**Lec. 5**

**Membrane Damaging Toxins**

**MDTs**

**The first membrane damaging activity of a bacterial culture fluid on erythrocyte was characterized by Paul Ehrlich ( 1888 ) and Alexandre Marmorck ( 1902 ) in culture fluid of *Cl . tetani* and *Streptococcus pyogenes* respectively .**

**The products were :**

**Tetanolycin for *Cl . tetani*.**

**Streptolycin ( S,O )for *Streptococcus pyogenes*.**

**MDTs were identified by their lytic action *in vitro* on erythrocytes suspension of human and other animals and the appearance of zone of hemolysis around the bacterial colonies growing on blood agar plates, ( still used for phenotypic characterization of bacteria for identification).**

* **Many if not all bacterial hemolysins acted on cells other than erythrocytes .**
* **Many of them also caused tissue damage or death when injected into experimental animals.**

**Certain members of MDTs are inactive on erythrocytes , while they damage other cells such as leucocytes ʺleucocidinsʺ some of them also named Cytotoxin ex : *S. aureus* leucocidin & *P. aeruginosa* leucocidin.**

**MDTs also named cytolysins or cytolytic toxins for their biological activity .**

**MDTs is a super family of toxins comprises 122 toxins ( about 36% ) verses 339 bacterial protein toxins, so far identified , thus it is the most important functional group .**

**Mechanism of action of MDTs :**

**Damage or disrupt the integrity**

**of the cytoplasmic membrane**

**of various eukaryotic cells**

**­­↓**

**Impairment of osmotic**

**balance**

**↓**

**Cell swelling**

**↓ subsequently**

**Cell lysis**

**↓**

**Release of intracytoplasmic**

**contents**

**Erythrocyte → hemoglobin**

**Various cells → lactale dehydrogenase**

**Following the cytoplasmic**

**membrane damage**

**Many MDTs**

**↓**

**Disrupt the membranes of**

**intracytoplamic organelleas**

**( Mitochondria , lysosome , phagosome )**

**↓**

**Release of pharmacologically action substances in the media**

**enzymes , inflammatory factors**

**cytokines , serotonin**

**The Role of MDTs in Pathogenicity :**

1. **Damage the host cells , tissue and organs .**
2. **Provoked apoptosis**
3. **Organelle vaculation**
4. **Production of inflammatory mediators ( cytokines )**
5. **Animal death**

**Classification of MDTs**

**MDTs can be classified according to the mechanisms of membrane damage of target cells to :**

**1- Toxins exhibiting detergent–like or ( surfactant ) activity resulting in membrane solubilization and ( or ) partial insertion into the hydrophobic regions of the target .**

**ex : Delta toxin of *S. aureus.***

**2- Cytolytic pore – forming toxins (PFTs ) characterized by their properties to create channals ( pores ) through the cytoplasmic bilayer membrane ( 7 – 9 nm ) of host cell.**

**ex : *S. aureus* α-toxin.**

**Listeriolysin O .**

**Streptolysin O .**

**3- Toxins that enzymatically hydrolyze the phospholipids of the membrane bilayers .**

**This group comprises hemolytic and some times lethal phospholipases .**

**ex :**

**- Phospholipases A ( A1 , A2 ) PLAs**

***E. coli***

***Salmonella enterica***

***Klebsiella pneumoniae***

**- Phospholipases C PLCs**

***B. cereus***

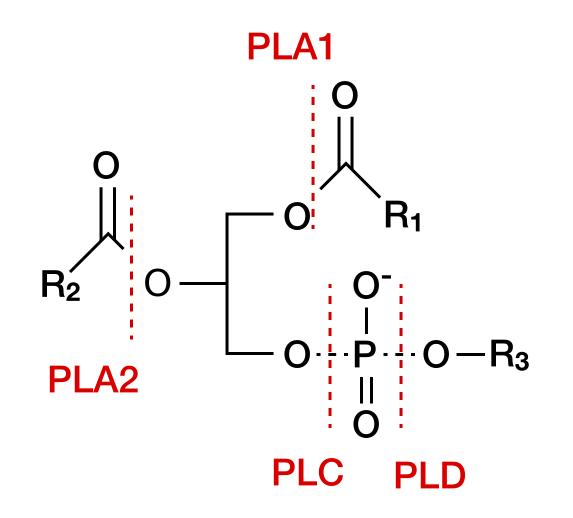
***Cl. Perfrengens***

**- Phospholipases D PLDs :**

**These toxins show 64 – 97 % sequence identical and related to those of PLD in the venom of brown recluse spider .**

**ex: *Corynebacteria pseudotuberculolosis***

***Haemophiless influenzae***

[](http://upload.wikimedia.org/wikipedia/commons/7/77/Phospholipases2.svg)