4. Set the initial condition (y\_0) for simulation as

y\_0=[22.0447; 6.1926; 17.8158; 201.5737; 5.0551; 6.3483; 59.8564; 7.3397; 0; 8.5270; 4.4444; 0.8939; 52.8060; 15.4442; 18.1709; 13.8821; 4.8854; 19.5717; 13.3581; 10.6108; 12.2203; 10.1635; 16.770; 13.7578];

1. Simulate the HNSCC model with for the following values of killer T cell proliferation rates cells(P(12))

P(12)[ 0 0.0500 21.0000 31.0000 41.0000 51.0000 61.0000 71.0000]

1. Plot the PDL1+ tumor cells vs PDL1- tumor cells normalized by their carrying capacities.

**For Figure 5(b)**

1. Set the value of barrier building CAF proportion (alpha) =0.005
2. Load the parameter set for given alpha and from the document ‘HNSCC\_parameters’. Store it in a vector P.
3. Set the value P(39)=150, P(40)=15, and P(41)=0.001.
4. Set the initial condition (y\_0) for simulation as

y\_0=[654.8; 354.5; 1227.8; 1997.2; 860.0; 1789.7; 29.3; 704.7; 0; 1615.7; 1287.4; 1536; 1395.2; 222.9; 314; 925.6; 1869.7; 1109.7; 521.1; 1011.7; 1468.4; 1724.2; 429.1; 117];

1. Simulate the HNSCC model with the following CAF-driven growth rate of tumor cells (P(14))

P(14)[ 7.5000 15.0000 22.5000 30.0000 37.5000 45.0000 60.0000 75.0000 82.5000 90.0000 97.5000 105.0000 135.0000 165.0000];

1. Plot the time profiles of the helper T cells. Adjust the time limit appropriate for the inset figure.

**For Figure 5(c)**

1. Set the value of barrier building CAF proportion (alpha) =0.005
2. Load the parameter set for given alpha and from the document ‘HNSCC\_parameters’. Store it in a vector P.
3. Set the initial condition (y\_0) for simulation as

y\_0=[22.0447; 6.1926; 17.8158; 201.5737; 5.0551; 6.3483; 59.8564; 7.3397; 0; 8.5270; 4.4444; 0.8939; 52.8060; 15.4442; 18.1709; 13.8821; 4.8854; 19.5717; 13.3581; 10.6108; 12.2203; 10.1635; 16.770; 13.7578];

1. Simulate the HNSCC model with the following -cell cytotoxicity (P(16))

P(16)[ 10 300 600 900 1200 1500 1800 2100 2400 2700 3000];

1. Plot the steady state ratio of PDL1- to PDL1+ tumor cells vs the Killer T cell cytotoxic levels P(16).
2. Repeat the exercise for different values of T cell exhaustion rate (P(36))

P(36)[ 16 32 50 80 128 150];

**For Figure 5(d)**

1. Set the value of barrier building CAF proportion (alpha) =0.005
2. Load the parameter set for given alpha and from the document ‘HNSCC\_parameters’. Store it in a vector P.
3. Use Latin-hypercube sampling to generate 10,000 different realizations of the influential parameters (P(i)) with i[12 14 30 32 33 36 37 38 39 40 41 42 43 44 45 48 49 50 51 53 54 55 58]
4. Simulate the model for each parameter combination without and with (anti-PD1 dosage=2) anti-PD1.
5. Use scatter plot to generate the points covered by the sampled parameters in the plane. The calculation of is outline in the main manuscript.
6. Each point in the plane is color modulated by the steady state values of Total tumor cells, Killer T, and CAF populations normalized by the respective carrying capacities.

**For Figure 5(e)**

1. Set the value of barrier building CAF proportion (alpha) =0.005
2. Load the parameter set for given alpha and from the document ‘HNSCC\_parameters’. Store it in a vector P.
3. Set the initial condition (y\_0) for simulation as

y\_0=[654.8; 354.5; 1227.8; 1997.2; 860.0; 1789.7; 29.3; 704.7; 0; 1615.7; 1287.4; 1536; 1395.2; 222.9; 314; 925.6; 1869.7; 1109.7; 521.1; 1011.7; 1468.4; 1724.2; 429.1; 117];

1. Simulate the model with anti-PD1 dosage=1 for following values of CAF-driven growth rate of tumor cells P(14).
2. P(14)[ 0 60 120 180 240 300 500 1000 2000];
3. Plot the total tumor cells vs. killer PD1- T cells.