

Function of CHIP E3 ligase regulating necroptosis

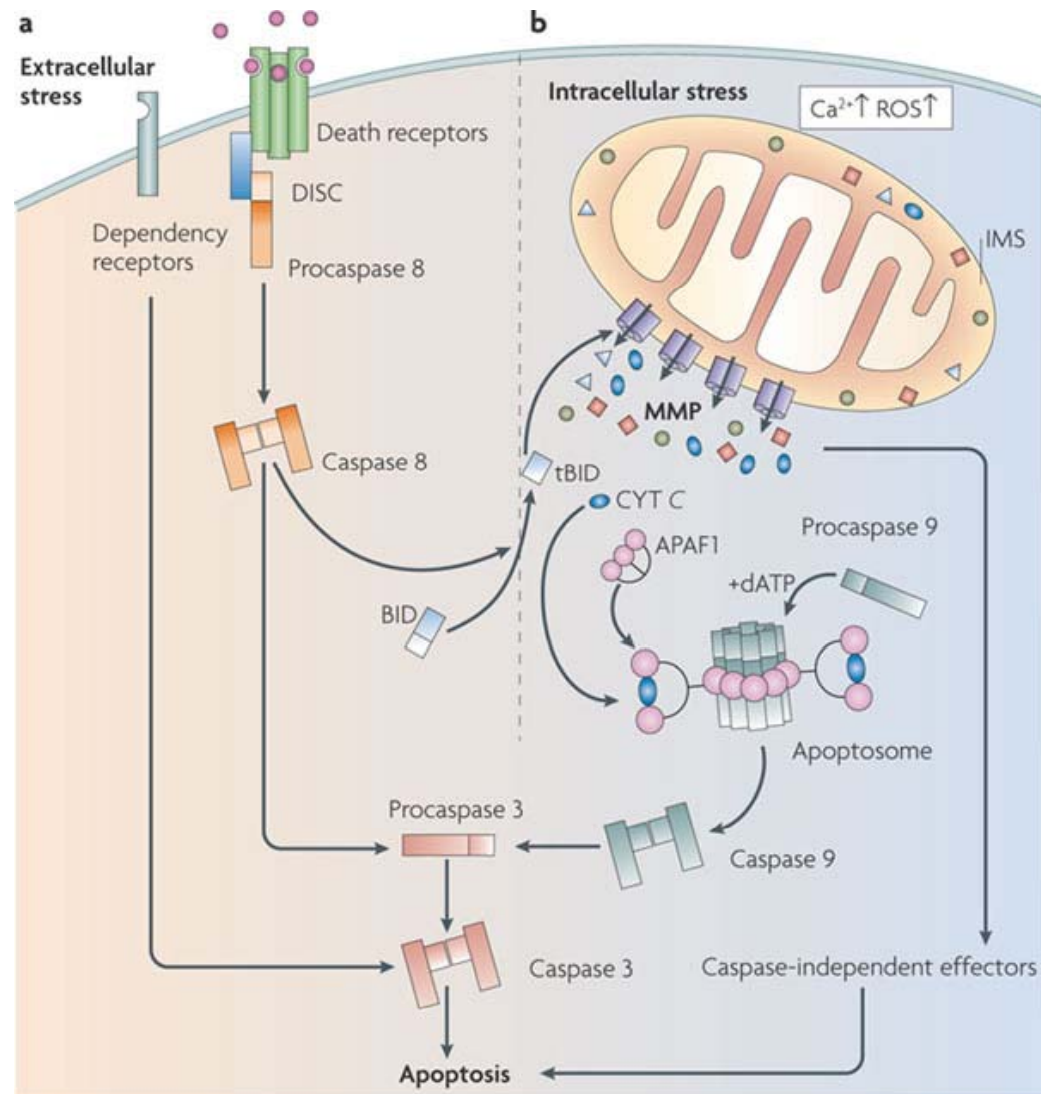


Jaewhan Song

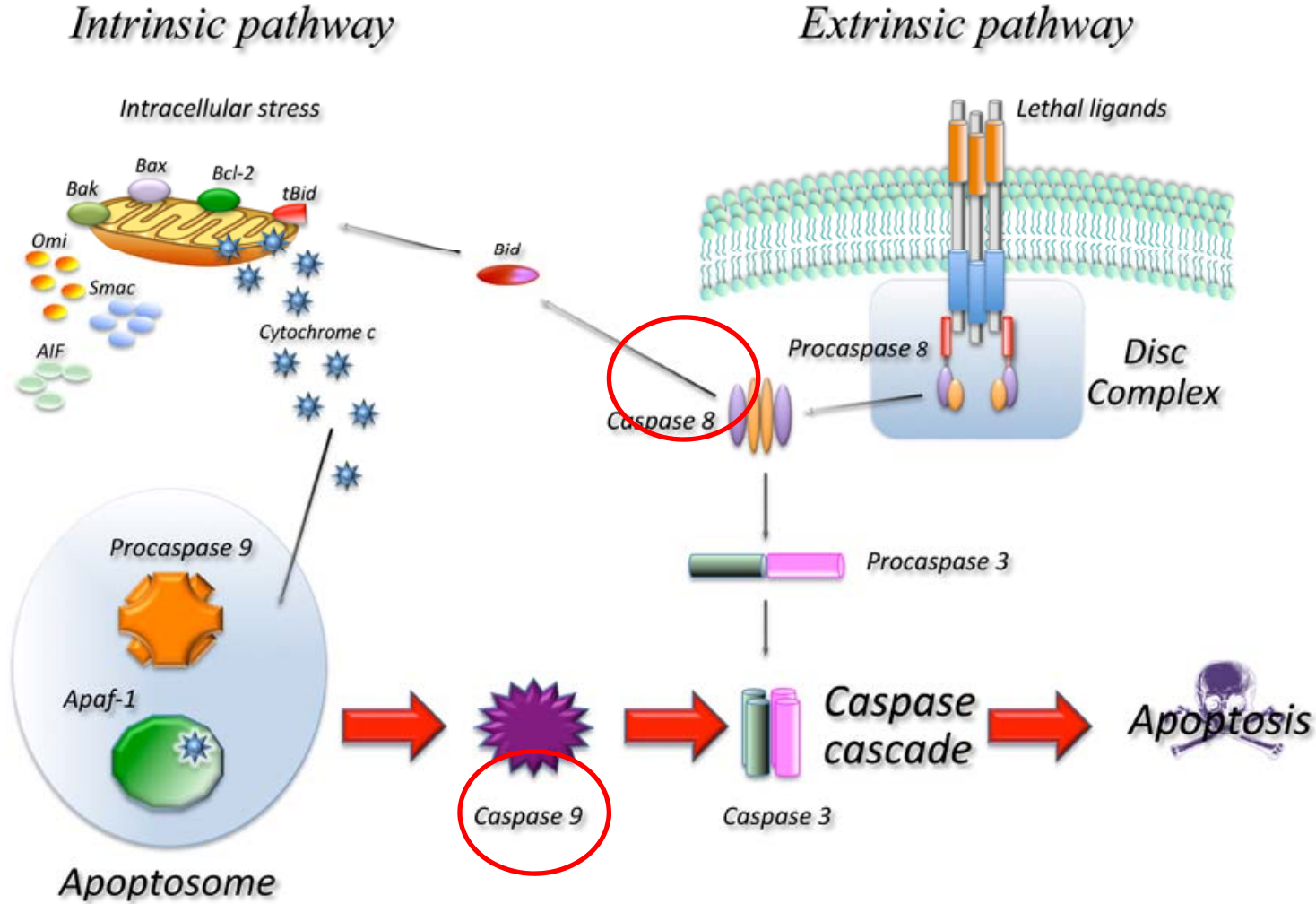
Cell death

- **Intrinsic Apoptosis**
- **Extrinsic Apoptosis**
- **Necroptosis**
- **Pyroptosis**

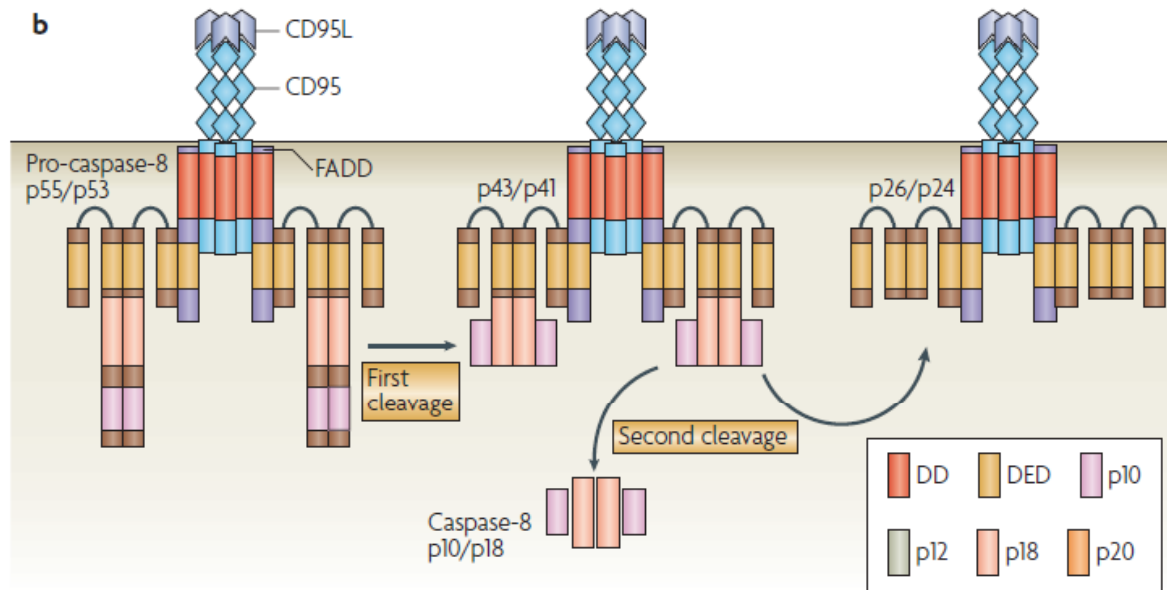
Intrinsic Apoptosis mediated by mitochondria



Crosstalk between intrinsic and extrinsic apoptosis



FADD and Caspase 8 are major factors inducing extrinsic pathways



DD: Death domain
DED: Death-effector domain

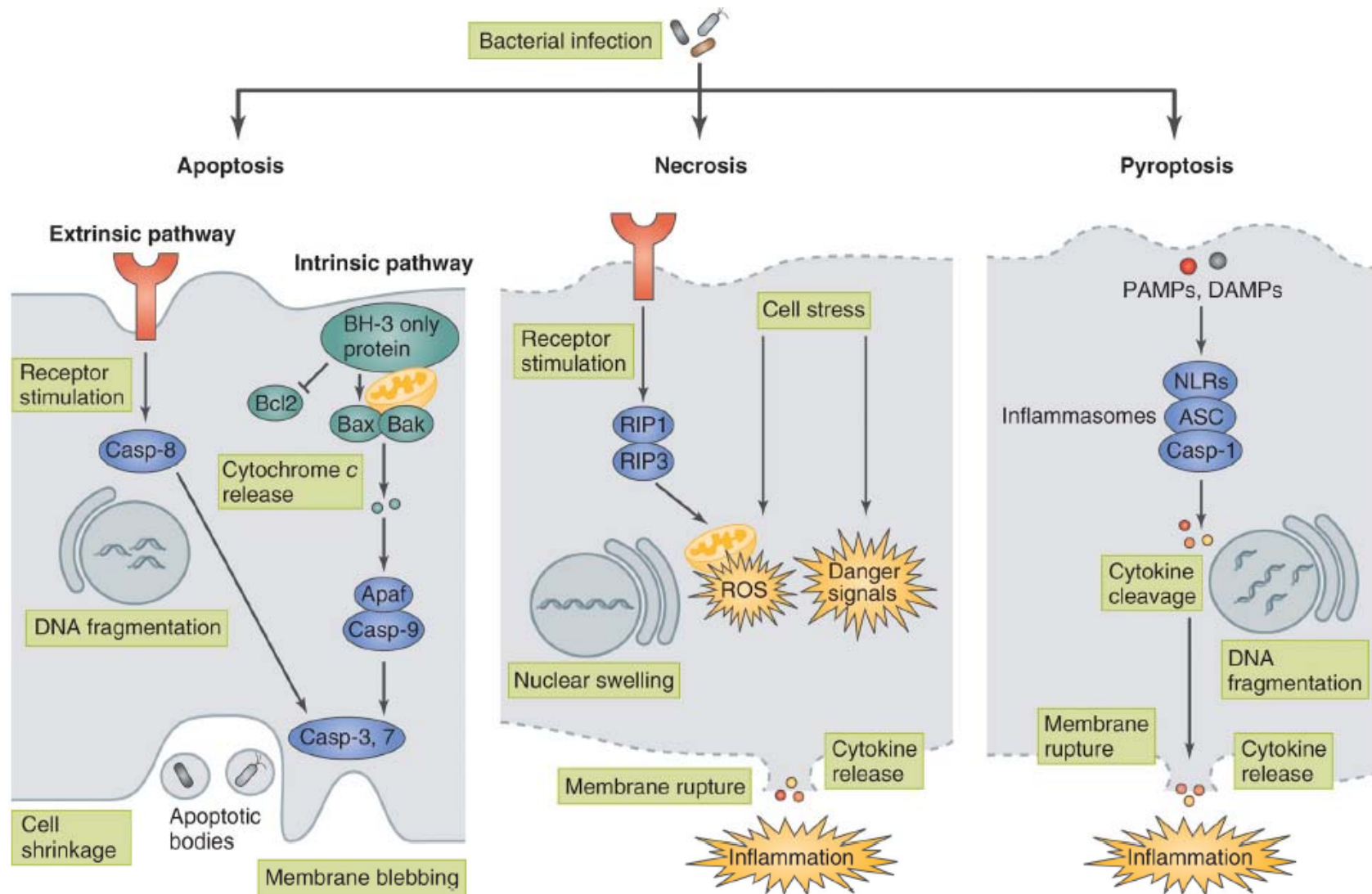
2007, Nat Rev Im
Life and death in peripheral T cells

Pyroptosis

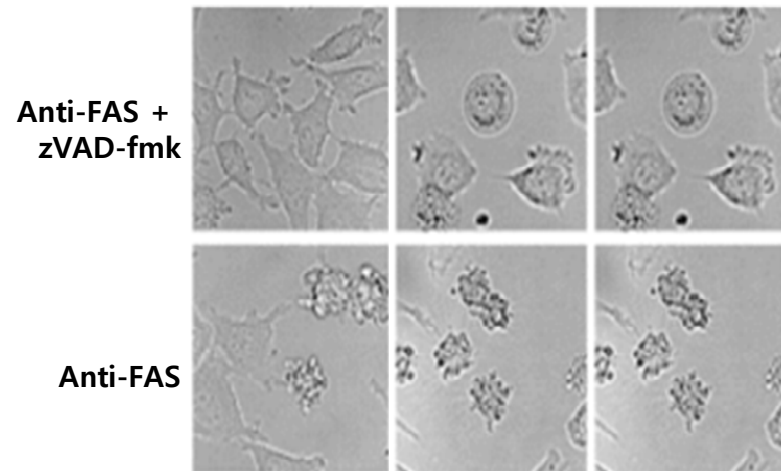
Pyroptosis is a form of programmed cell death associated with antimicrobial responses during inflammation. In this process, immune cells that recognize certain danger signals within themselves produce cytokines, swell, burst and die.

This releases the cytokines, attracts other immune cells to fight the infection and contributes to inflammation. Some examples of pyroptosis include salmonella-infected macrophages and abortively HIV-infected T helper cells.

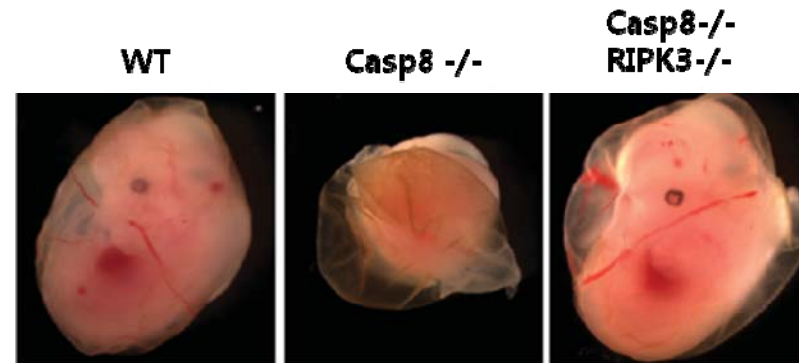
Pyroptosis



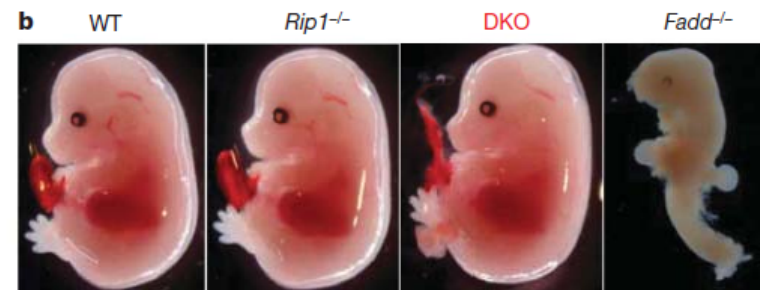
네크로토시스의 발견!



Peter Vandenabelle, JEM. 1998, 188 (5): 919-930



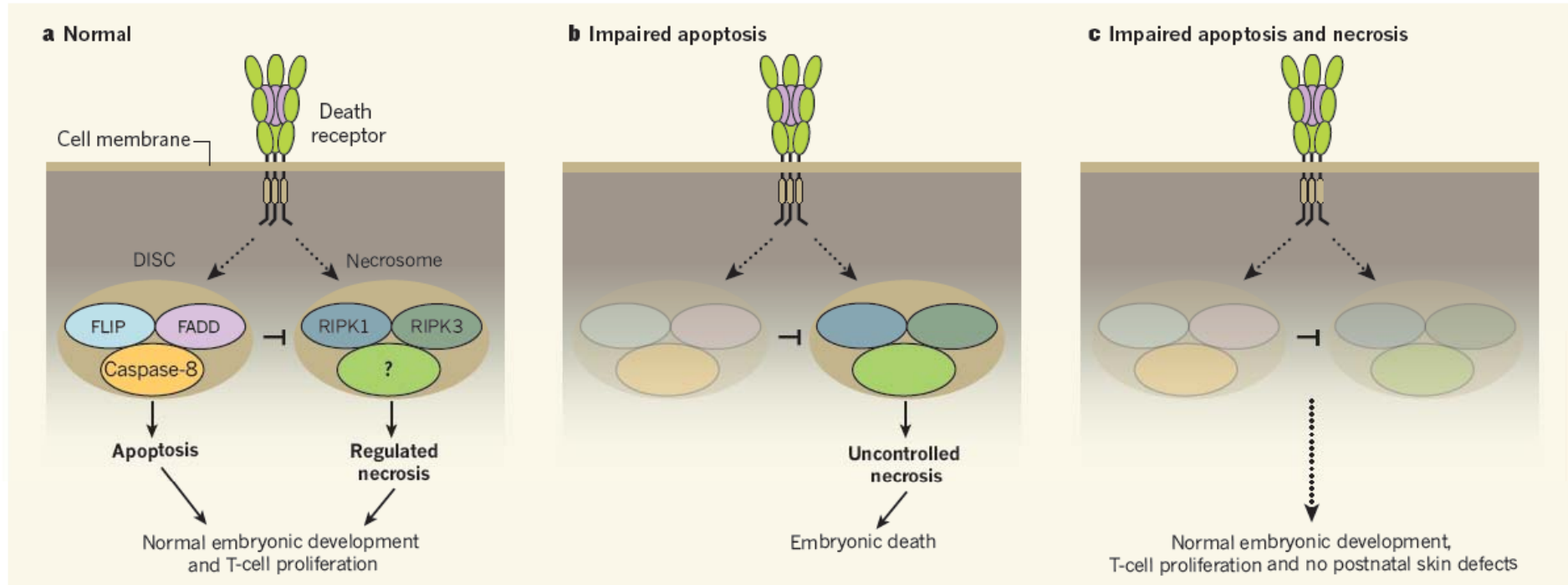
Edward Mocarski, Nature. 2011 Mar 17;471(7338):368-372, RIP3 mediates the embryonic lethality of caspase-8-deficient mice



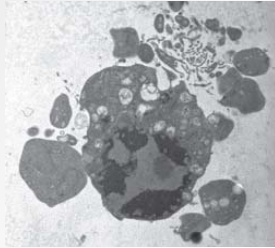
Jianke Zhang, Nature. 2011 Mar 17;471(7338):310-2. Functional complementation between FADD and RIP1 in embryos and lymphocytes .

Non-apoptotic programmed cell death

Embryonic lethality of FADD or Caspase-8 KO mice are rescued by RIP1/RIP3 deficiency



네크롭토시스에 의한 세포 사멸의 특징



1972 (Kerr 관찰)
2002 (Nobel 수상: Brenner 등)

프로그래밍화 자살기작

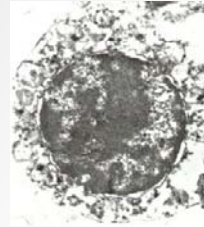
능동적 세포사멸

최소한의 면역반응

세포막 수포화

**아팍토시스
(Apoptosis)**

능동적 세포 자살 기작
(질병, 감염, 발생, 노화, 개체 항상성유지, 세포증식)



1998 Vandenabeele 최초관찰,
2012년 기전발견 (Wang)

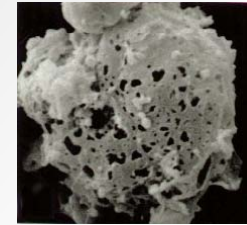
프로그래밍화 자살기작

능동적 세포사멸

강한 면역반응 수반

세포막 파열

**네크롭토시스
(Necroptosis)**



오래된 일반적 개념의 세포괴사

비프로그래밍화 기작

수동적 세포사멸

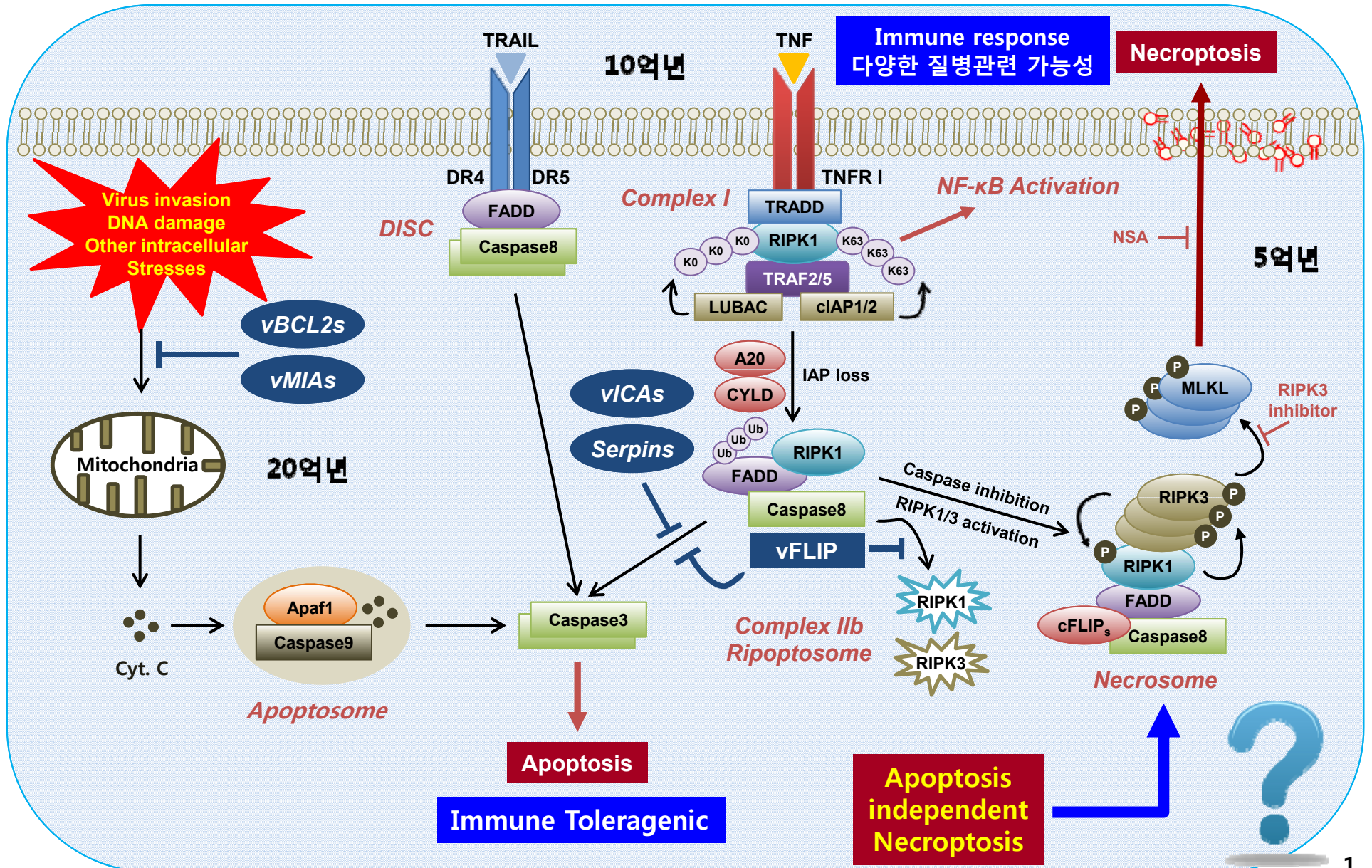
강한 면역반응 수반

세포막 파열

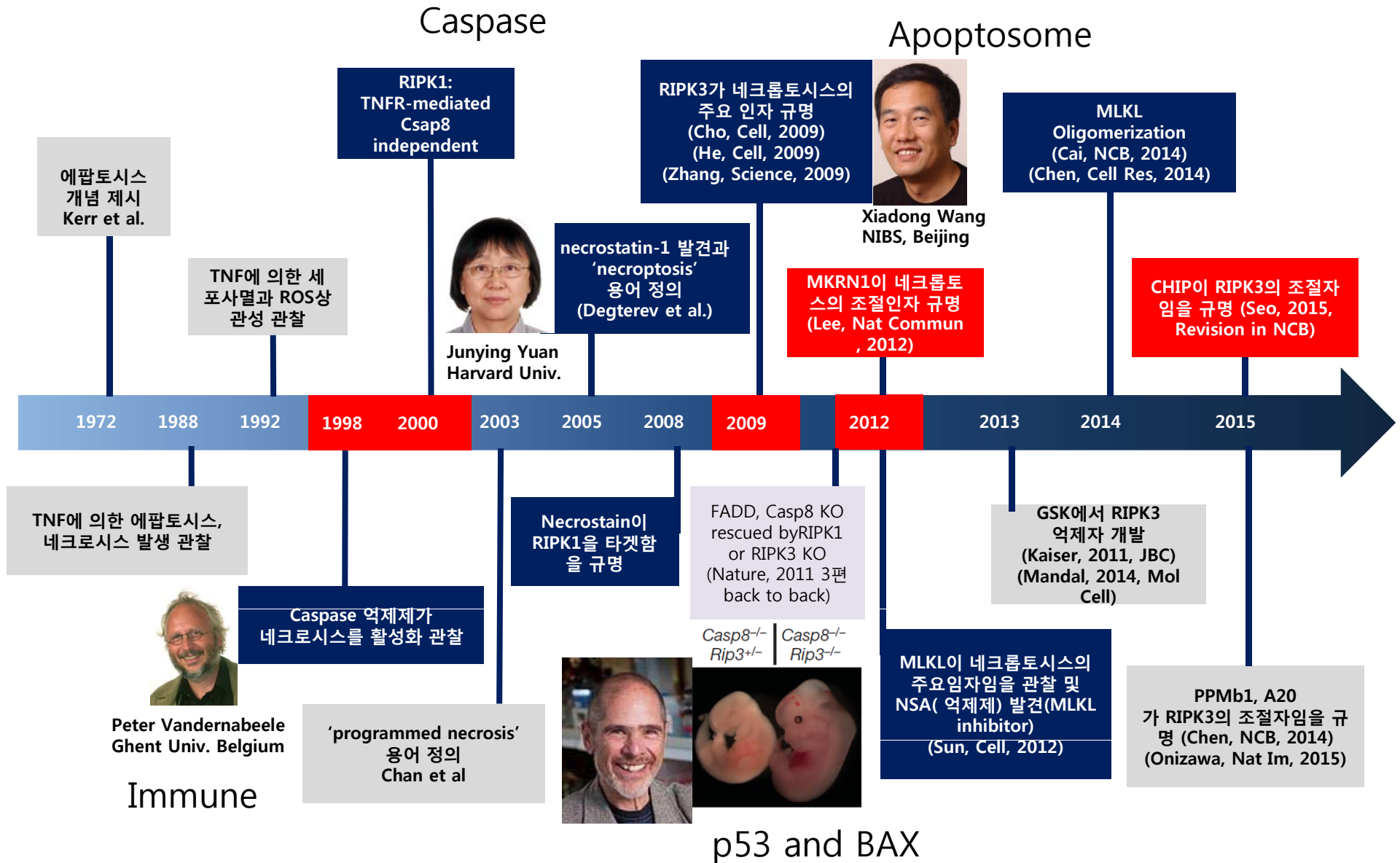
**네크로시스
(Necrosis)**

물리화학적 자극에 의한 수동적, 우연적
세포사멸 (상처, 화상, 감염)

세포사멸의 진화론적 발전



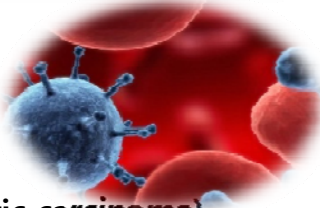
네크로토시스의 역사적 배경



Necroptosis 관련 질병

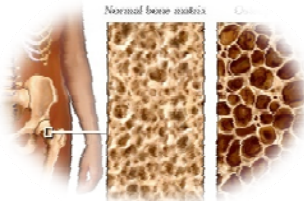
네크롭토시스의 낮은 활성화도 Undesirable low rates

암



- 폐암 (HCC)
- 뇌종양(Glioma)
- 췌장암(Pancreatic carcinoma)
- 유방암(Breast carcinoma)
- 난소암(Ovarian carcinoma)
- 대장암(Colon carcinoma)
- etc....

네크롭토시스의 항상성 붕괴 Deregulated rates



항상성 파괴

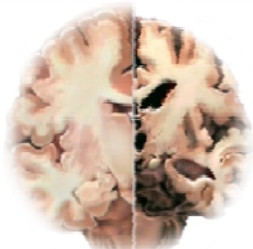
- 크론병 (Chron's disease)
- 괴사창자염(necrotizing enteritis)
- 위소장염(entrogastritis)
- 대장염(Colitis)



발생과정 이상

- 태아사망 (Fetal death)

네크롭토시스의 높은 활성화도 Undesirable high rates



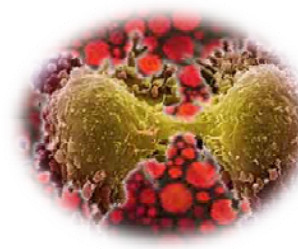
신경퇴화
Neuro-
Degeneration

- 루게릭병(Amyotrophic lateral sclerosis)
- 헌팅턴병(Huntington's disease)
- 망막색소변성증(Retinitis pigmentosa)
- 노인성 근육퇴화증 (Age-related muscular degeneration)



허혈성 질환
Ischemia-
Reperfusion

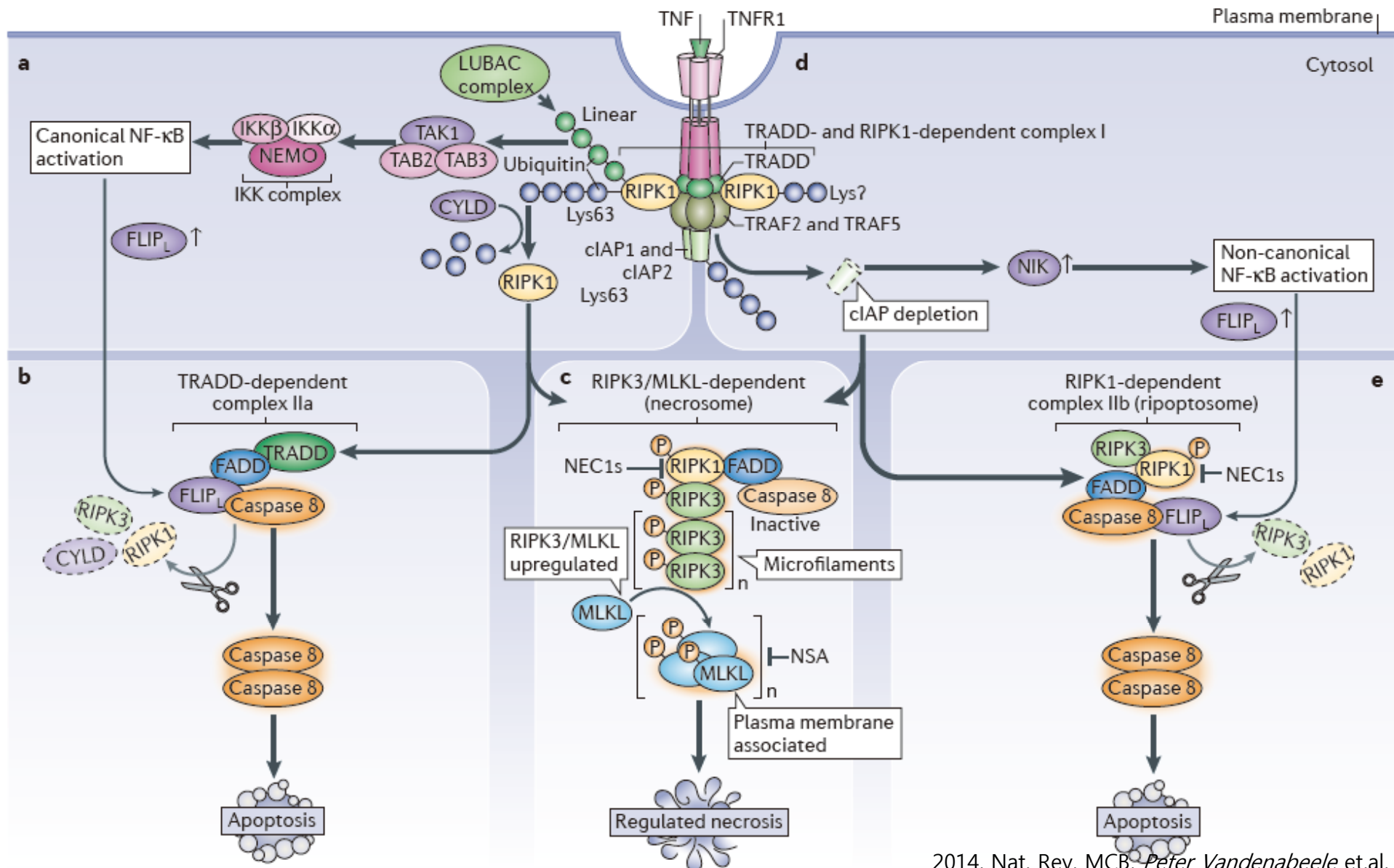
- 뇌허혈 Brain I/R injury
- 망막허혈 (Retinal I/R injury)
- 허혈성 심장질환 (Myocardial I/R injury)



면역관련 질병
Defect Immune
response

- 폐혈증(Lethal systematic inflammation)
- 자가면역반응(Systematic autoimmunity)
- 간염 (hepatitis)
- 감염성질환(Pathogen infection)

TNF- α superfamily-mediated cell death pathways include apoptosis and necroptosis



Regulators affecting apoptosis or necroptosis

