**Steps to reproduce Figure 3 of main manuscript.**

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

**For Figure 3(a-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\_immune\_desert\_modelling’. Store it in a vector P.
3. Set the values of P(30)=P(31)=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; 3.8821; 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 T cell exhaustion rate (P(36))

P(36)[ 0.8000 4.8000 8.8000 12.8000 16.8000 20.8000 24.8000]

1. Plot the time profiles of Exhausted and Killer T cell populations normalized by their carrying capacities (P(29))

**For Figure 3(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\_immune\_desert\_modelling’. Store it in a vector P.
3. Set the value P(30)=P(31)=10, P(36)=72.
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; 3.8821; 4.8854; 19.5717; 13.3581; 10.6108; 12.2203; 10.1635; 16.770; 13.7578]

1. Simulate the HNSCC model with the following values of CAF-Treg interaction (P(40))

P(40)[ 1 3 5 7 9];

1. Plot Regulatory T cell vs. Killer T cell population. Both the population are log-normalized with respect to the carrying capacity.

**For Figure 3(d-f)**

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\_immune\_desert\_modelling’. Store it in a vector P.
3. Set the value P(11)=5, P(16)=1500,
4. For the dotted plot (Low-proliferation scenario), set P(30=P(31)=0.5
5. For the solid plot scenario, set P(30)=P(31)=50, P(36)=72.
6. Set the initial condition (y\_0) for simulation as

y\_0=[222.0447; 206.1926; 217.8158; 401.5737; 205.0551; 206.3483; 259.8564; 207.3397; 200; 208.5270; 204.4444; 200.8939; 252.8060; 215.4442; 218.1709; 203.8821; 204.8854; 219.5717; 213.3581; 210.6108; 212.2203; 210.1635; 216.770; 213.7578]

1. Simulate the HNSCC model with anti\_PD1 dosage of 1and the following values of anti-PD1 binding rate (P(35))

P(35)[ 0.5000 5.5000 10.5000 15.5000 20.5000];

1. Plot the exhausted vs Killer T cell population, PD1- Killer T cells vs Post-ICI tumor cells (Fig: 3(d-e)).
2. Repeat the steps 1-8 with the Lactate clearance rate C\_LAC=10