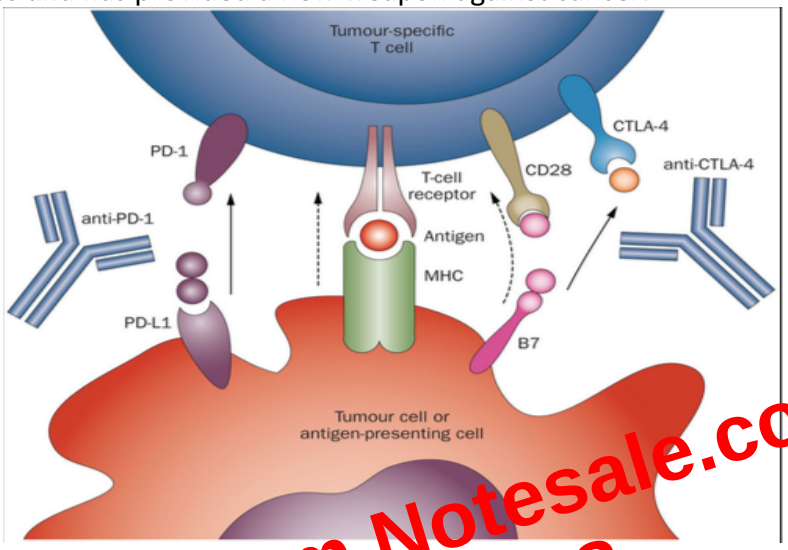
4. Tumours co-opt/exploit inhibitory receptors and ligands ('immune checkpoint' molecules) that impair T cell survival, activation, proliferation and effector functions.
    - Anti-tumour T cells are held in check by immune checkpoint molecules that **suppress T cell activation and effector functions.**

Immune checkpoint blockade (ICB) immunotherapy:

1. ICB immunotherapy (including **anti-CTLA4, anti-PD1 and anti-PDL1 antibody drugs**) which target and block immune checkpoint molecules can unleash anti-tumour responses and has provided a new weapon against cancer.



2. T cells from cancer patients exhibit **defective F-actin immunological/immune synapses.**
3. T cell activation leads to the formation of the immunological synapse in healthy patients, whereby there is **F-actin polymerization ('the kiss of death')** and leads to the release of cytolytic granules.
4. However, T cells acquired from lymphoma patients exhibit **no immunological synapses,** due to the lack of T cell activation. Immune checkpoint therapy aims to return T cell function and this can be measured via F-actin polymerization.

T cell Activation:

1. T cell activation requires 2 signals:
2. **Signal 1:** T cell receptor (TCR) signalling:
    - T cell activation occurs after interaction between the TCR and antigen (Ag) in the context of MHC (signal 1).
    - TCR signalling occurs when the TCR is engaged by cognate peptide (Ag)-MHC.

3. **Signal 2:** co-stimulatory signalling (i.e. CD28) amplifies TCR signalling and the recruitment of signalling molecules at the immune synapse to drive T cell activation.
    - T cell activation occurs after interaction between the TCR and antigen in the context of MHC (signal 1) plus **CD28 co-stimulation** ('stimulator') (signal 2).