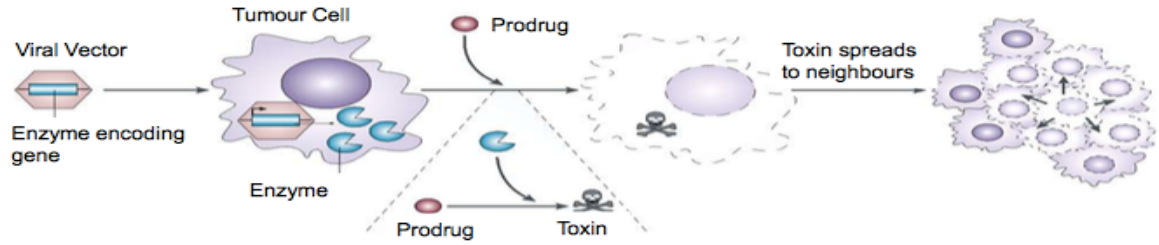
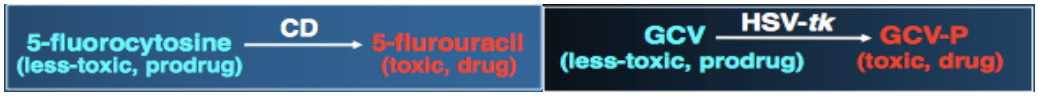
- **Cytosine deaminase/5-fluorocytosine**
- **HPV/ganciclovir**



3. The therapeutic **transgenes have the ability to convert a non-toxic pro-drug**, which penetrates the tumour, into cytotoxic drug or to express the toxic gene expression product.
4. This takes places inside the tumour with the help of an administered viral or bacterial cell suicide inducing gene.
5. The normal cells are not affected.



- The replicating **murine leukaemia virus (MLV):**
  1. Simple virus, well understood
  2. RNA virus with no oncogene and preferential random integration (when it hits 'correct' gene, it becomes oncogenic)
  3. Infects proliferating cells only
  4. Reduced immunogenicity of retroviral vectors
  5. Transcriptional control of replication – use of tissue/tumour specific promoters
  6. Stable integration, not directly cytolytic and there is the possibility of sustained presence.
  7. Can provide **pro-drug activated cell death by suicide genes**

  8. However, some things to consider:
  - HSC transduction unlikely with intra-tumoural injection
  - Inability to infect HSCs *in vivo* without growth factors
  - **No selective advantage for the infected cells**
  - Suicide gene-mediated elimination of infected cells
  - **Availability of anti-retroviral drugs (safety feature)**
  - Risk vs. benefit ratio in poor prognosis maliganancies

- **Replication competent retrovirus (RCR) vectors for suicide gene therapy:**
  1. The yeast cytosine deaminase (CD) as a suicide gene: CD converts the non-toxic 5-FC into the **toxic** metabolite 5-FU. This has a better bystander effect than HSV-tk/GCV vector.