- NK2GD is a receptor on NK cells, and tumour cells that express this receptor are more susceptible to be killed by NK and T cells.
- NKG2D receptor is an essential regulator of the activity of such effector immune cells, triggering potent cytotoxic mechanisms against target cells expressing its stress-induced ligands, even when normal levels of inhibitory MHC-I molecules are present.

- Tumour-induced immune suppression:

1. Tumour cells express enzymes that alter metabolism and results in the starvation of the tumour microenvironment of amino acids needed by the lymphocytes in order to function.
2. For example, tryptophan, arginine or i-NOS depletion.
3. Additionally, the tumour cells increase the production of immune suppressive factors, i.e. TGF-beta, which drives the activity of **T regulatory cells (T reg)** that dampen down the immune response.
4. The cells can also express **CCL22 that attracts its receptor, CCR4 on the Treg cells.**
5. An accumulation of Tregs in tumours **predicts a poor outcome** for the individual due to the suppressed immune response.
6. Within the immune system, there exist **inhibitory immune receptors – Programmed death (PD1) and PD-L1 –** which maintain the immune checkpoint.
7. The tumour cells exploit this mechanism by increasing the expression of PD-L1. An increased expression of PD-L1 by tumours predicts poor outcome.

→ Therapies created to circumvent tumour-induced immune suppression include:

- IDO inhibitors
- Selective Treg elimination
- Immune checkpoint blockade: anti-PD1 or anti-PDL antibodies

THE ROLE OF THE IMMUNE SYSTEM IN INITIATING & PROMOTING TUMOUR GROWTH:

1. Acute inflammation is good for the body, however, persistent, chronic inflammation **can facilitate malignant transformation** and **promote tumour growth.**
2. Chronic inflammation contributes to:
   - Cancer initiation by generating genotoxic stress
   - Cancer promotion by inducing cell proliferation
   - Cancer progression by enhancing angiogenesis and tissue invasion

3. Evidence linking cancer and inflammation include:
   - Chronic inflammatory diseases increase cancer risk, i.e. H.pylori infection and stomach cancer
   - NSAIDs reduce the risk of developing certain cancers, i.e. colon and breast cancer
   - Signalling pathways involved in inflammation operate downstream of oncogenic mutations, i.e. RAS and Myc