Pyroptosis (pro-inflammatory programmed cell death)

- The term pyroptosis is derived from the Greek roots “pyro,” relating to fire or fever, and “ptosis” (pronounced “to-sis”), denoting falling, to describe pro-inflammatory programmed cell death.
- Pyroptosis is a more recently recognized form of regulated cell death with morphological and biochemical properties distinct from necrosis and apoptosis.
- Pyroptosis has been described in monocytes, macrophages and dendritic cells infected with a range of microbial pathogens.
- In contrast to apoptosis, pyroptosis requires the function of caspase-1.
- Recently, it was shown that Caspase-1 is activated during pyroptosis by a large supramolecular complex termed the pyroptosome.
- Only one large pyroptosome is formed in each macrophage, within minutes after infection.
- Biochemical and Mass Spectroscopic analysis revealed that this pyroptosome is largely composed of dimers of the adaptor protein ASC. (Apoptosis-associated speck-like protein containing a CARD or ASC)

TLRs

- TLRs present on macrophages and dendritic cell, recognize Pathogen-Associated Molecular Patterns (PAMPs) that are located either in cell surface or within endosomes.
- The resulting recognition will initiate the signaling pathway, including the activation of transcription factors NF-κB and MAPKs.
- This in turn will be responsible for the production of inflammatory cytokines such as IFN α/β, TNF and IL-12.
- In addition, pro-IL-1β and pro-IL-18 will be released to be processed by cysteine-mediated caspase-1.

- The term “pyroptosis” was originally introduced to describe a particular form of cell death in macrophages, which is induced by bacterial infection, is accompanied by caspase-1 activation and hence leads to the release of pyrogenic interleukins;
- however, it is still controversial whether pyroptosis – which can also be triggered by non-bacterial pathological stimuli – truly represents a cell death modality on its own or whether it constitutes a special case of apoptosis or necrosis.
NLRs

- NLRs consist of more than 20 subsets, including NOD1 and NOD2, NLRP3, NLRC4.
- All recognize bacterial, viral and toxic foreign products that are introduced into the host cell cytosol.
- Upon recognition, NOD1 and NOD2 function similarly to the TLRs, producing and processing inflammatory cytokines.
- Some of these subsets such as NLRP3 could also activate caspase-1 dependent cell death, accompanied by pore-formation.
- NLRC4 can specifically recognize flagellin and then trigger caspase-1 dependent pyroptosis.
- NOD’s recognize molecular pattern danger signals and build up the inflammasome.

Inflammasome

- Formation of the multi-protein complex inflammasome is achieved through the binding of intracellular bacterial, viral or host danger signals to the NLRs receptor, whose assembly leads to the activation of caspase-1.

PM AUTOLYSIS VS NECROSIS

AFTER DEATH

- Respiration ceases (Total Diffuse Anoxia)
- Anaerobic glycolysis
  - Rapid Depletion of Glycogen
  - Decrease in pH -- High lactic acid production
- Low pH Activate
  - Proteases, Lipases, Esterases, DNAses, RNAses, etc.
  - Release of Lysosomal Enzymes -- Autolysis
- Change Occur in All cells

MICROSCOPIC

- Living and Dead Tissue (Necrosis)
  - Not Always True
- Erythrocytes
  - Outline Sharpness
  - Staining Bright Red
- Inflammatory Zone and Hyperaemia (Necrosis)
  - In Kidney, If no Inflammation and Oedema present
    - Degeneration

PM AUTOLYSIS VS NECROSIS
**PM AUTOLYSIS VS NECROSIS**

- Rectal Prolapse
- Muscles
  - Soft, Pale red, Watery (Cooked Appearance)
- Omentum/Mesentry
  - Postmortem imbibitions

**PM AUTOLYSIS VS NECROSIS**

- Foul Smelling --- Putrefaction
  - AMONIA, HYDROGEN SULPHIDE
  - INDOLE, SKATOL
  - PUTRESCINE, CADVARINE
- Left Ventricle
  - Un-clotted blood -- Recent
  - Empty -- 2 hours after
  - Dark haemolysed blood -- Late
  - Clotted Blood -- Lingering Death
- Rumen, Reticulum, Omasum
  - Desquamation of Epithelium
- Black or Dark Green Colour
  - Fe + S or H2S

**References:**

2. Manual on meat inspection for developing countries, FAO.