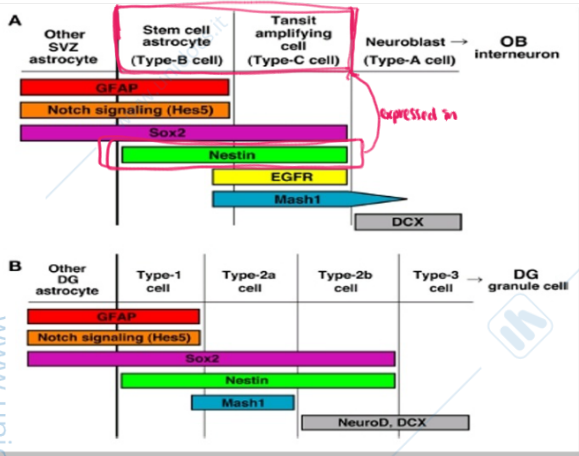
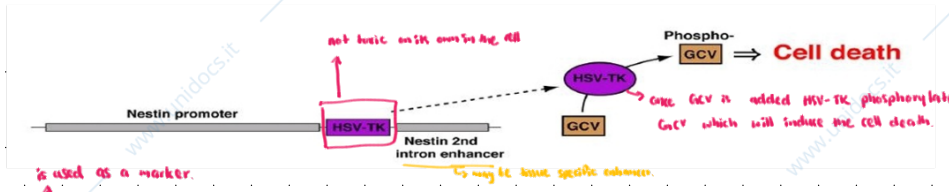


Tissue specific expression and inducible systems can also be used to obtain inducible tissue specific death.



Example: Genetic methods to identify and manipulate newly born neurons in the adult brain.

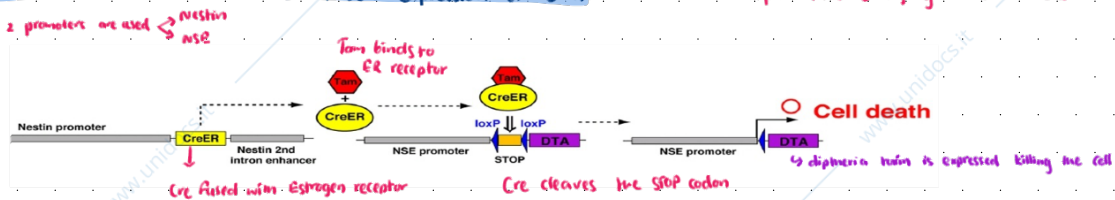


Nestin: an intermediate filament protein specifically expressed by neural stem/progenitor cells in the developing nervous system and the adult brain.

Administration of **Ganciclovir [GCV]** to mice carrying the transgene **Nestin-TK** results in death of dividing cells expressing herpes simplex virus thymidine kinase (HSV-TK).

HSV-TK produces toxic metabolites that disrupt DNA synthesis and results in the death of dividing cells.

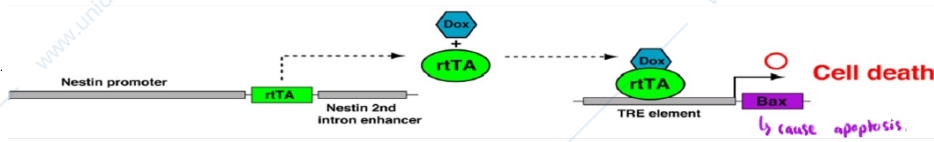
Tamoxifen-Cre/ER recombinase driven expression of **DTA** → used in experiments studying roles in cells (neurons) in diseases.



In the **Nestin-CreER / NSE-DTA** mouse

- Nestin-CreER drives the expression of a tamoxifen (Tam)-inducible form of Cre in NSCs
- Cre-inducible diphtheria toxin fragment A (DTA) is engineered into the locus of the neuron-specific enolase (NSE) gene.
- Activated CreER leads to the recombination of loxP sites and removal of the STOP cassette upstream of the DTA gene, thus allowing the expression of DTA from the NSE promoter.

Doxycycline induced expression of Bax



- In the Nestin-rTA/TRE-Bax mice, doxycycline [Dox] activates the rTA protein, which binds to seven TetO sequences (TRE) to drive the expression of the pro-apoptotic protein Bax, which activates the apoptosis pathway in NSCs.
- Alternatively, also DTA could be used.