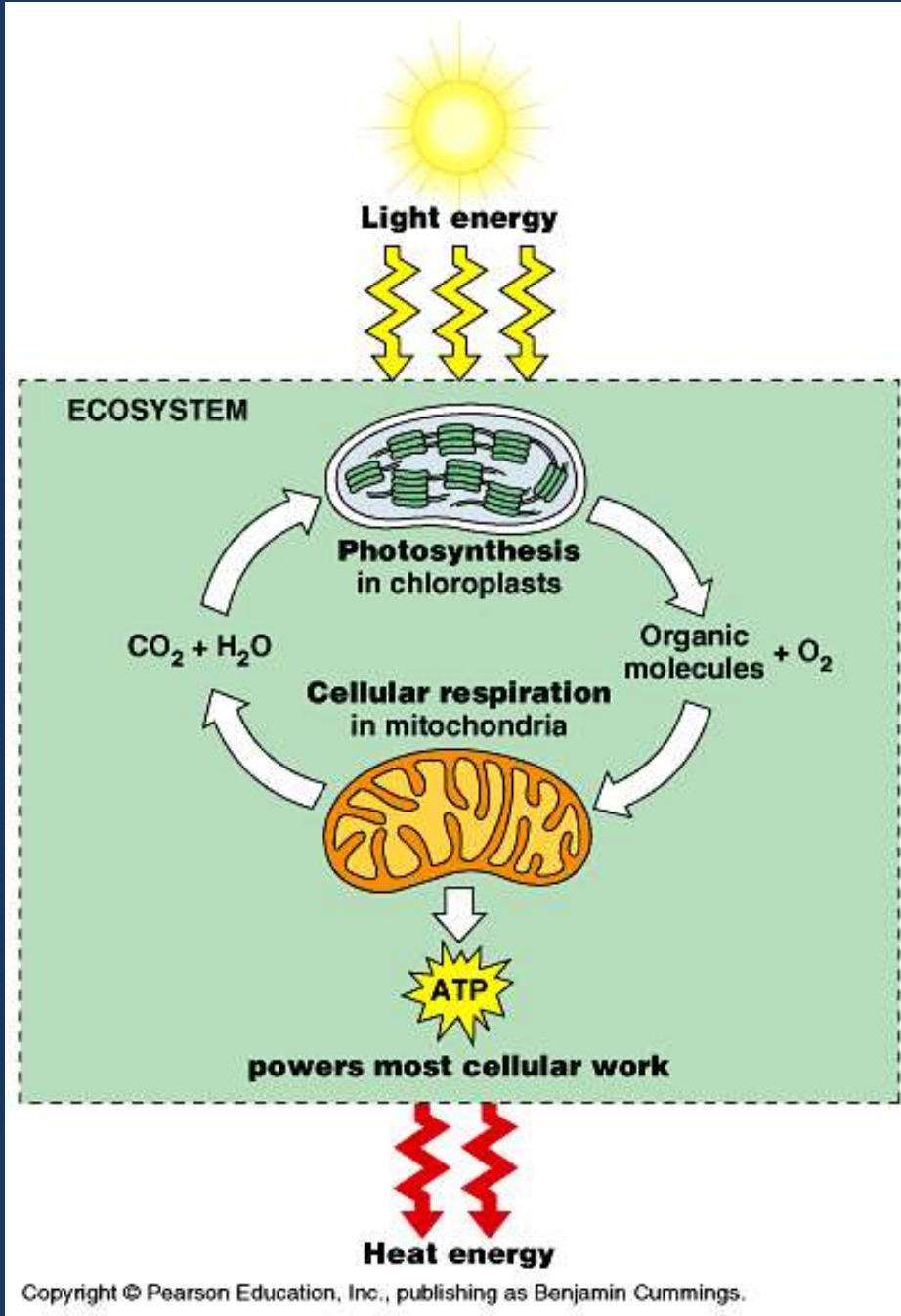


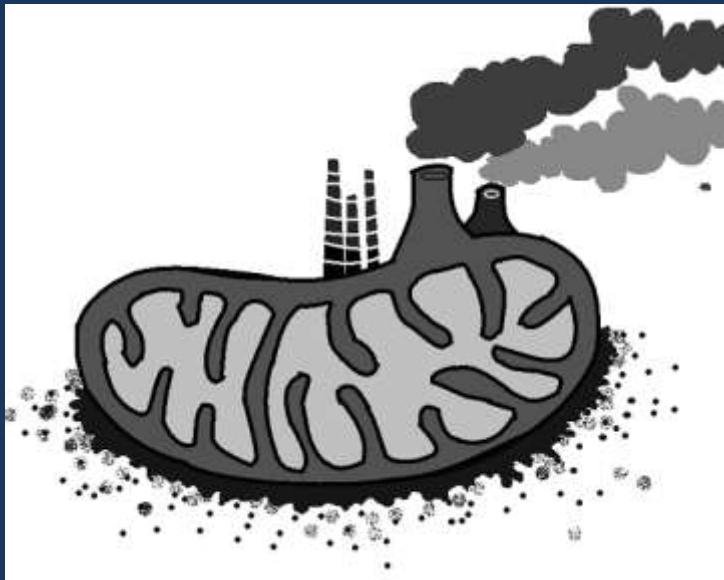


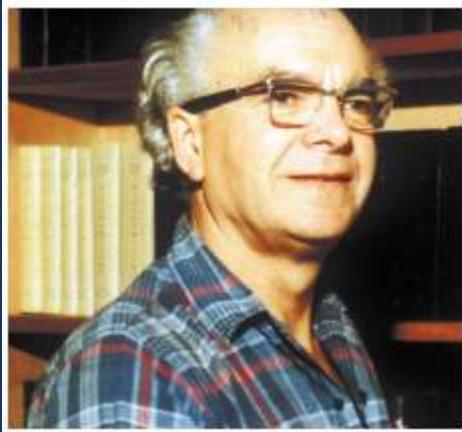
# Kanserde mitokondrinin önemi: Güçün aydınlık ve karanlık yüzü

Doç. Dr. Cenk ARAL  
[caral@nku.edu.tr](mailto:caral@nku.edu.tr)



- ATP sentezi
- ROS/RNS
- Krebs siklusu
- Üre siklusu
- Hem biyosentezi
- Stereidogenez
- Aminoasit metabolizması
- B-oksidasyon
- Glukogenez
- Ketogenez
- Hücre içi kalsiyum düzeyi regülasyonu
- Apoptoz
- ....

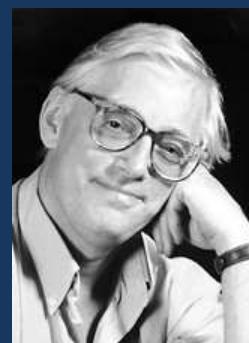




**Peter Mitchell, Kemiozmotik teori, 1978**

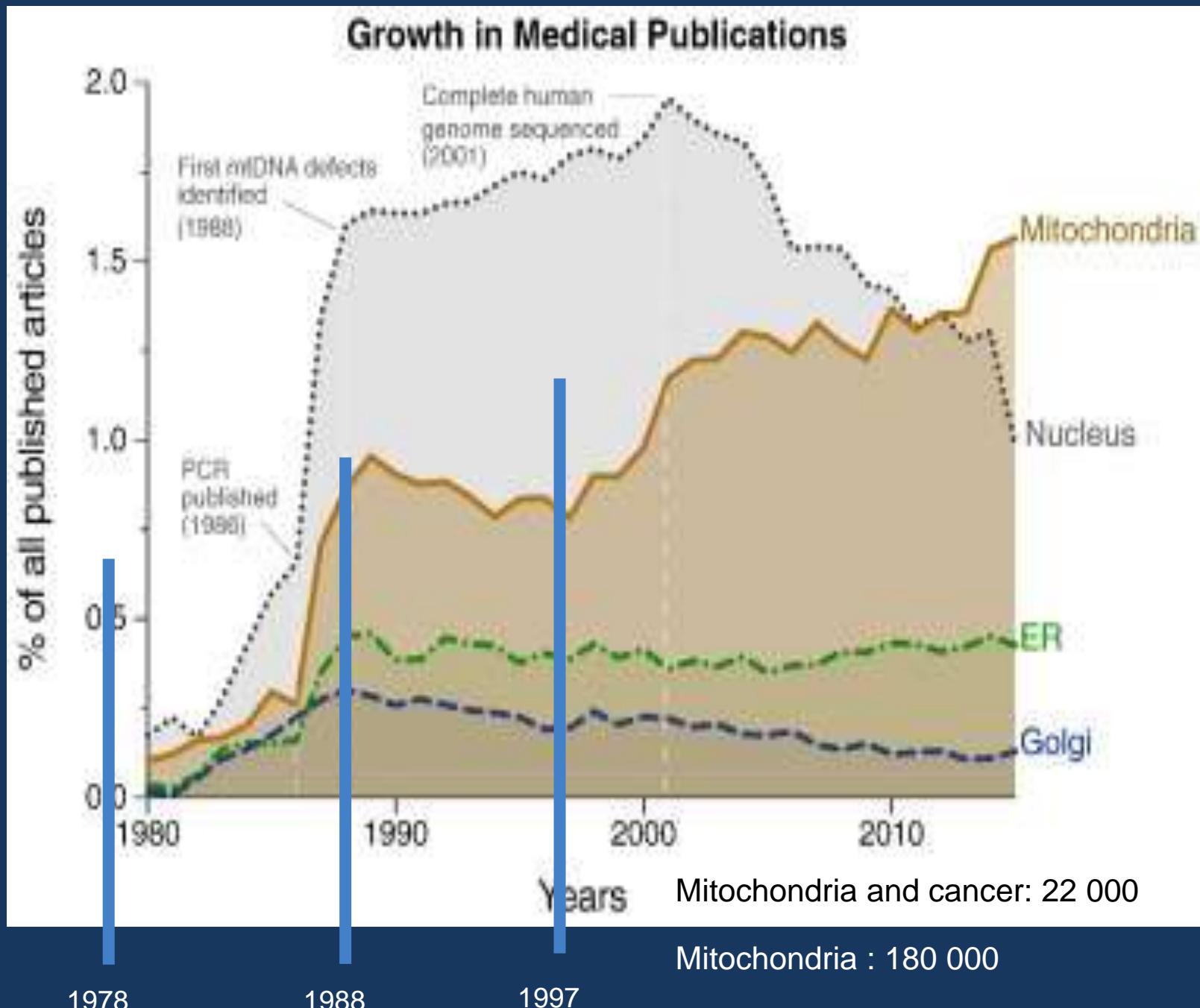


**Johann Deisenhofer Hartmut Michel,  
Robert Huber, 1988**  
Bakteriyal fotosentetik reaksiyon



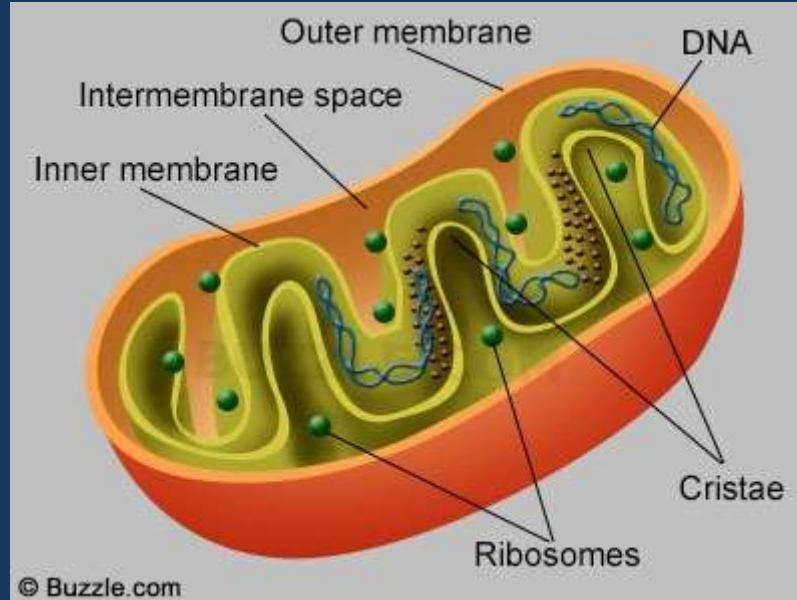
**Paul D. Boyer, John E. Walker, 1997**  
ATP sentaz



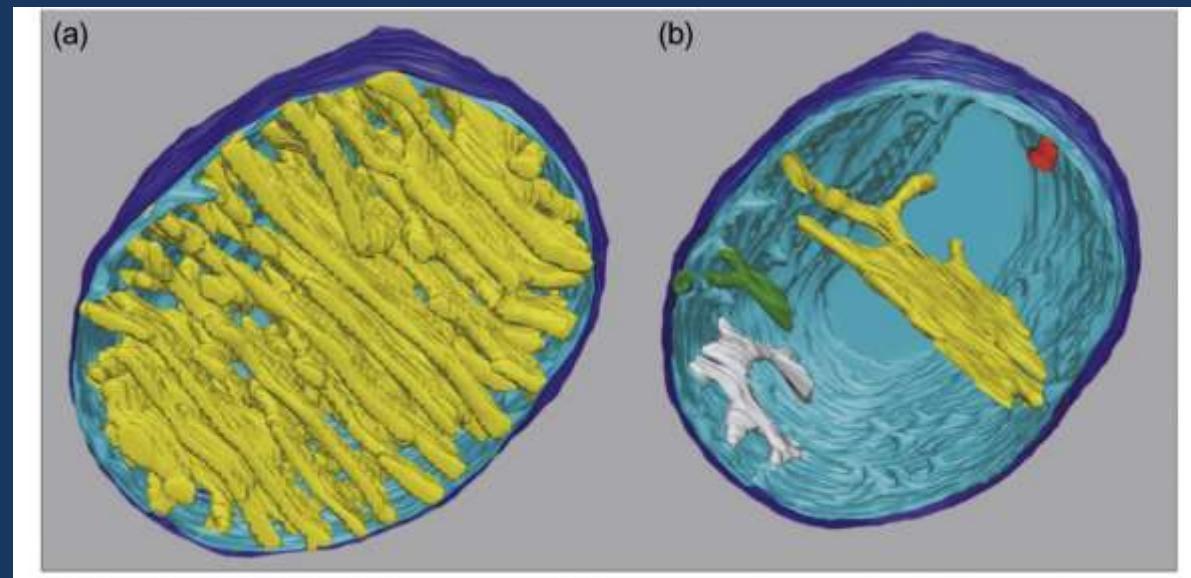


# Hanahan D, Weinberg RA, The Hallmarks of Cancer

- Cell, 100(1) 57-70, 2000
  - Kendi kendine kontolsüz proliferatif uyarım
  - Anti-proliferatif sinyallerden kaçınma
  - Anjiyogenez
  - Replikatif ölümsüzlük
  - Apoptozdan kaçınma
  - İnvaziv/metastatik potansiyel
- Cell, 144(5) 646-674, 2011-The next generation
  - Metabolik değişimler (programlama)

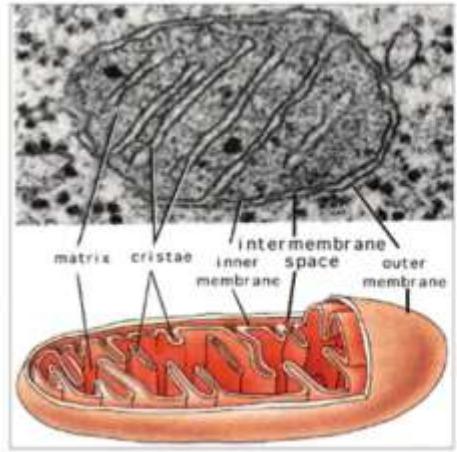


© Buzzle.com

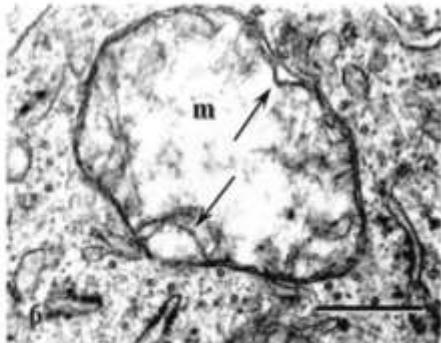


Frey ve Mannella (2000)

Normal Mitochondria



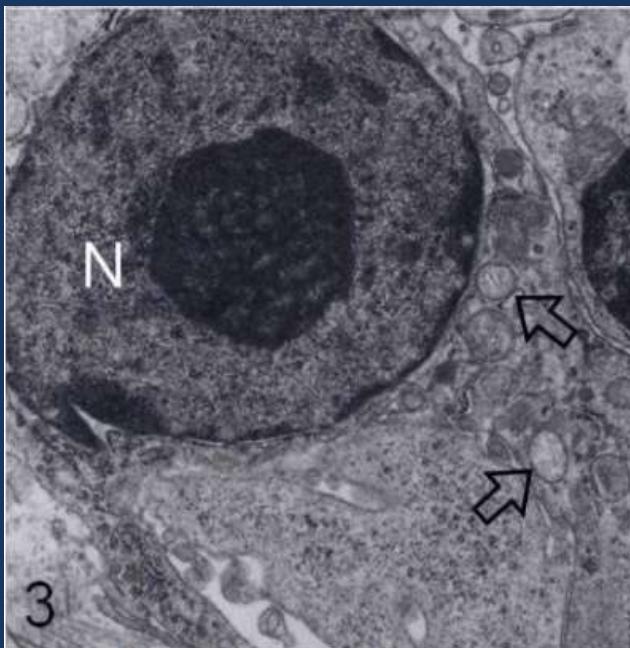
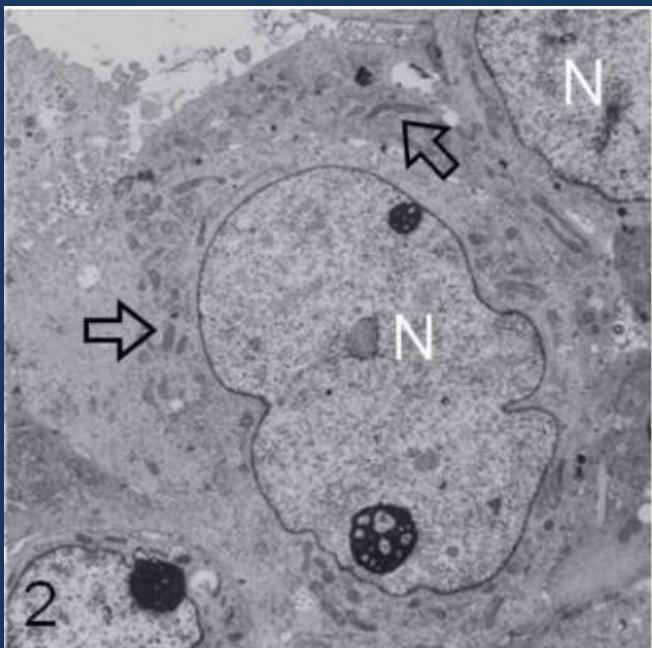
GBM Mitochondria



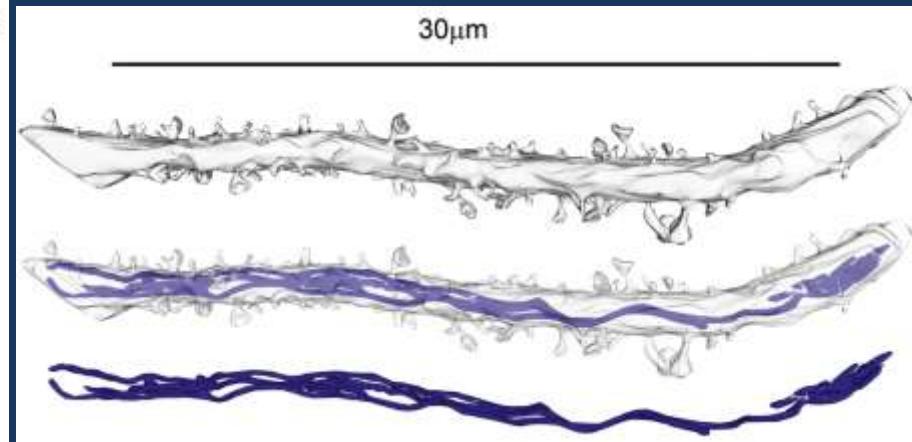
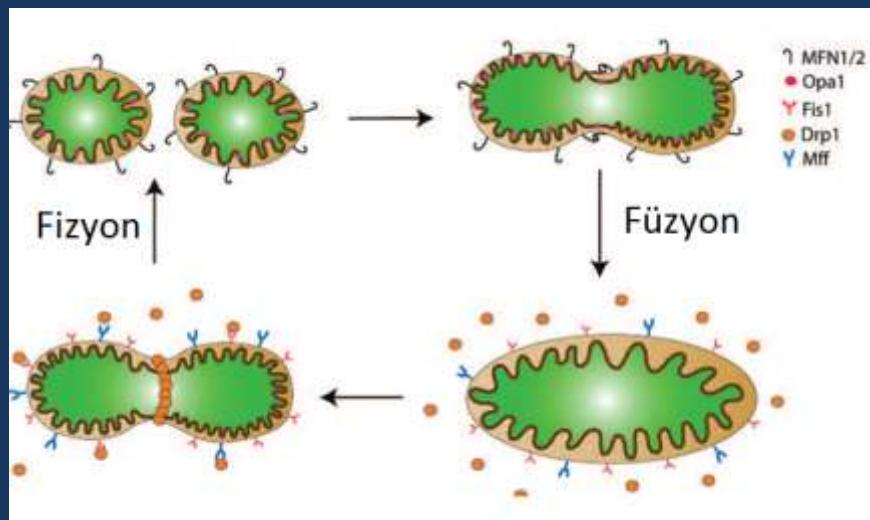
Seyfried ve ark. (2013)



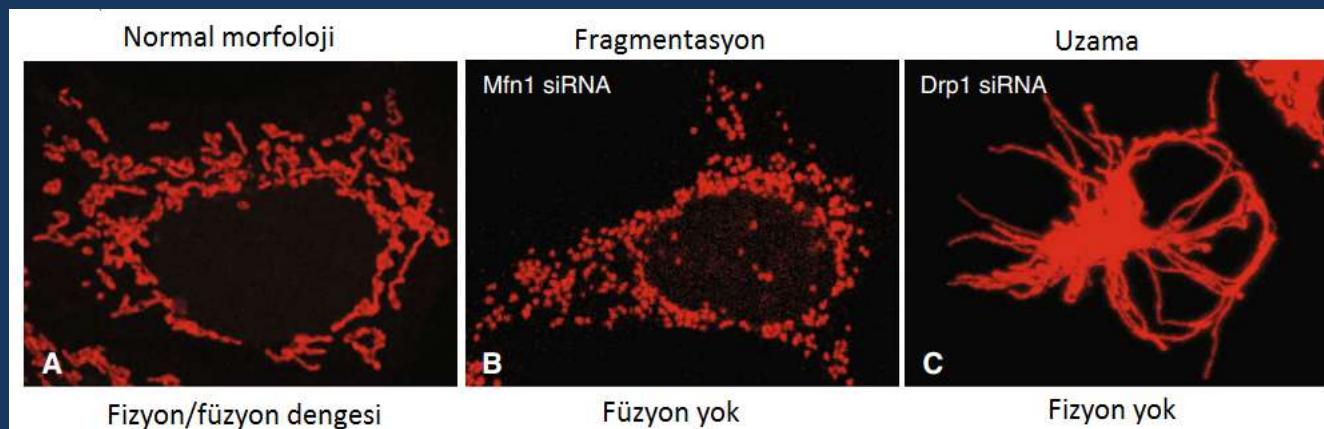
Arismendi-Morillo (2009)



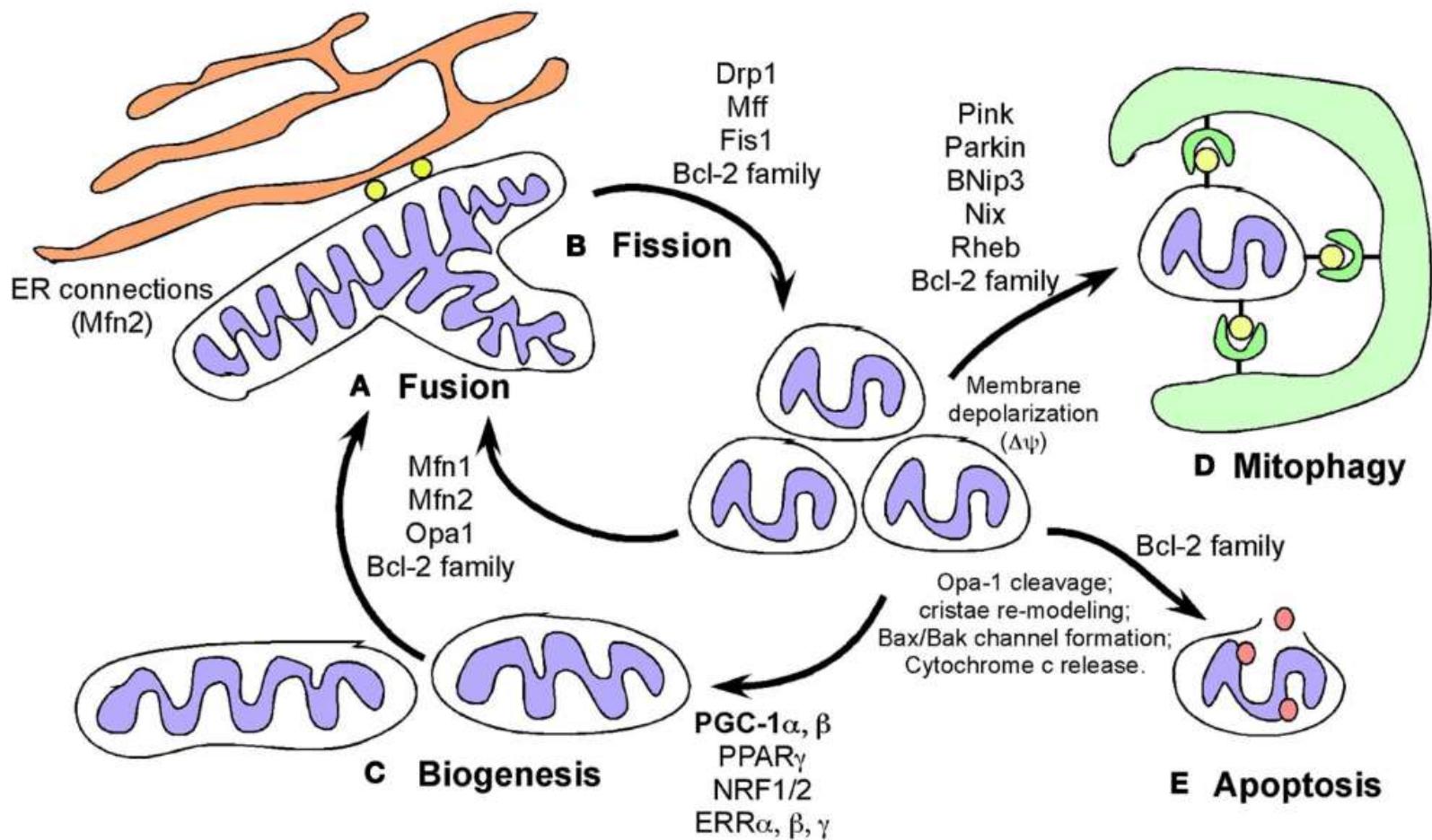
Elliot ve ark. (2011 ve 2012)



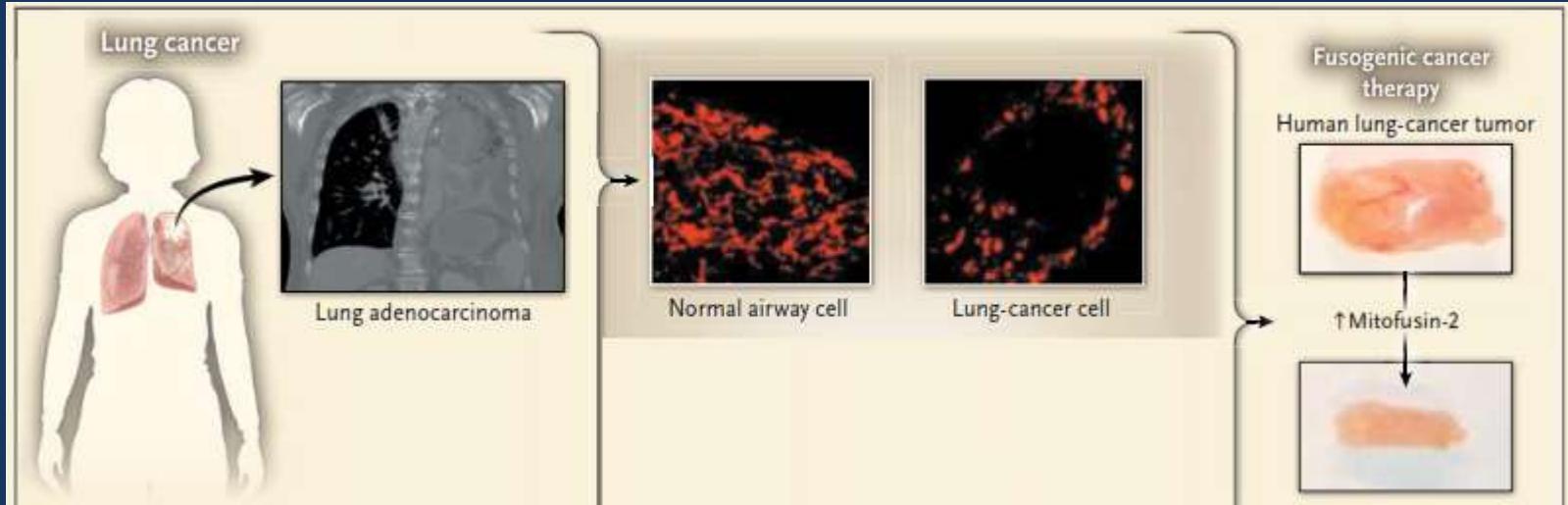
Popov ve ark. (2005)



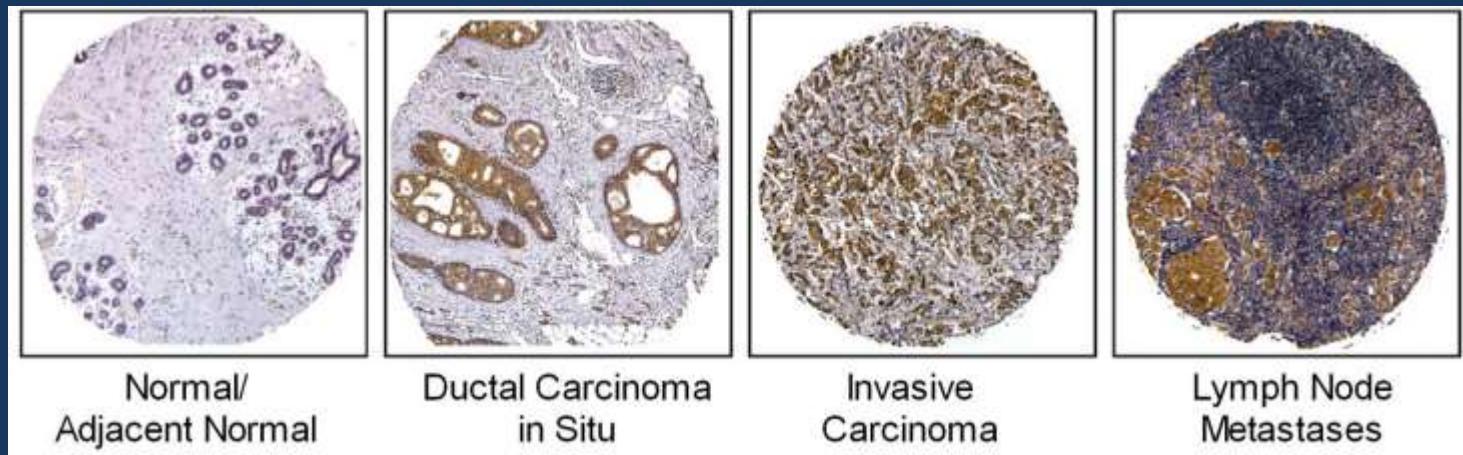
Zhao ve ark. (2013)



Boland ve ark. (2013)

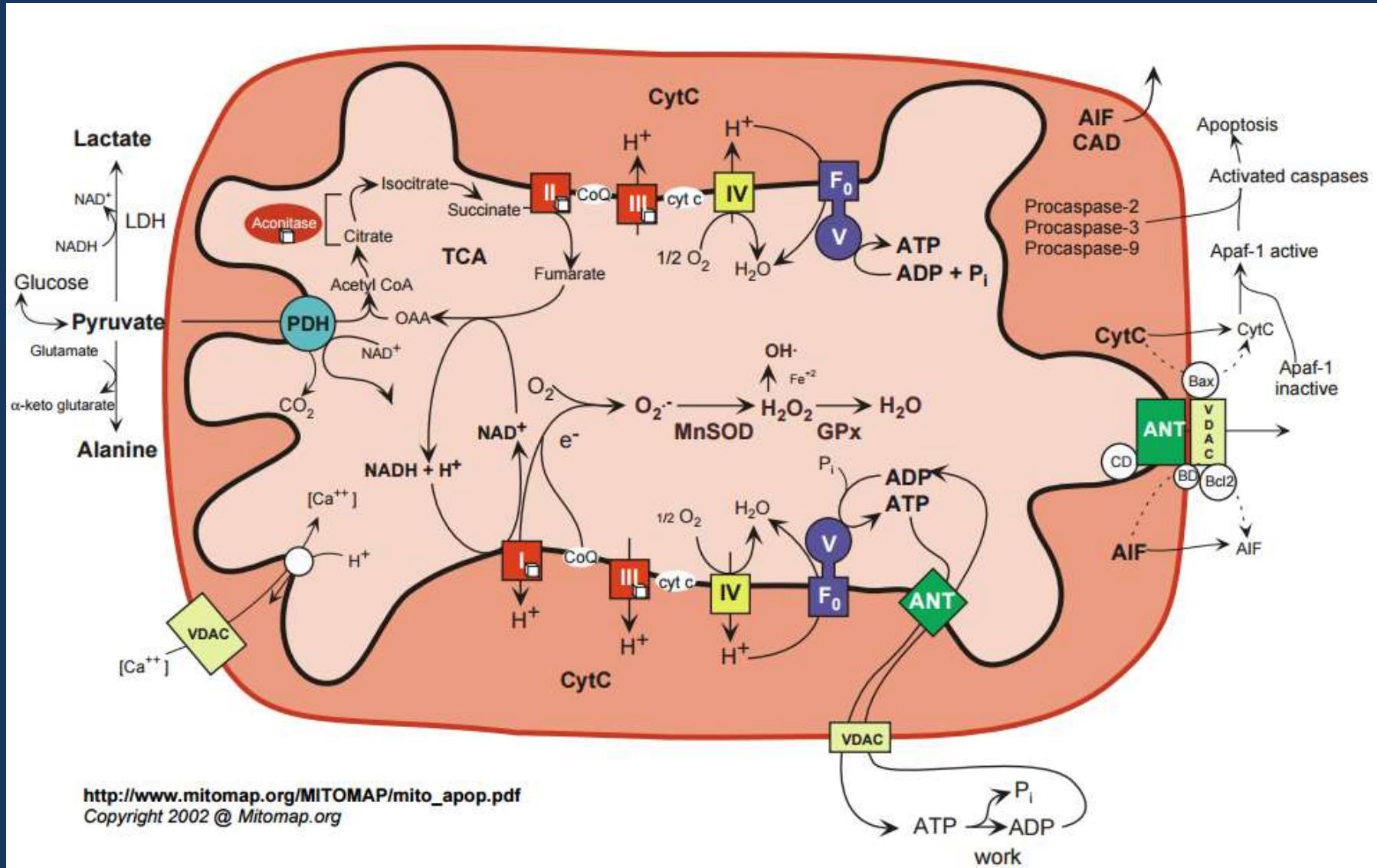


Archer (2013)



Zhao ve ark. (2013)

Drp1

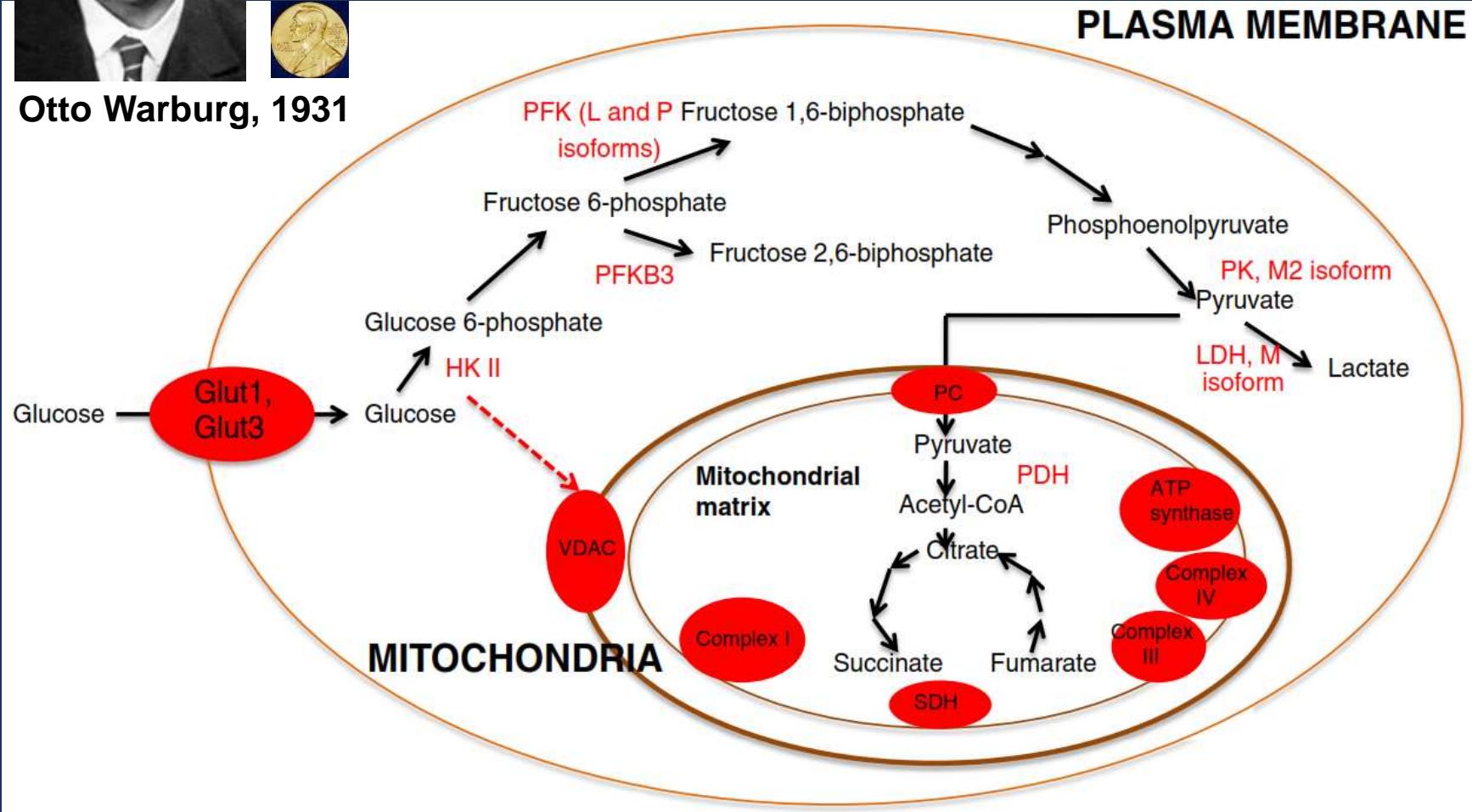




# Warburg etkisi



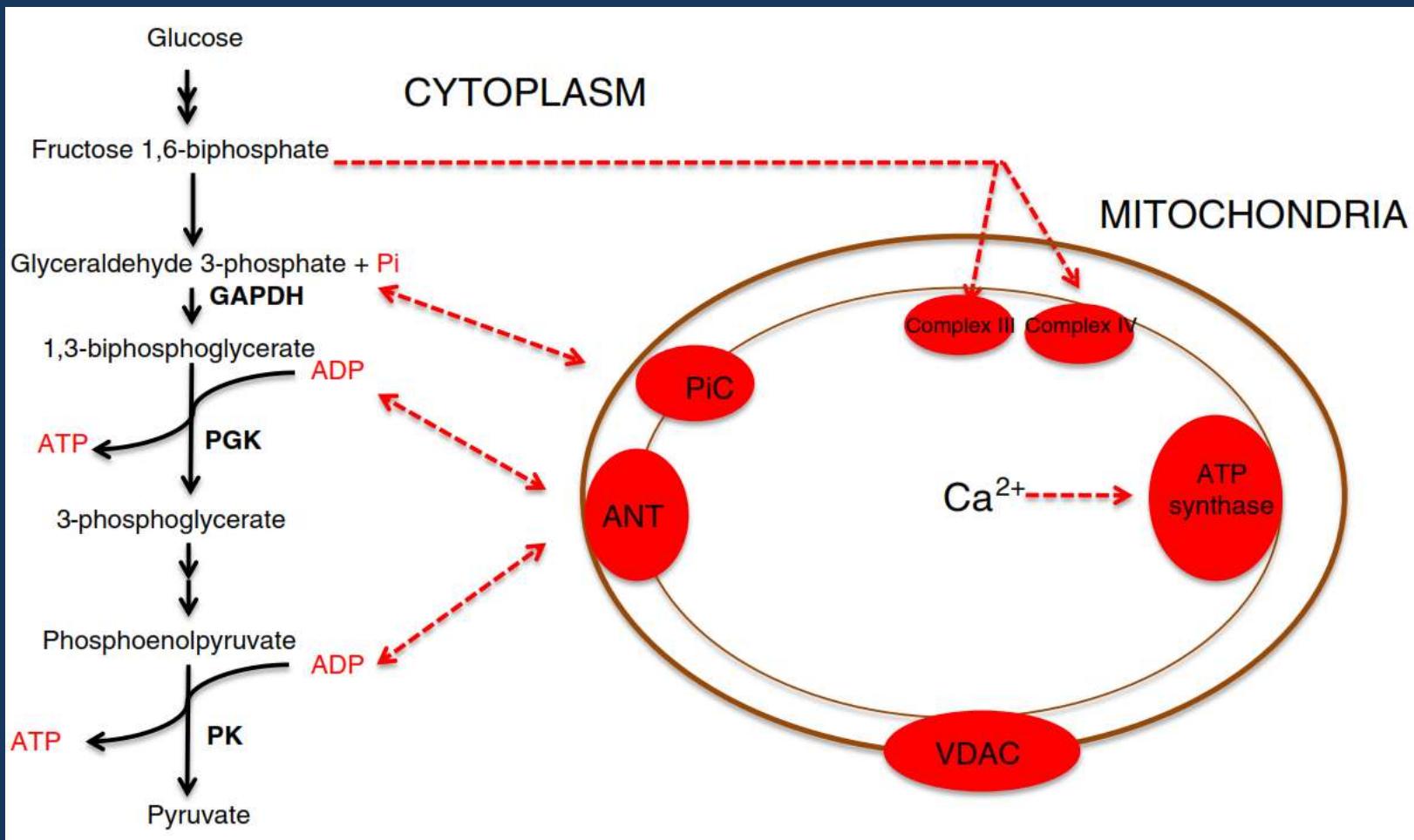
Otto Warburg, 1931

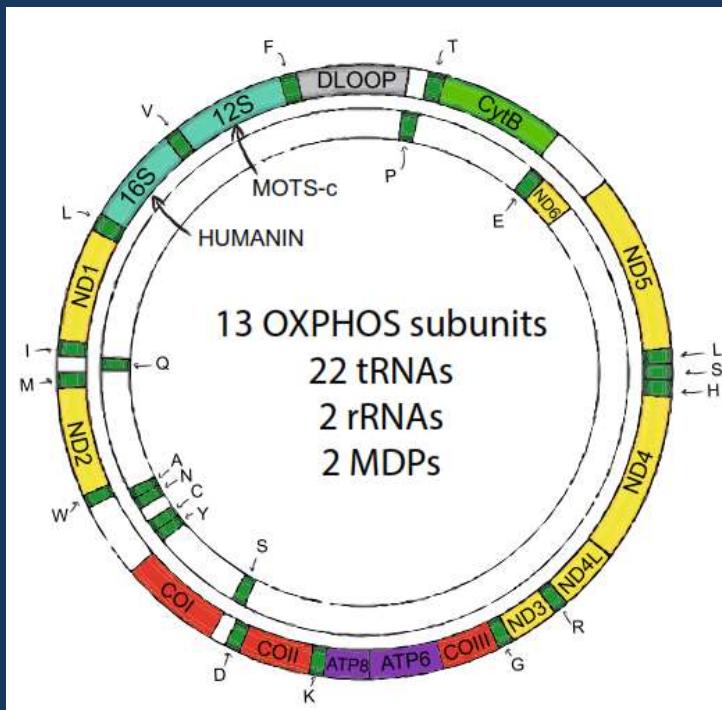


# Glikoliz artışının olası mekanizmaları

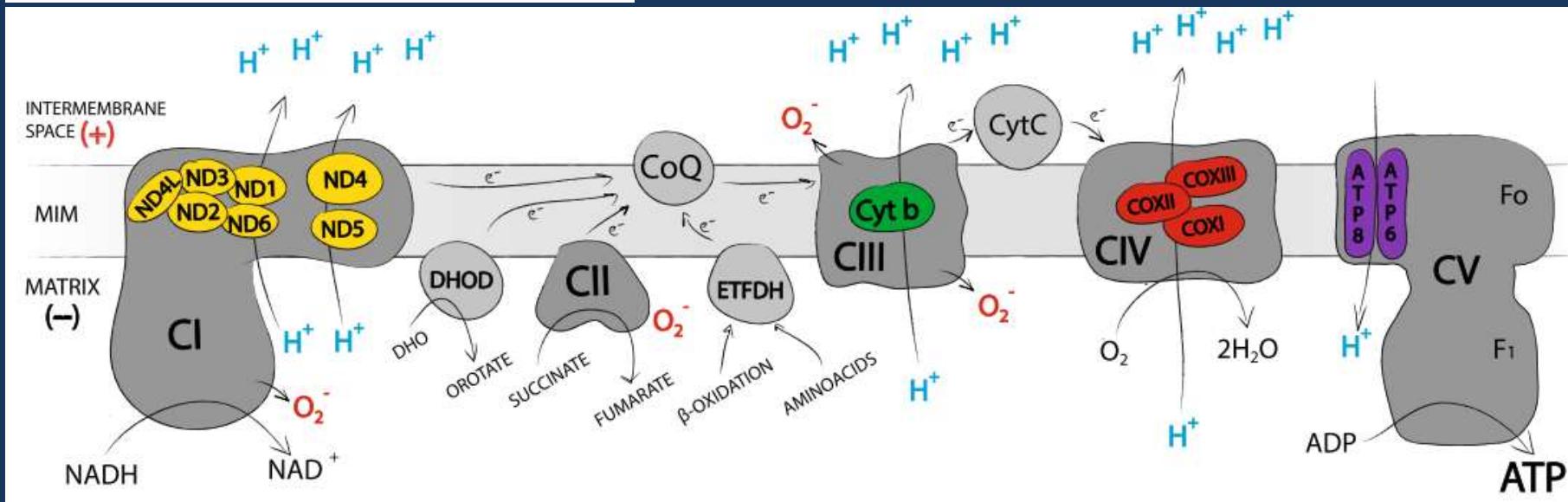
Mitokondri defektleri	mtDNA mutasyonları
Hipoksi	O <sub>2</sub> eksikliğine adaptasyon
Onkojen sinyaller	Ras, Src, Akt
Metabolik enzimlerde değişim	Hekzokinaz II, süksinat dehidrokinaz mutasyonu...

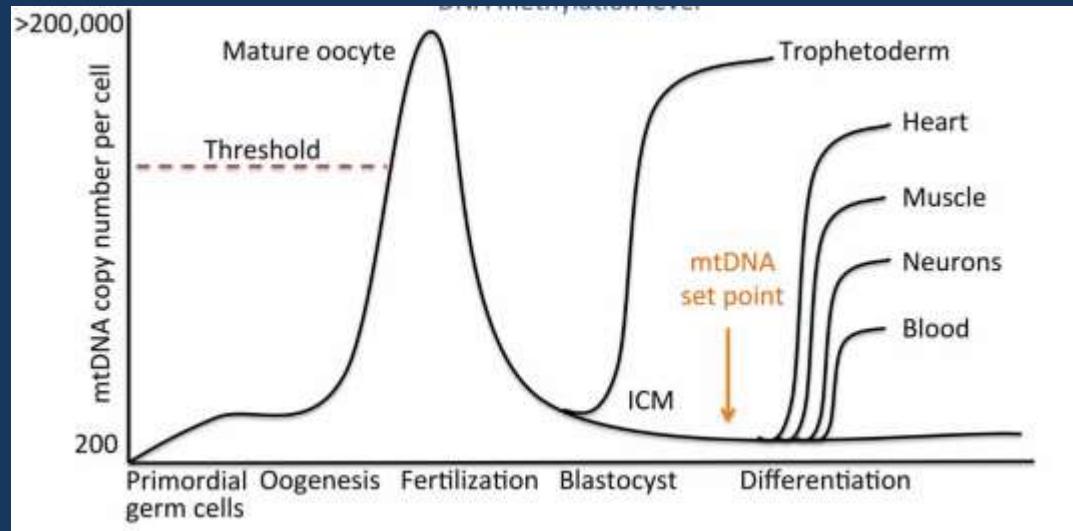
# Crabtree etkisi



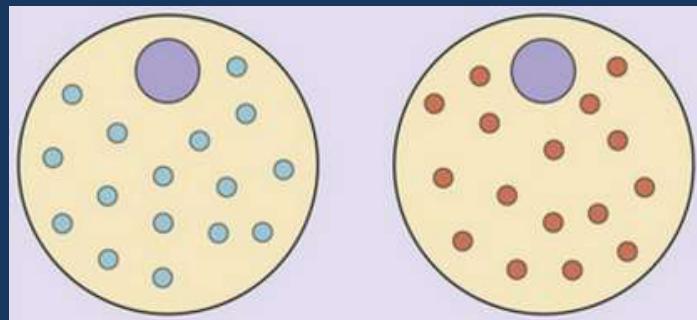


# Mitokondriyal genom

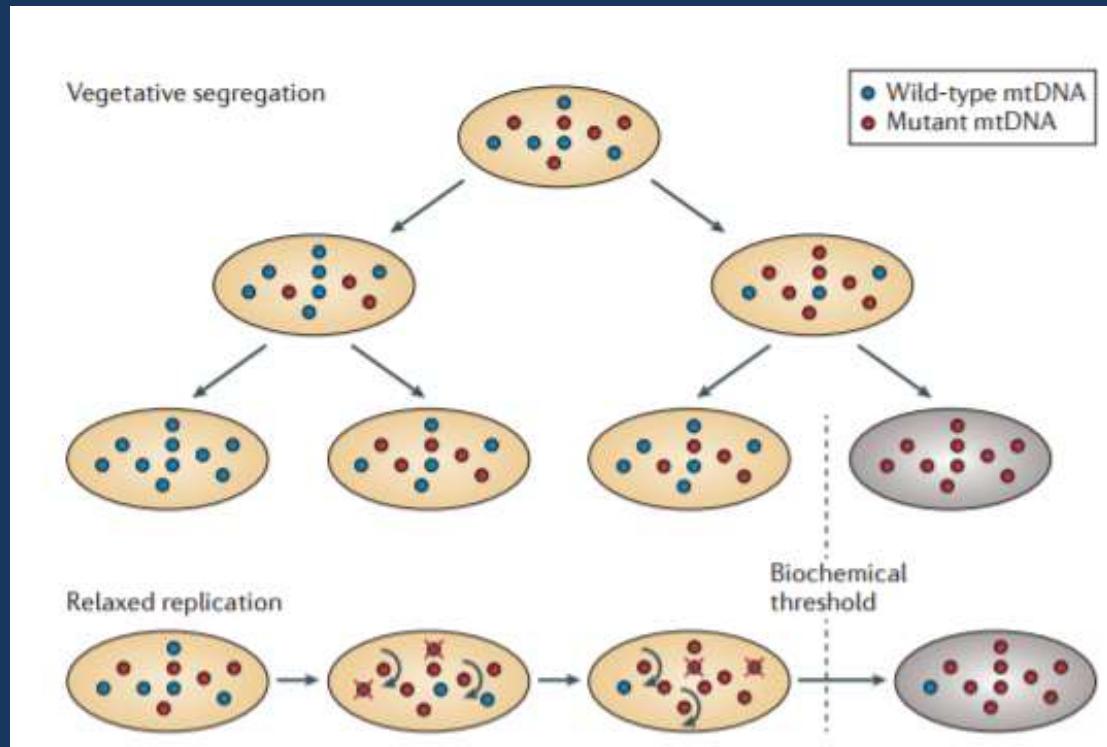
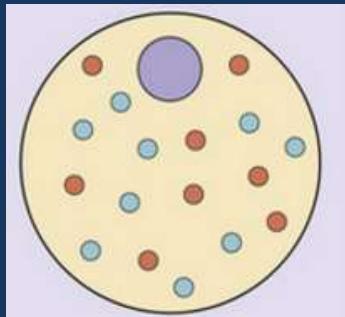




Sun ve John (2016)

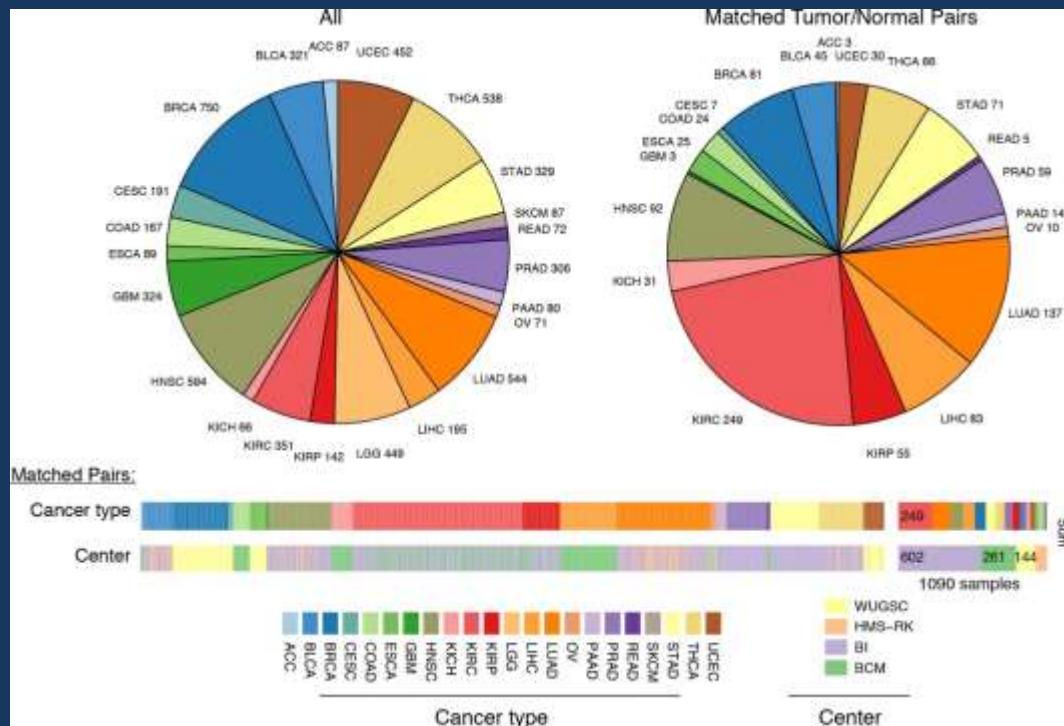


HOMOPLAZMI



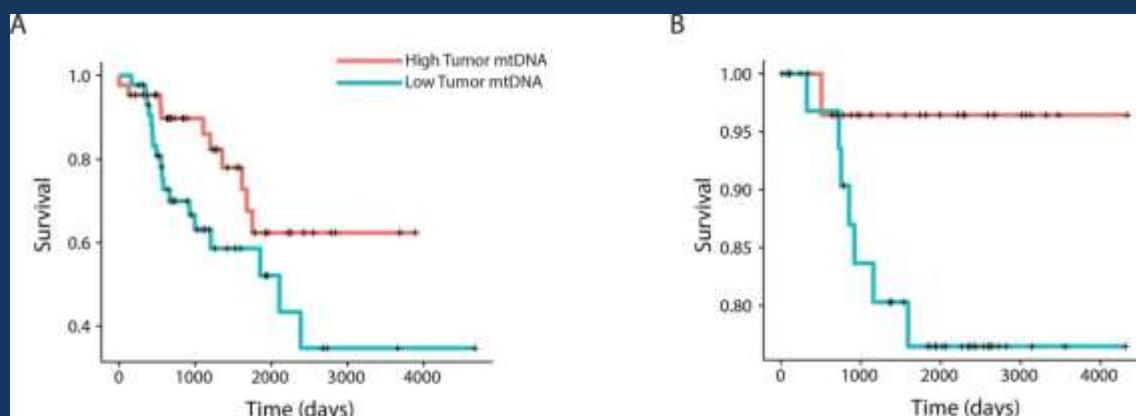
Steward ve Chinnery (2015)

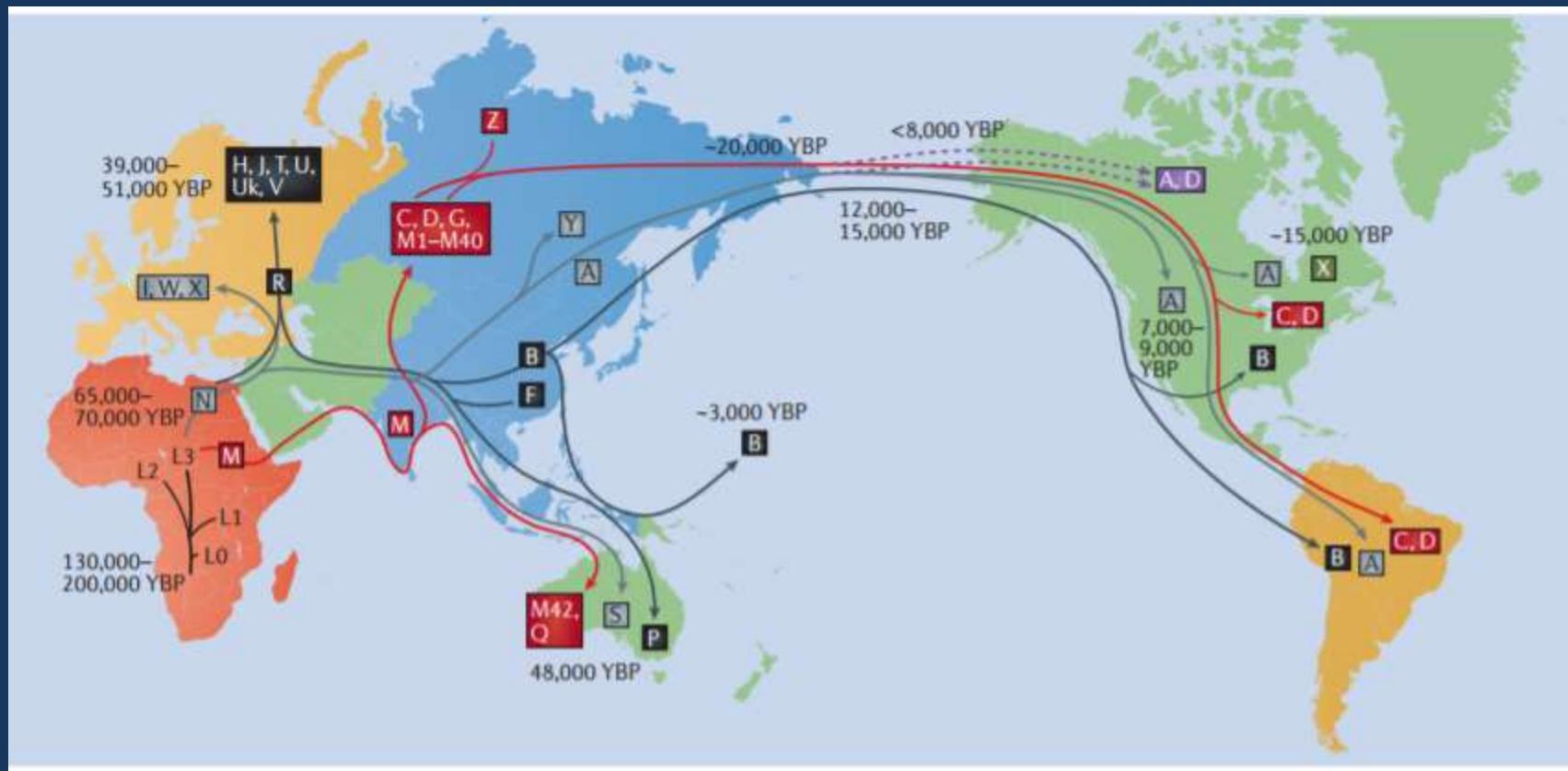
# mtDNA kopya sayısı (CANCER GENOME ATLAS)

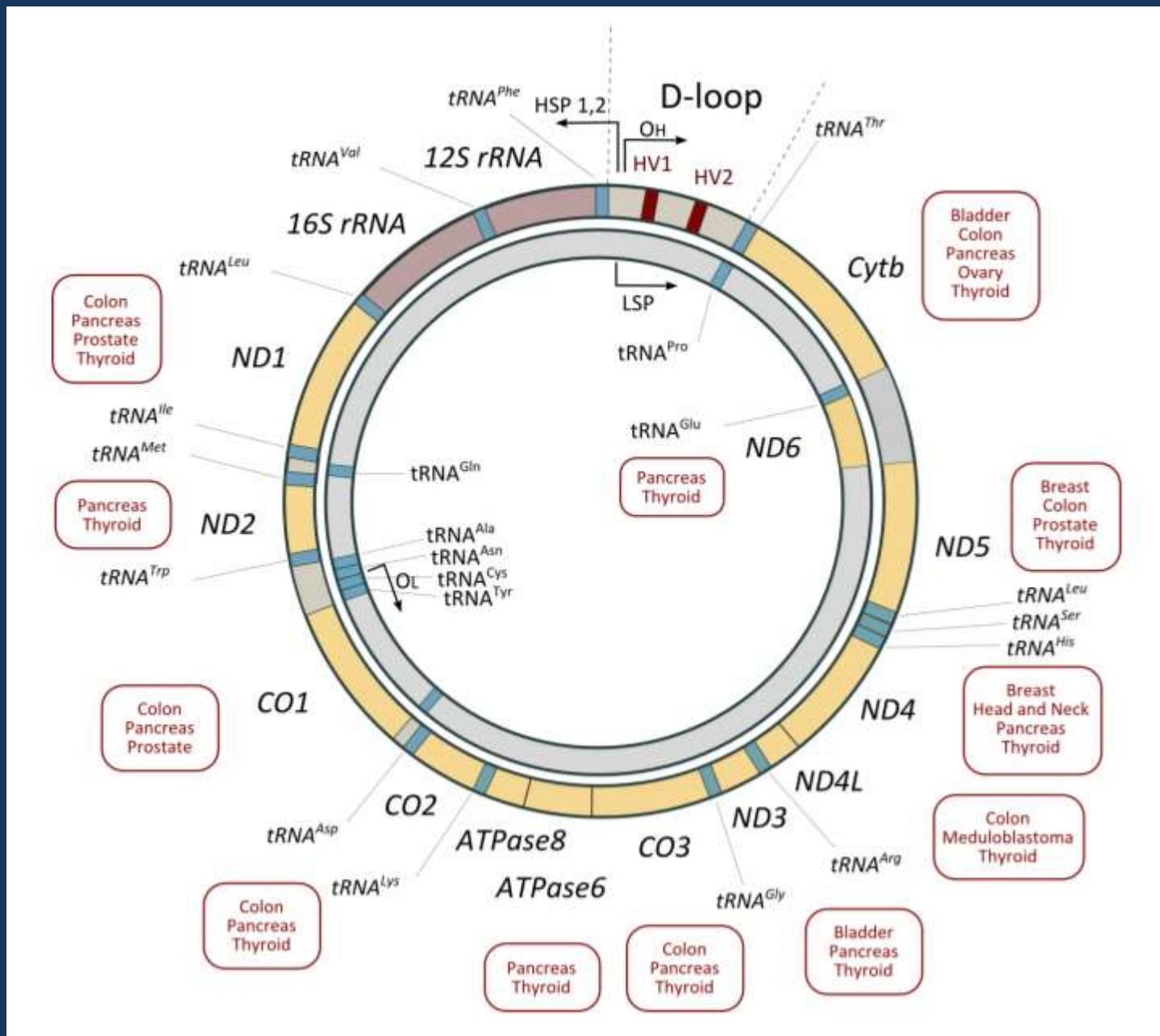


Azalma.  
Böbrek, mesane,  
meme, karaciğer, baş-  
boyun, özofagus,  
kolorektal....

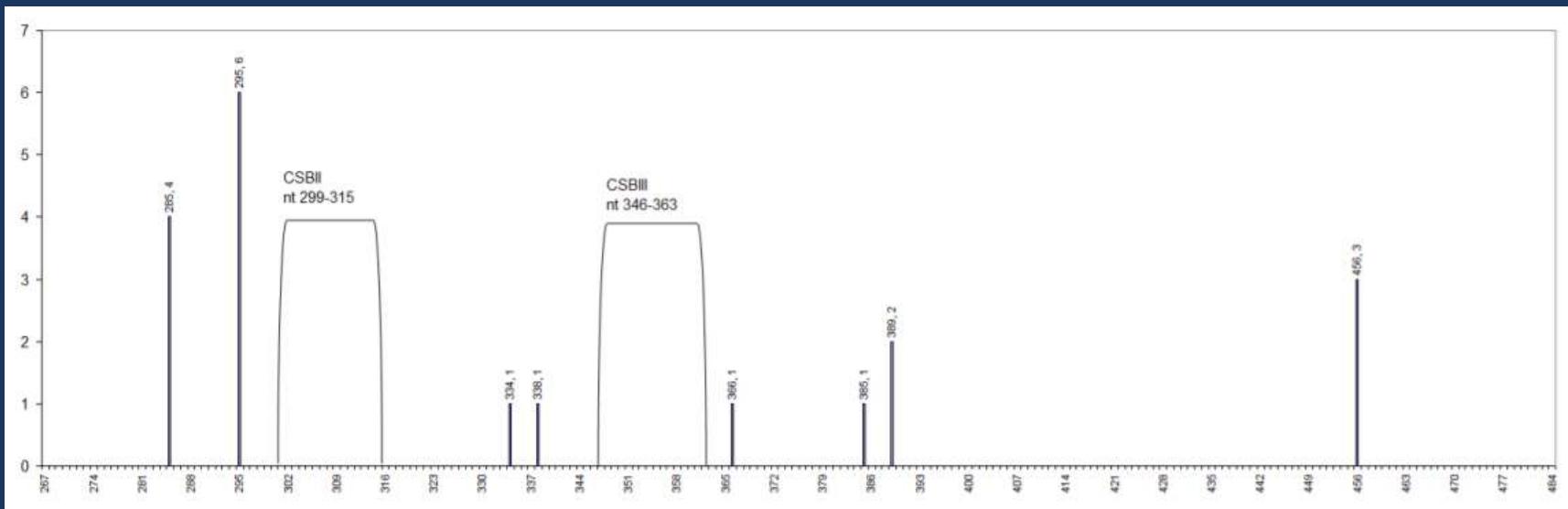
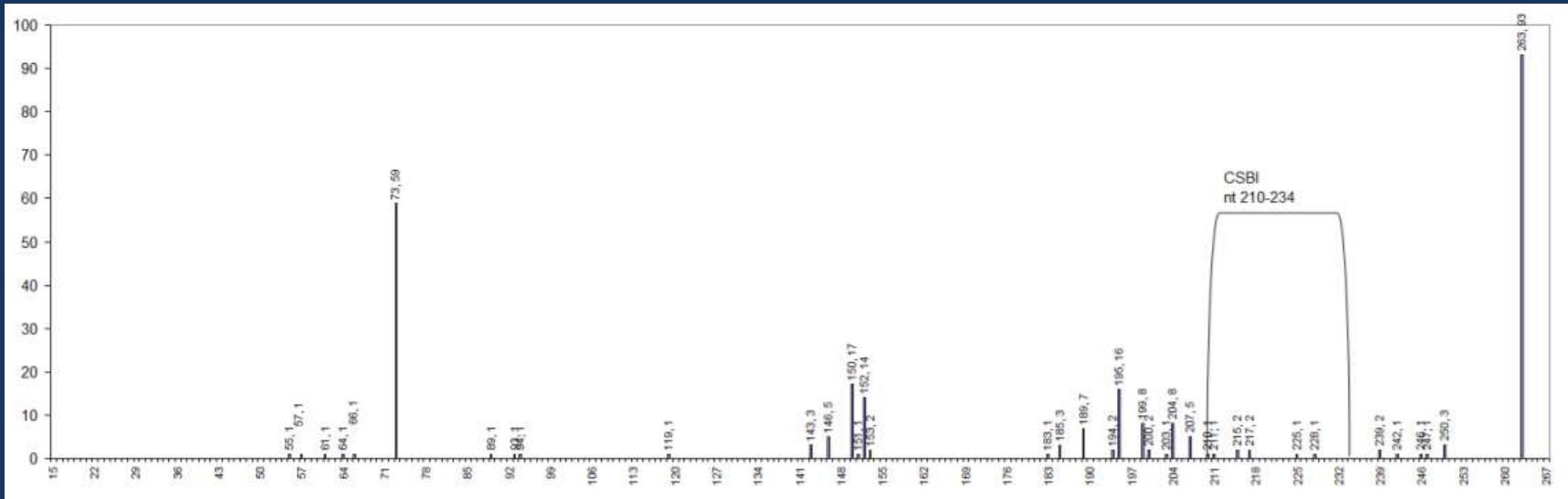
Artış  
Akciğer  
adenokarsinomu

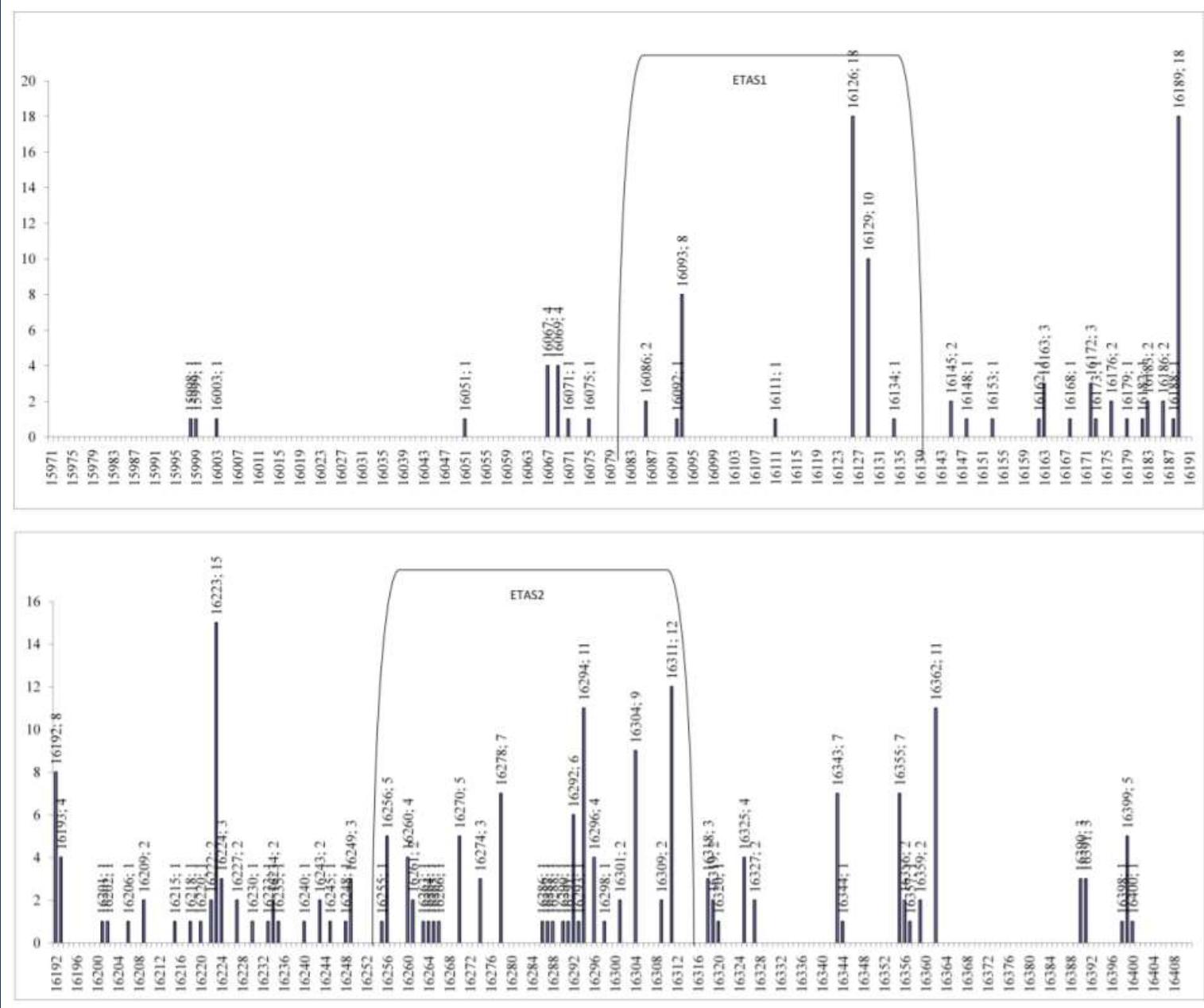






Tokarz ve Blasiak (2014)





# Bundan sonra?

- Mitokondriyal proteomiks: Bilinen mitokondriyal proteinler buz dağının görünen tarafı
- Mitokondriyal DNA: Bilmediğimiz genler
- Türk populasyonuna özgü çalışmalar
- Metodoloji: Fonksiyonel mitokondri izolasyonu, BN-PAGE, Oksijen tüketim hızı tayini, konfokal mikroskobi...
- İlaçların mitokondriyal fonksiyon üzerine etkisi