

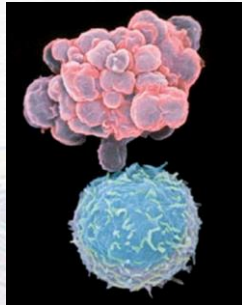
GENERAL PATHOLOGY

CELL INJURY – 14

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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) ²

- 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.

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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-1 β and pro-IL-18 will be released to be processed by cysteine-mediated **caspase-1**

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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**

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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

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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

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PM AUTOLYSIS VS NECROSIS

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

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PM AUTOLYSIS VS NECROSIS

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

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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

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QUESTIONS
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