Lecture_2

- **Full Forms:**
  - ATM - Serine Theronine Kinase : Ataxia telangiectasia Mutated
  - CHK : Check Point Kinases
  - p53 : TUmour supressor protein
  - PUMA : p53 upregulated modulator of apoptosis
  - BAX : BCL2 associated X protein
  - BAK : BCL2 activating kinase
  - BCL2 : B Cell lumphoma
  - VDAC : voltage dependent anion channel
  - MAC : Mitochondria Apoptotic inducer channel
  - Caspase: Calcium dependent nucleases
- **Cell death**
  - Cell death is required to protect other cells from damage
  - Cancerous cells kill themselves to prevent spread
  - In viral infection the infected cells die to prevent spread
  - In cases of random mutation the cells kill themselves to prevent further damage
  - **Intrinsic Pathway**
    - Also known as mitochondrial pathway
    - Signal arises inside cell
    - In case of DNA lesions [DNA damage] intrinsic apoptotic pathway starts
    - Intrinsic Pathway starts with DNA Damage [Nucleotide shift, Mising nucleotide, Breakage]
    - ATM serine Threonine kinase / CHK [Checkpoint kinase] which sense DNA damage and give message to system and activates p53 [Tumor supressor protein]
    - p53 activate PUMA [p53 upregulated modulator of apoptosis]
    - PUMA activates 2 protens BAX [BCL2 associated X protein] and BAK [BCL2 activated kinase] BCL2 = B-cell lymphoma
    - BAX and BAK will bind to mitochondria to open up VDAC [voltage dependent anion channel]
    - There will be opening of MAC [mitochondrial apoptotic inducer channel]
    - Opening of channel will lead to release of cyt-C
    - cyt-C will bind to APAF [Apoptotic protease activating factor] to form a complex called as apoptosomes

- Procaspase9 gets converted into caspase9 under the influence of the apoptosomes
- Procaspare3 gets converted to caspase3 [calcium dependent nucleases] under the influence of caspase9
- Caspase3 with degrade DNA thoroughly, during this APAF will degrade the proteins thus the basic structural unit of cell ie. atkin fibres, cytoskeletons will be damaged and eventually the cells will be broken into pieces and the small fragments will be digested by phagocytosis

- **Extrinsic Pathway - TNF alpha Pathway**
  - TNF [Tumor necrotic factor]: cytokines released by some macrophages
  - It starts with release of TNF alpha which is a type of cytokine
  - This molecule binds to the TNFR1 [Tumor necrotic factor alpha receptor 1] which in turn leads to dissociation of SODD [Silencer of death domain]
  - The death domain recruits TRADD [Tumor necrotic factor associated with death domain] and FADD [First apoptotic signal associated death domain]
  - All of this together forms a complex TNFalpha-TNFR1-DD-TRADD-FADD and is called DISC [Death inducing signalling complex]
  - This DISC will nor recruit Procaspase8 which after activation turns into caspas8 which converts Procaspase3 into Caspase3
  - Caspase3 will recruit and activate calcium dependent nuclease and proteases.
  - These nucleases and proteases will degrade proteins and nucleic acid and lead to the eventual cell death
- **FAS-Ligand pathway**
  - Cytotoxic cells have a specific antigen called **FAS [*First Apoptotic Signal*] ligand**
  - This cytotoxic cell binds to FAS receptor via the *FAS-ligand*
  - This receptor is always in complex with a *Death Doman* and *SODD*
  - After binding dissociation of *SODD* takes place
  - After dissociated *FADD* binds with the Death domain
  - This complex of FAS-ligand-FAS-receptor-Deathdomain-FADD is known as *DISC*
  - This leads to activation of *Procaspase8* into *caspase8*
  - *Caspase8* will convert *Procaspase3* to *caspase3*
  - This will lead to the degradation of proteins and will lead to eventual cell death