- Bcl-2 regulators promote cell killing by either interfering with the protectors or activating the killers.
- 2. These genes are defined by the presence of one to four short blocks of conserved protein sequences called Bcl-2 homology domains (BH).
- 3. Anti-apoptotic Bcl-2 protectors typically have four of the domains, whilst proapoptotic Bcl-2 killers have 3 of these domains.
- 4. The pro-apoptotic Bcl-2 regulators have **only** the BH3 domain, which is a short segment of helix that fits into a groove on the surface of both Bcl-2 protectors and killers, forming a complex that regulates their activity.
- 5. Bcl-2 protectors regulate the activity of Bcl-2 killers by forming a complex, thus interfering with the ability of Bax (a killer) to kill cells.

Mechanisms of regulating the pro-apoptotic proteins:

- 1. Apoptosis can be regulated transcriptionally or through post-translation modifications, which depends on the time requirements of the system.
- 2. For example, CTL-mediated destruction of virus infected cells undergoes in minutes due to the danger this poses to the animal and is thus post-translational modification, whereas, the loss of tail in tadpole development occur over works and tesale.co. thus transcriptionally regulated.
- Transcriptional Regulation:
- C ramily 3. P53 activates the expression of pre-activates the expressio members, i.e. Bax and Bid and members, i e ecl-2 and Bcl-X₁. represses the anti-apost reti
- Post-trais a ional Regulation
- pH3-only pro-apoptotic Bc-2 family members are sequestered in the cytoplasm and can bind to calcium, resulting in a translocation so it can go to the mitochondria and bind to Bcl-2.

Bcl-2 Family & The Mitochondria:

- 1. In C.elegans, there is a sequestration model where via protein-protein interactions, where you can free a dangerous protein that can lead to the activation of caspases.
- 2. Within the mammalian system, there is a more complex model the mitochondrial integrity model, where the Bcl-2 family is responsible for the health and well-being of the mitochondria.
- 3. Anti-apoptotic proteins keep it healthy and pro-apoptotic are responsible for destroying it.
- 4. You can have direct or indirect activation of the family.
- 5. Additionally, some Bcl-2 family members can act as ion channels but cannot make pores big enough to allow cytochrome C out of the cell.