**Steps to reproduce Figure 9 of main manuscript.**

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

**For Figure 9(a)**

1. Load the parameter set for given alpha and from the document ‘HNSCC\_parameters’. For the following proportions of Barrier constructing CAF cells (alpha)

alpha[ 0.0050 0.0800 0.1000 0.1500 0.2000 0.3000 0.4000 0.5000]

1. Set the initial condition (y\_0) for simulation as

y\_0=[5.6304; 7.6874; 8.0805; 3.9277; 7.5001; 0.1805; 0.8207; 2.5095; 0; 7.9163; 7.5867; 8.0238; 6.3413; 0.4928; 9.4814; 6.1741; 9.7238; 7.2642; 5.0844; 8.1333; 7.8140; 1.8921; 0.9877; 5.9869 ];

1. Simulate the HNSCC model with for the parameter vectors against each alpha.
2. Plot the time profile for IL-8 concentration for different alpha and thereby steady state immune accessibility index.

**For Figure 9(b)**

1. For the fibro-desert scenario, use alpha=0.05 to load the parameters from the file ‘HNSCC\_parameters\_fibro\_desert\_modelling’
2. Set the initial condition (y\_0) for simulation as

y\_0FD=[ 2000; 0; 2500; 4000; 0; 0; 59.8564; 50; 0; 40; 20; 30;150; 150; 18.1709; 13.8821; 4.8854; 19.5717; 13.3581; 10.6108; 12.2203; 10.1635; 0; 13.7578]; for the pre-anti-PD1 setting. For the simulation in the presence of anti-PD1 set the initial condition as the final value of pre-anti-PD1 simulation.Set anti\_PD1 dosage=2

1. Simulate the HNSCC model with the aforementioned setting. Store the IL-8 and killer T cell data.
2. For fibro-dominated and immune-dominated setting, use the initial condition as

y\_0IFR=[5.6304; 7.6874; 8.0805; 3.9277; 7.5001; 0.1805; 0.8207; 2.5095; 0; 7.9163; 7.5867; 8.0238; 6.3413; 0.4928; 9.4814; 6.1741; 9.7238; 7.2642; 5.0844; 8.1333; 7.8140; 1.8921; 0.9877; 5.9869];

1. Load the parameters form the file ‘HNSCC\_parameters’ for alpha=[ 0.005 0.5];
2. Simulate the HNSCC model for both the values of alpha and plot IL-8 concentration vs killer T cells in all the scenarios.

**For Figure 9(c)**

1. For fibro-dominated scenario, set the value of barrier building CAF proportion (alpha) =0.5
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=[108.2087; 602.6678; 350.1559; 937.5152; 556.5256; 33.2473; 888.2395; 244.3348; 0; 722.0367; 78.8519; 697.2312; 793.8480; 450.4767; 541.5014; 253.9598; 961.2047; 294.3169; 172.0025; 859.1064; 766.1546; 641.7523; 484.2232; 132.2313];

1. Simulate the HNSCC model without the anti-PD1. Collect the steady state vector (y\_s).
2. Use the y\_s as the initial condition to simulate three scenarios (a) anti-PD1 with OPN knockout (b) anti-PD1 with LIF knockout, and (c) anti-PD1 with OPN and LIF knockout.
3. Plot IL-8 concentration vs Total tumor cells in all four (fibro-rich+3 knockout strategies).