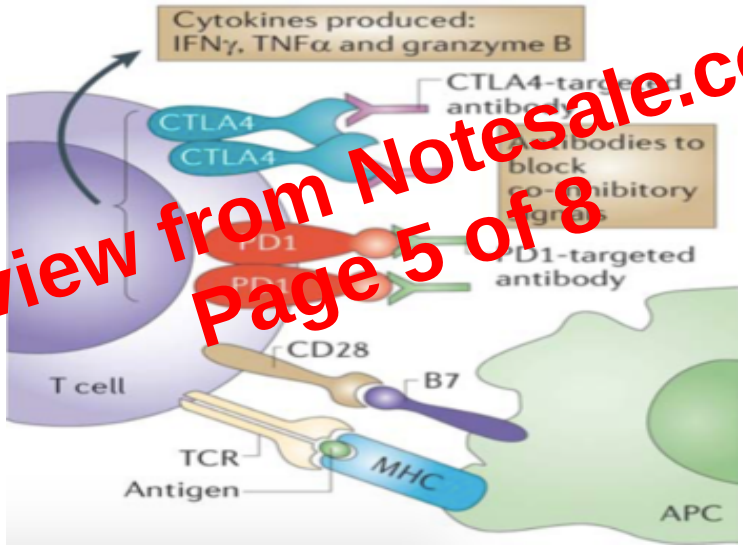
Potential targets for antibody therapy of cancer:

1. Blood vessels are an important component to cancer metastasis and induction of angiogenesis is dependent on growth factors, i.e. VEGF.
2. MA-bs can be used to attack a number of cancer associated targets including:
   - Tumour-associated blood vessles
   - VEGF
   - Diffuse malignant cells (i.e. leukaemia)
   - Tumour cells within a solid tumour
   - Tumour-associated stroma – attack stroma that supports the cells

Activation and suppression of antigen specific T cells:

1. Uncontrolled activation of T cells is a key mechanism exploited by cancer cells and T cell activation is regulated by **PD-1 and CTLA4.**
2. These compete with T cells to inhibit them further inappropriate activation, and thus a potential immunological mechanism would be to target these "exhaustive" marks and the immune cells.
3. However, **autoimmunity** is a possible side effect.



4. Blocking mAb, such as alpha-CTLA4 and alpha-PD1, neutralize these co-inhibitory receptors
5. These **mAbs block intrinsic immune checkpoints**, allowing sustained T cell responses, including increased cytolytic activity and production of cytokines, such as IFN-gamma.

OVERALL: Monoclonal antibodies work by:

1. Blocking receptor mediated signalling for tumour cell survival and/or growth: reduced/loss of efficacy when downstream signalling components are deregulated (i.e. mut-RAS for anti-EGFR therapy, loss of PTEN function, etc).
2. Marking tumour cells for immune mediated destruction: