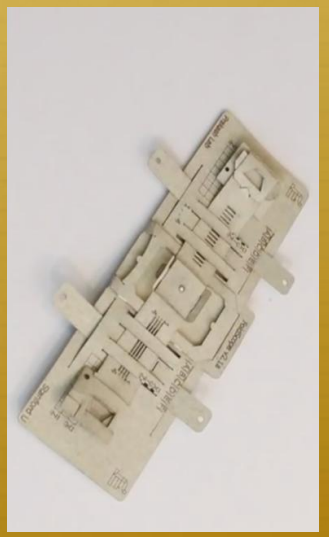
Leeuwenhoek'dan Foldoskopa Semmelweis'dan Semmelweis'a Mikrobiyolojinin Evrimi

Prof. Dr. Tanıl Kocagöz

ACIBADEM ÜNİVERSİTESİ

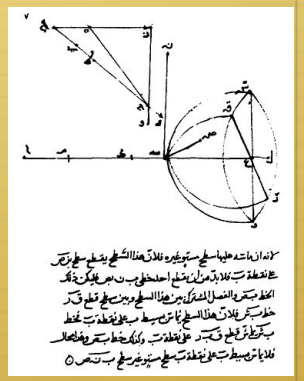


Su Cam ve Işık

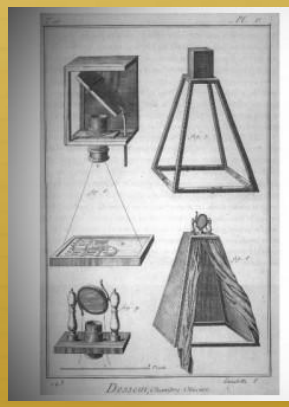
- Claudius Ptolemy: M.Ö. 2.yy. Suya daldırılan çubuğun eğilmiş gibi görüldüğünü gözlemleyip, suyun ışığı kırma açısını hesaplıyor.

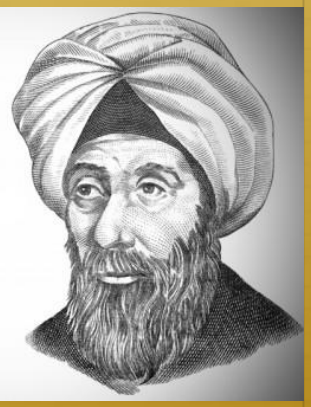
- 1. yy'da Roma'da farklı şekli olan camların altındaki cisimlerin görüntüsünü büyüttüğü gözleniyor. Bunlar mercimeğe benzediği için mercek (lentil – lense) ismini alıyor. Filozof Seneca su dolu bir kürenin büyüteç görevi yaptığını bildirmiş.

Orta Çağda Optik

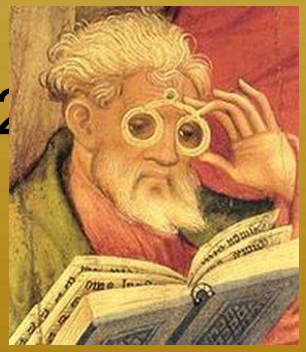


- Al Hasan Ibn Sahl (940-1000) Matematikçi, fizikçi, optik cisim mühendisi. Kırılma yasasını bulan kişi. Bunu kullanarak kusursuz lensler tasarlamış ve yapmış.





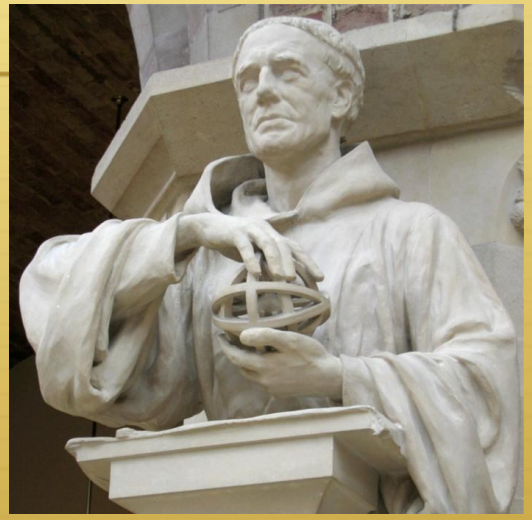
- Ibn al-Haytham (Alhazen) (Basra 965-1039): Optikler kitabı: Modern optik fiziğinin temelleri.



- Salvino D'armate (İtalya 12 1312). İlk gözlük

Deney ve Gözleme Dayalı Bilim

Dr. Mirabilis



Oxford Üniversitesi önündeki heykeli

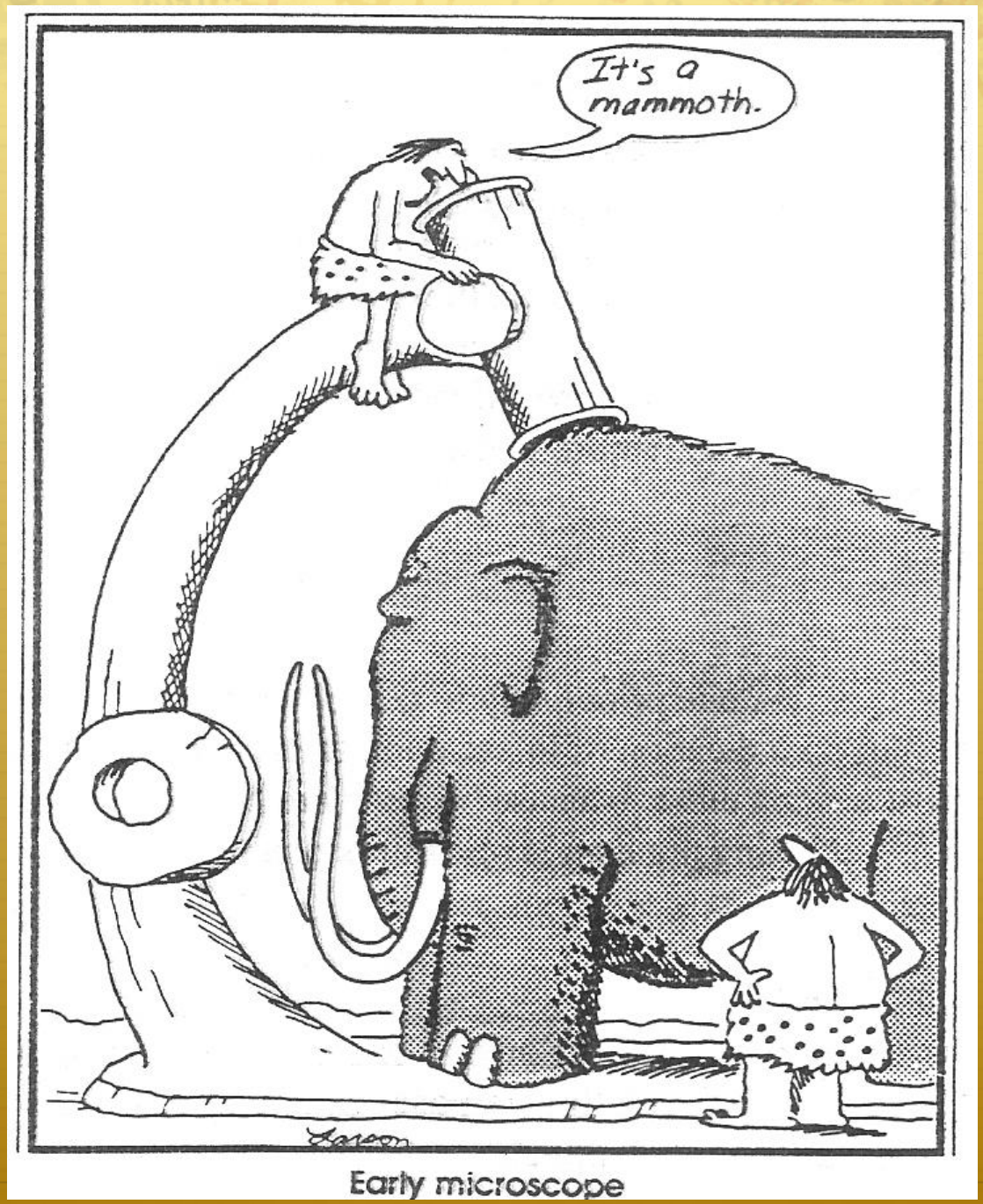
- Roger Bacon (1214-1294) İngiliz bilim adamı, filozof. Gerçeğin akıl ve deney ile bulunabileceğini savunuyor.
- Çift lensi ilk kullanan kişi.
- Hastalıkların küçük canlı yaratıklar tarafından oluşturulabileceğini söylemiş.

İlk Bileşik Mikroskop

- Hans ve oğlu Zacharias (1580 – 1638) Janssen

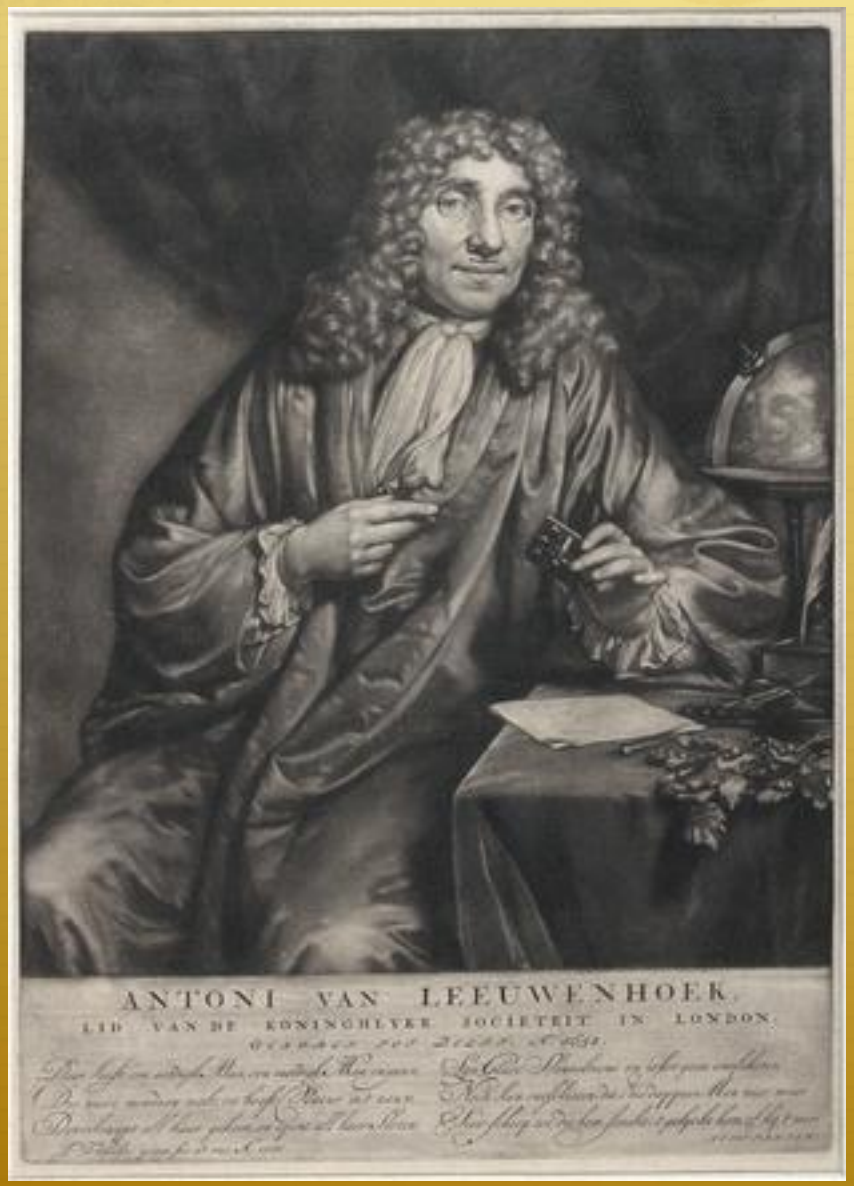
- Galileo Galilei (1609) bir dış bükey bir de iç bükey lens ile bileşik mikroskop yapıyor.


16

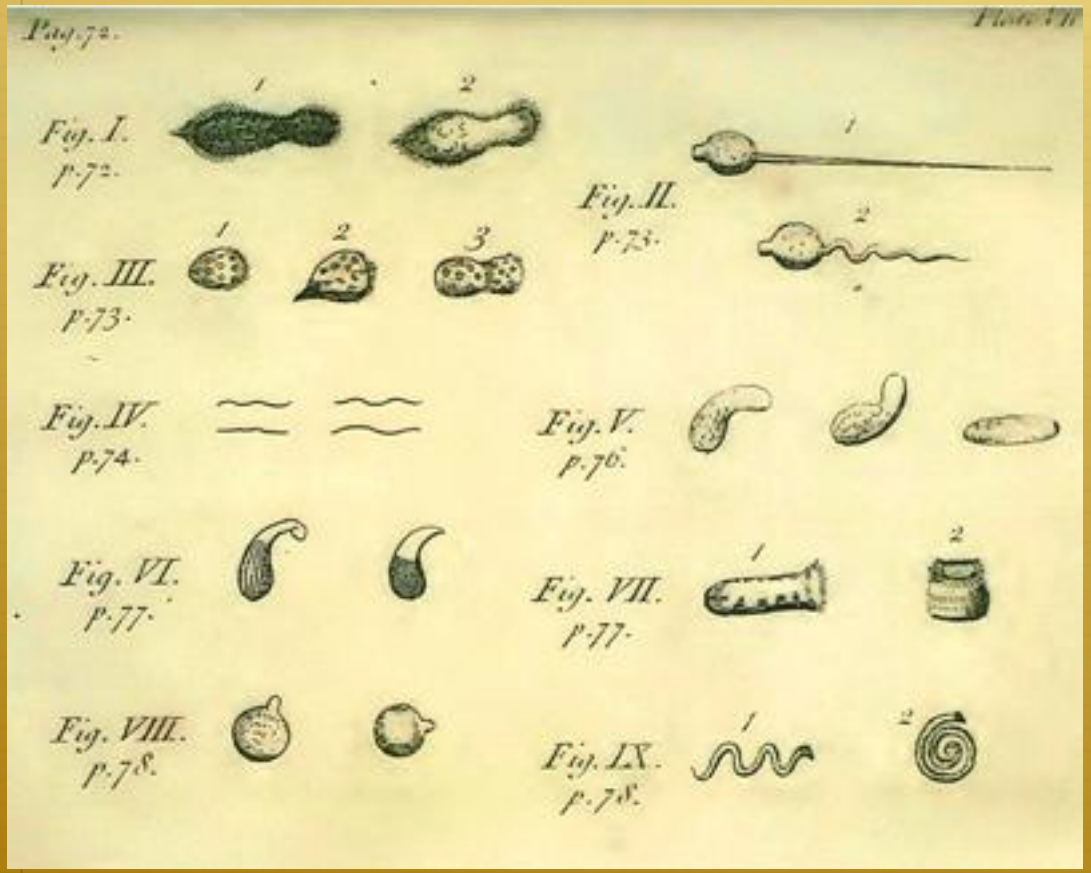


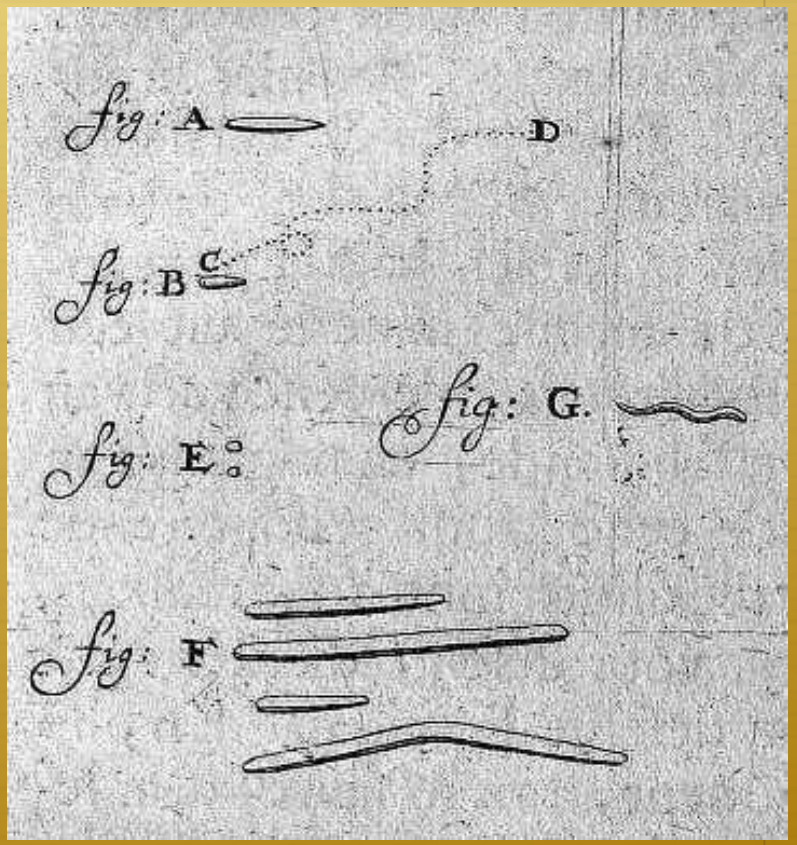
Early microscope

Anton van Leeuwenhoek



Protista ve Bakterilerin Görülmesi

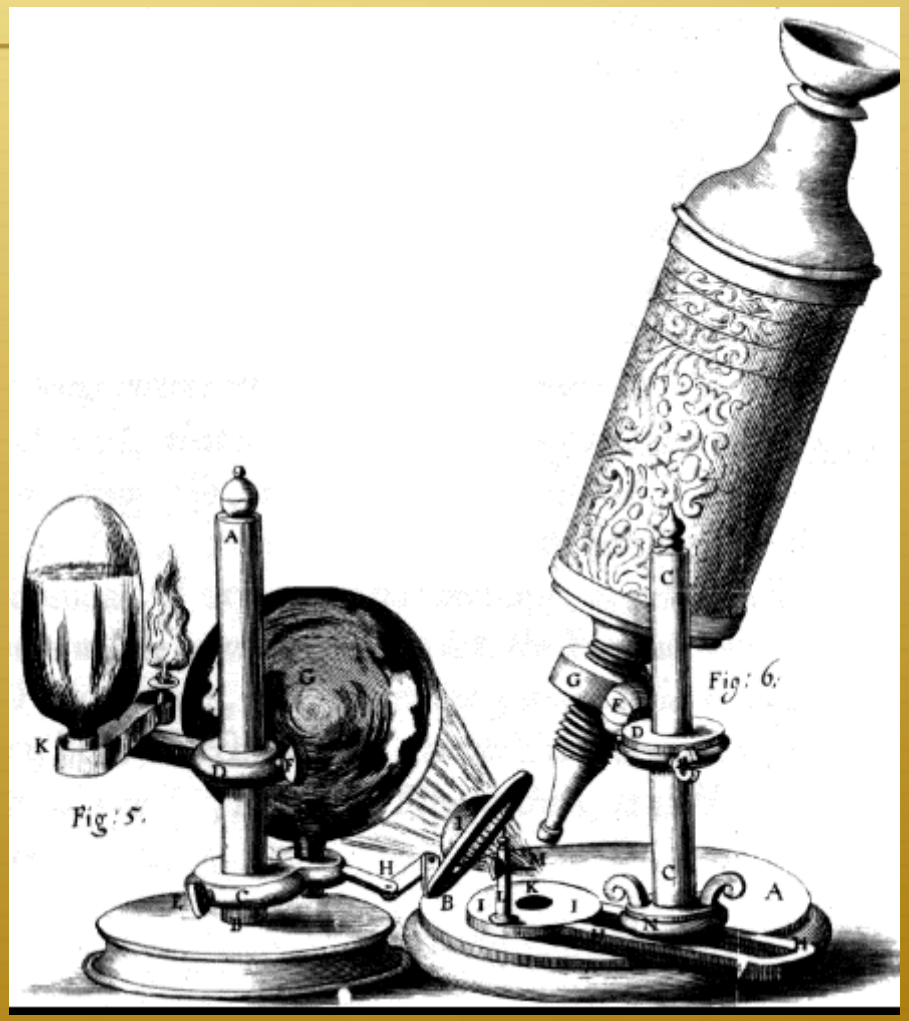




Çift Lensli Mikroskop

- Robert Hooke

1635-1703 İngiliz bilim adamı

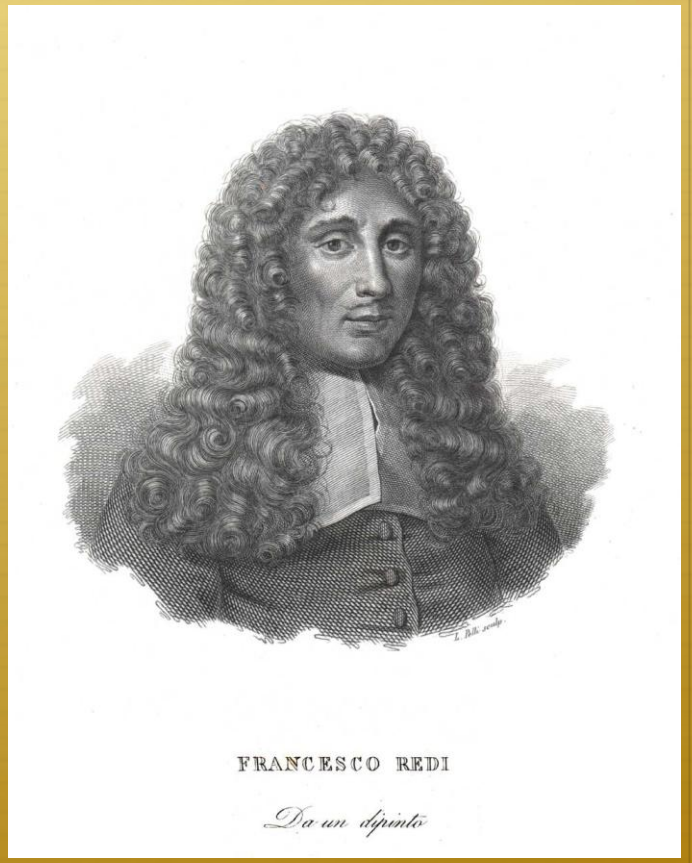


Kendiliğinden Canlı Oluşma Kuramları

- M.Ö. 384-320 Aristo hayvanlar topraktan oluşabilir.
- Samson ve M.Ö. 40 Virgil baldan arı oluşturma tarifleri.
- Güneşe bırakılan etten kurtlar oluşur.
- Kirli çorap ve buğday çuvalı bekletilirse fareye dönüşür.

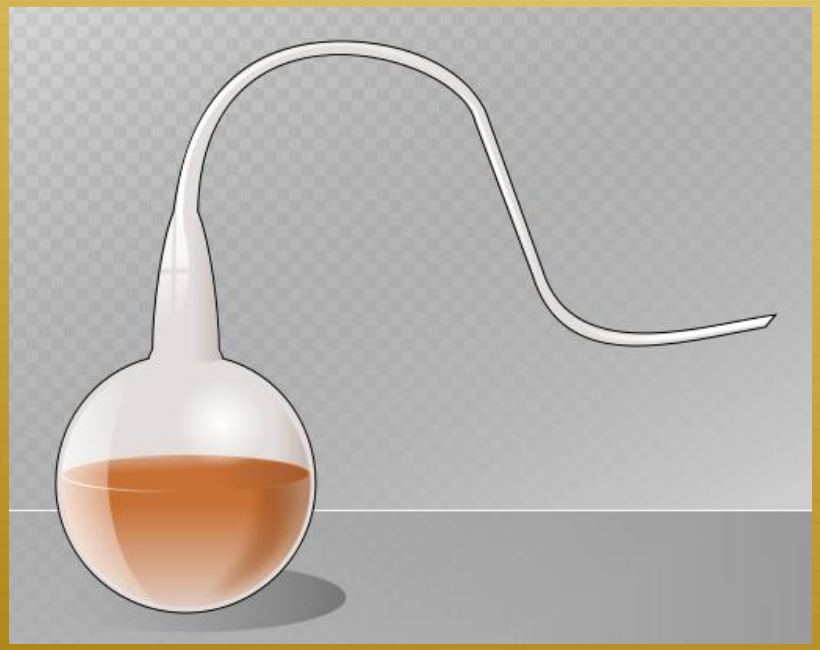
Kendiliğinden Canlı Oluşamayacağı Kuramı

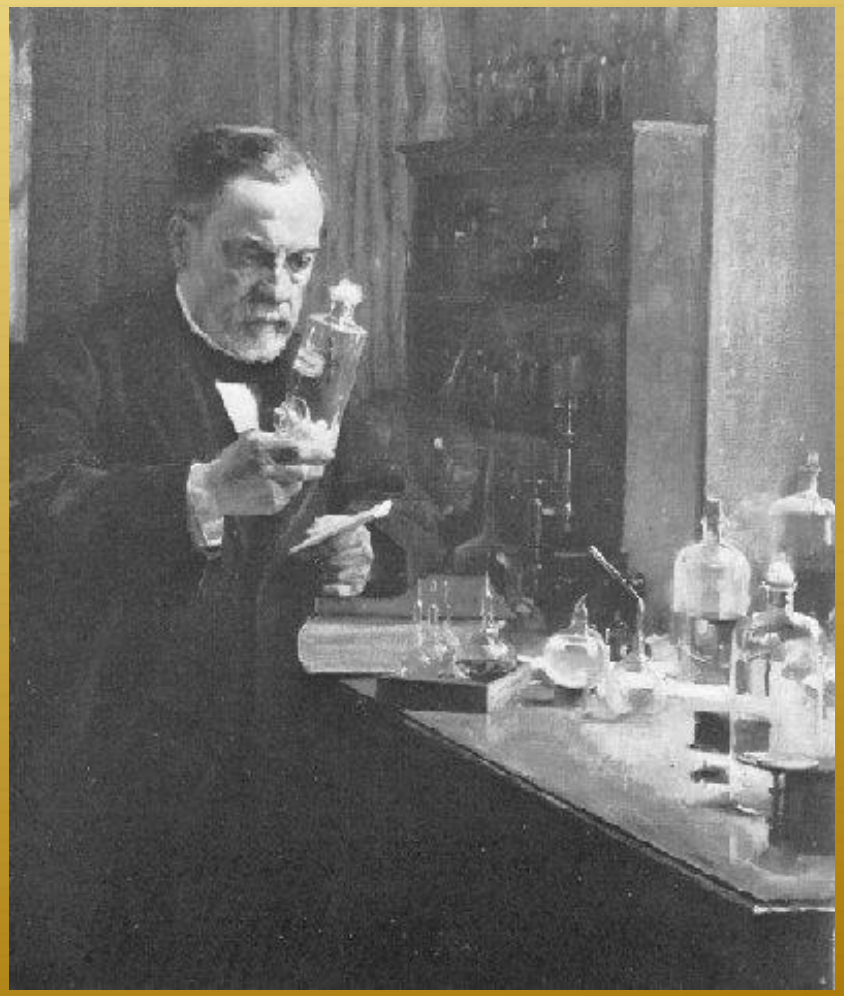
- Francesco Redi (1626-1697) Pisa'lı bilim adamı



Louis Pasteur (1822-1895)

- Fransız bilim adamı





İbn-i Sina (Avicenna)

- Türk filozof ve doktor. Şu anda Pakistan'daki Afşana kentinde doğdu. 10. yüzyıl başlarında «*El-Kanun fi El-Tıb*», (Tıbbın kanunları).

- İbn-i-Sina'nın kitabı üç asır boyunca Avrupa'nın temel tıp kitabı olarak okutulmuş. Tüberkülozun bulaşıcı bir hastalık olduğunu anlatmış. Menenjitin bulgularını yazmış. Enfeksiyon hastalıklarının su, gıdalar ve topraktan bulaştığı hipotezini ortaya atmış.

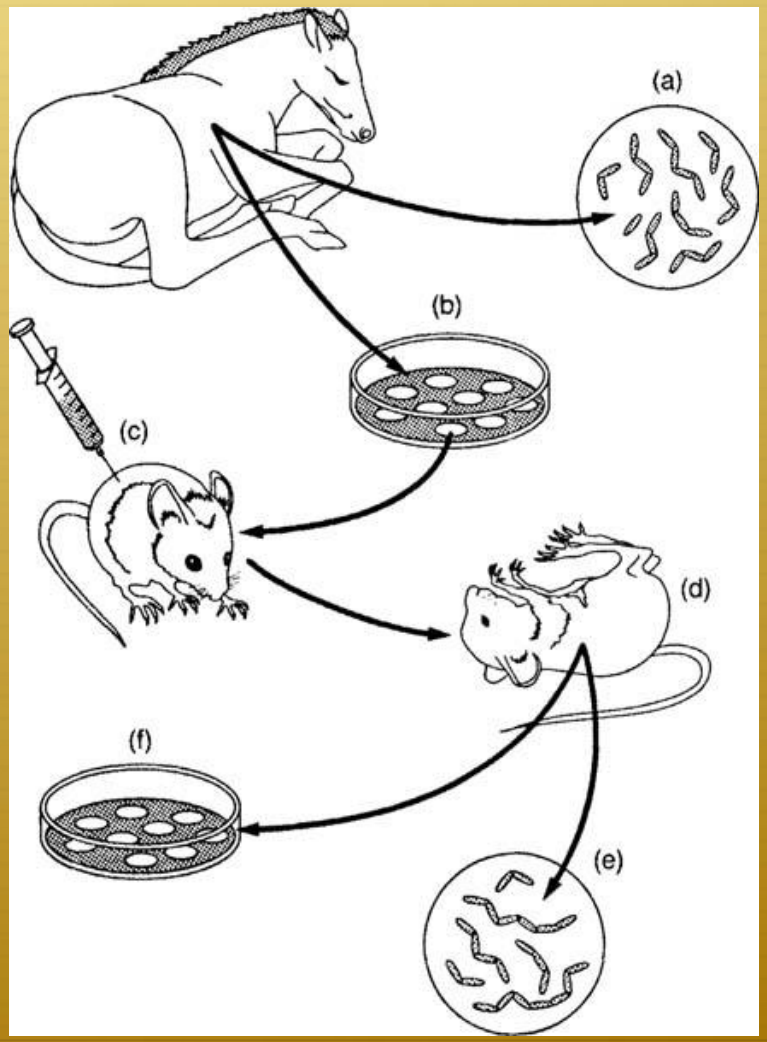
Bulaşıcı Hastalık ve Mikroplar

- **Hieronymus Fracastorius** (1478-1553) Venedikli bilim adamı. Sifiliz ve diğer bulaşıcı hastalıkların mikroplarla oluştuğu, herbirine gözle görülmeyen farlı küçük canlıların yol açtığını söylemiş.

Hieronymus Fracastorius, epidemiologist (1483-1553) named syphilis.

Robert Koch (1843-1910)

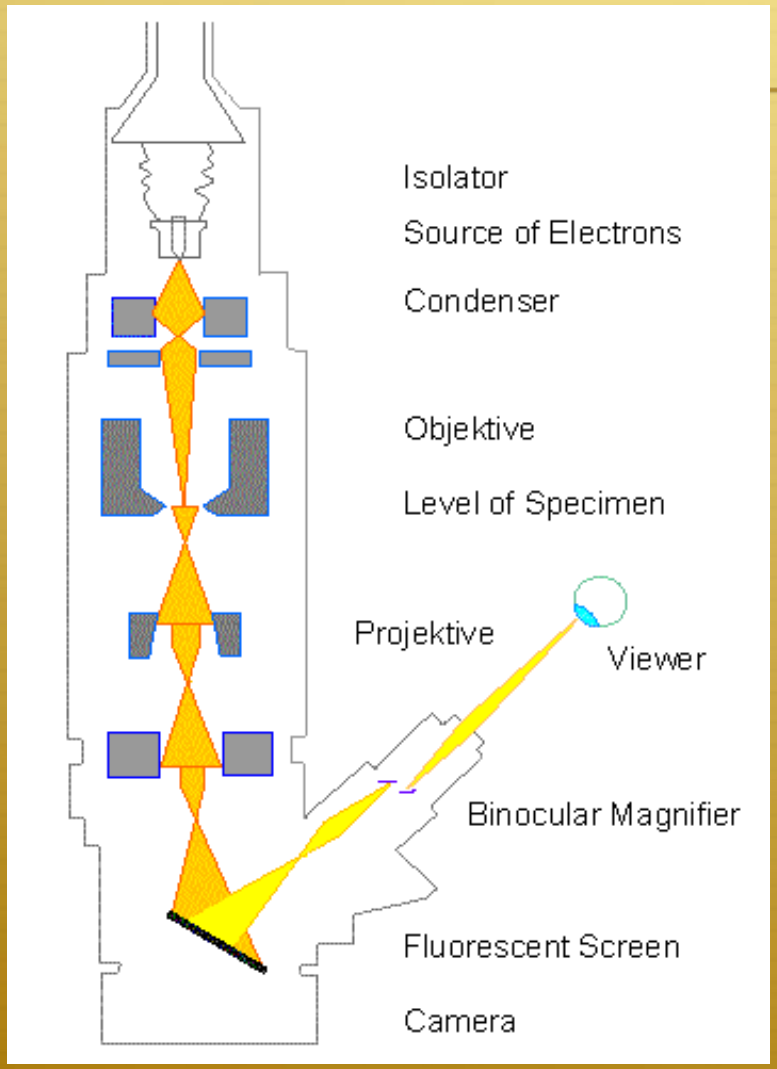
- Katı besiyeri. Bakteri kolonileri.
- Koch postülaları
- 1877'de Bacillus anthracis, 1882'de Mycobacterium tuberculosis, 1883'de Vibrio cholera'yı izole etmiş.

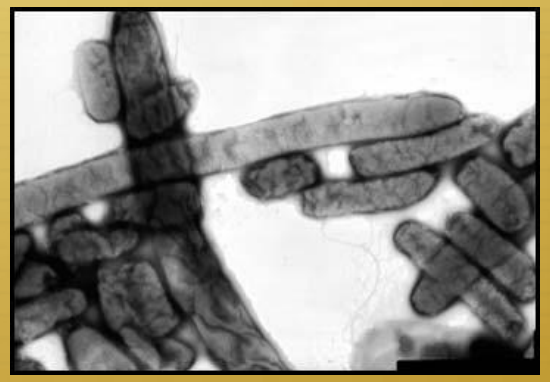


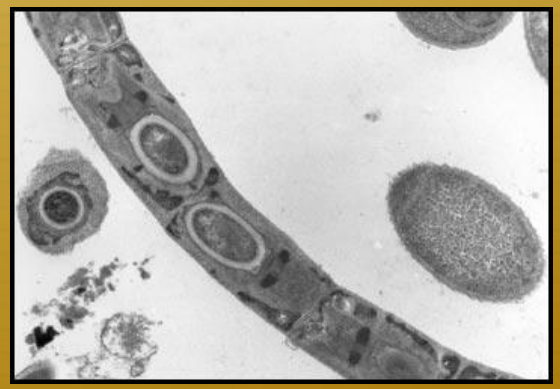
1900 başlarında Mikrobiyoloji ve Virüslerin bulunması

- Koch' dan sonraki 20 yıl mikrobiyolojinin altın çağı.
- 1900' e dek *Corynebacterium diphteria, Salmonella Typhi, Neisseria gonorrhoeae, Clostridium perfringens, Clostridium tetani, Shigella dysenteria, Treponema pallidum* tanımlanmış.
- 1892 Ivanowsky tütün mozaik virüsü porselen filtreden geçiyor.
- 1898 Beijernick virüs (latincede zehir) terimini kullanıyor.
- 1911 Rous tavuklarda kanser yapan sarkoma virüsü
- 1914-1918 Twort ve d' Herelle bakteriofaj

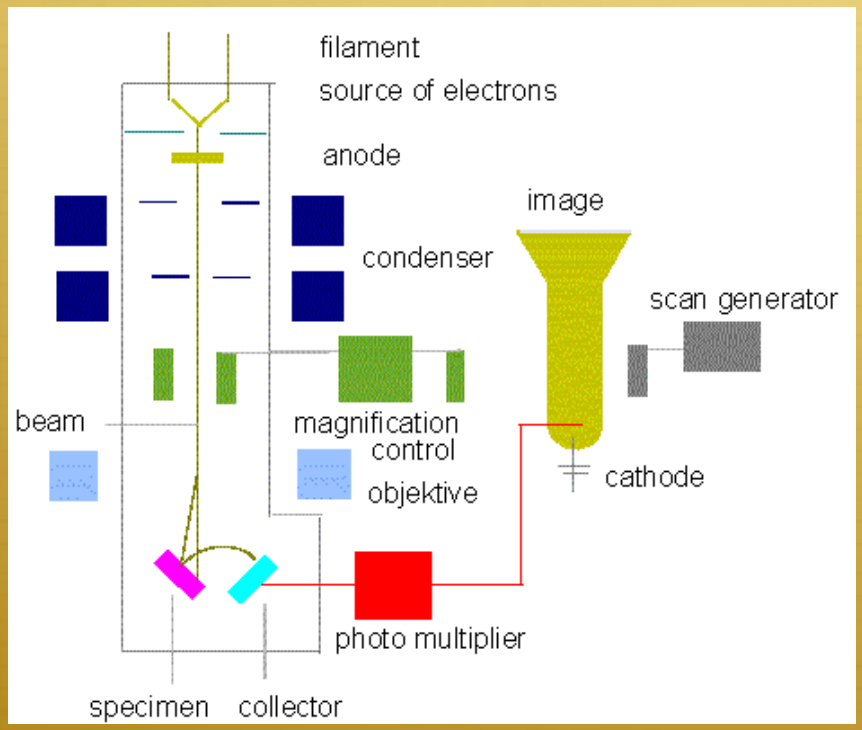
Aktarımlı Elektron Mikroskobu

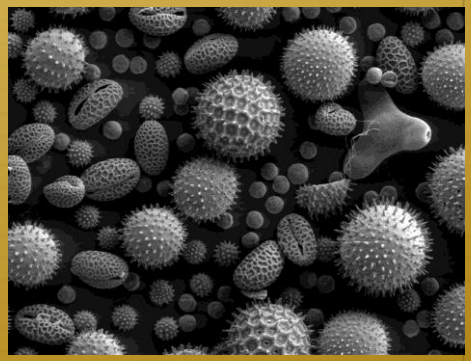




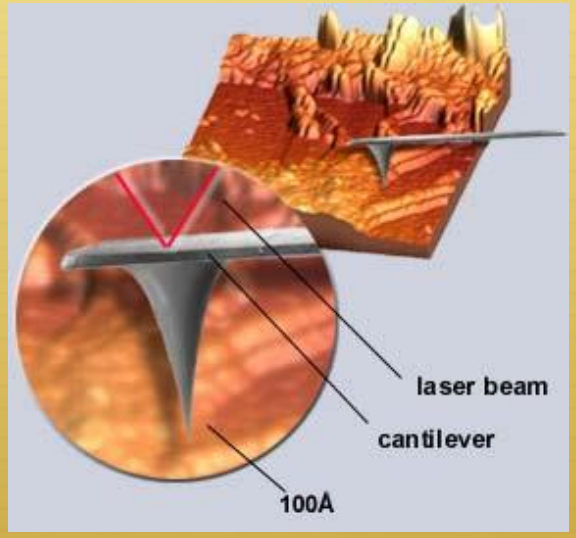


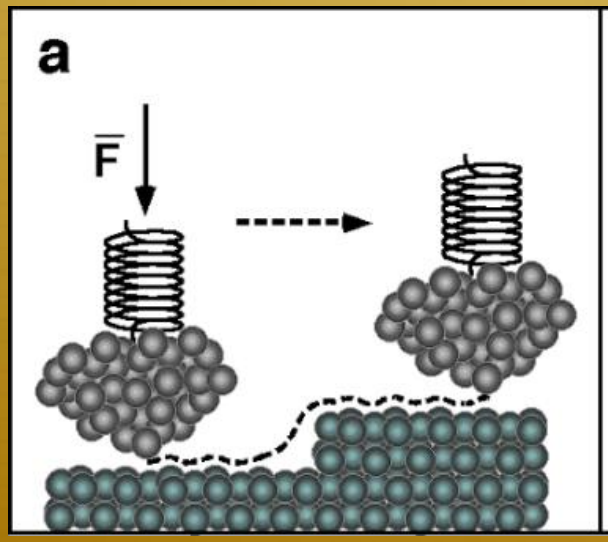
Tarama Elektron Mikroskobu

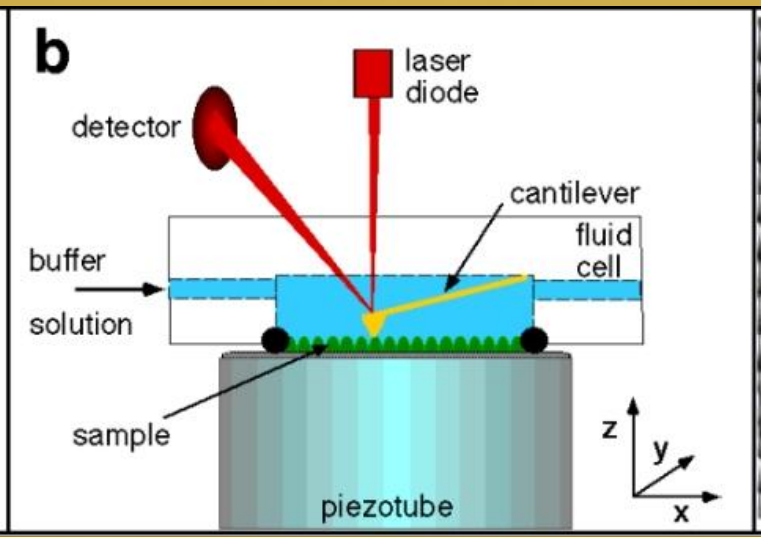


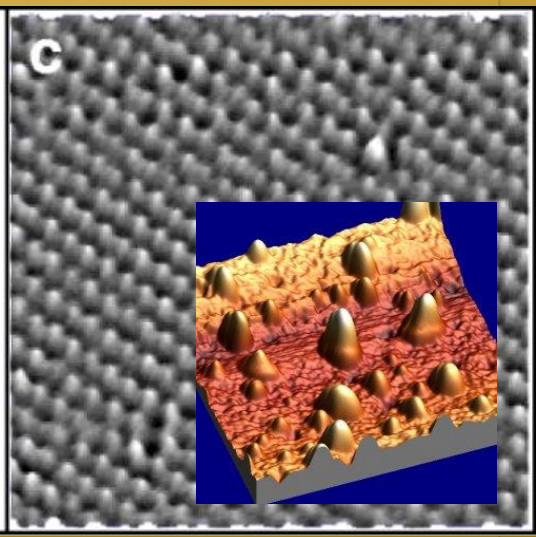


Atomik Güç Mikroskobisi





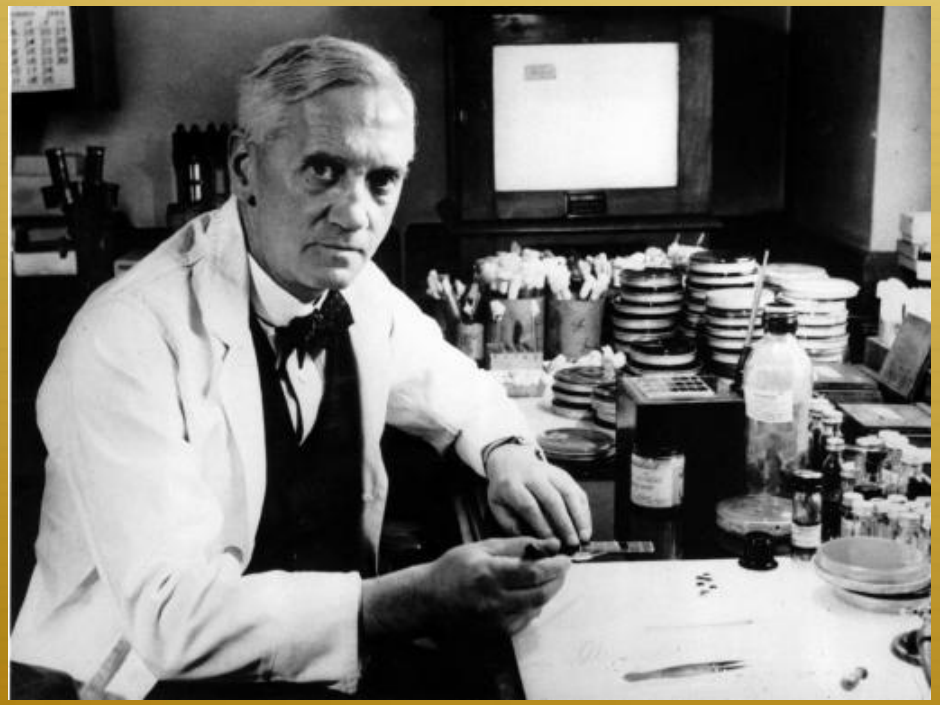


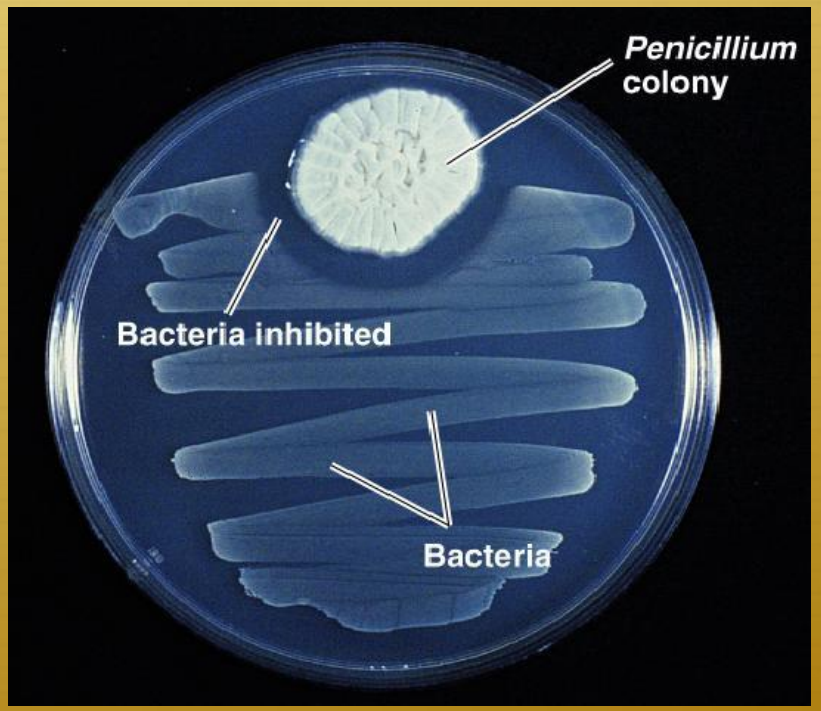


Semmelweis

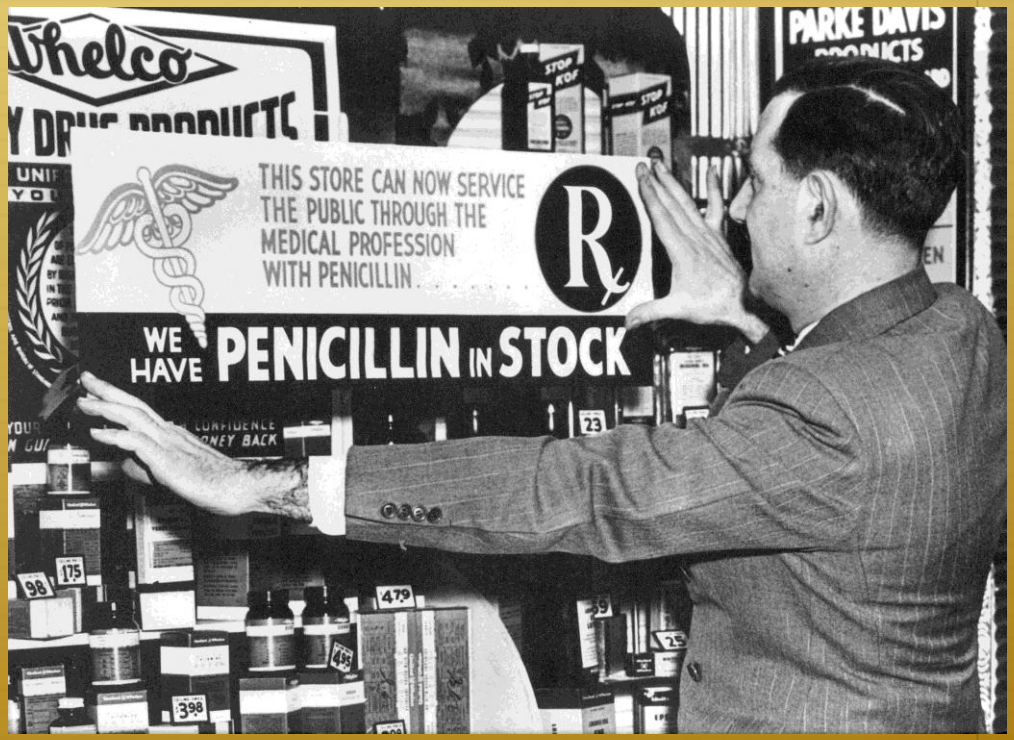
Antibiyotik Çağı

- Fleming 1929'da *Penicillium* (mantar) kolonisi çevresinde bakterilerin üreyemediğini gözlemiştir.
- 1935 yılında Domagk sentetik ilaçlar sülfonamitleri bulmuştur.

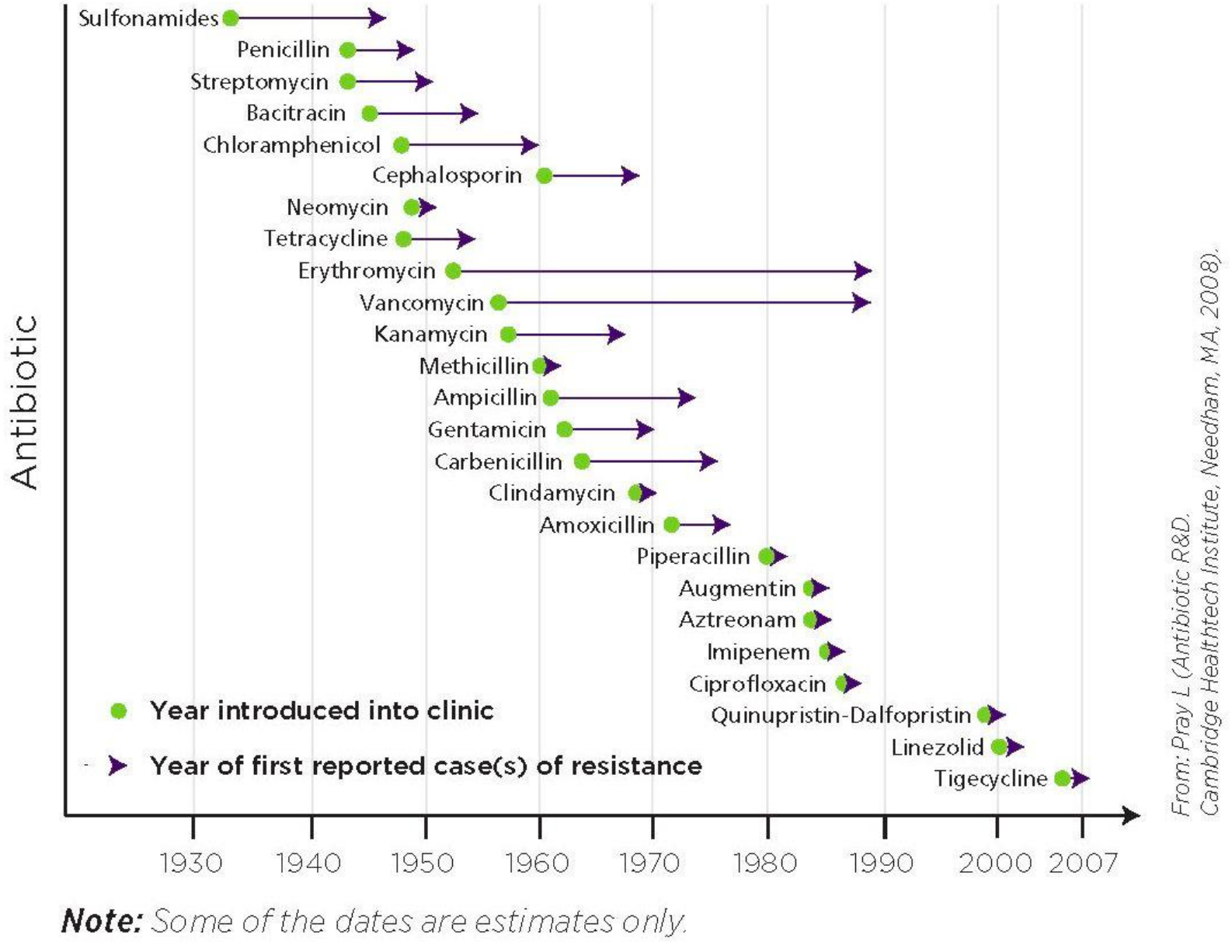




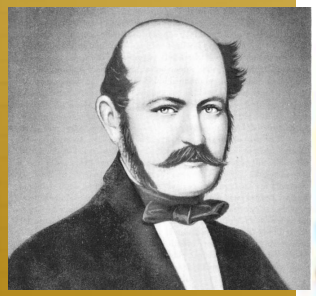
- İkinci Dünya Savaşı'nda penisilin birçok yaralının yaşamını kurtardı

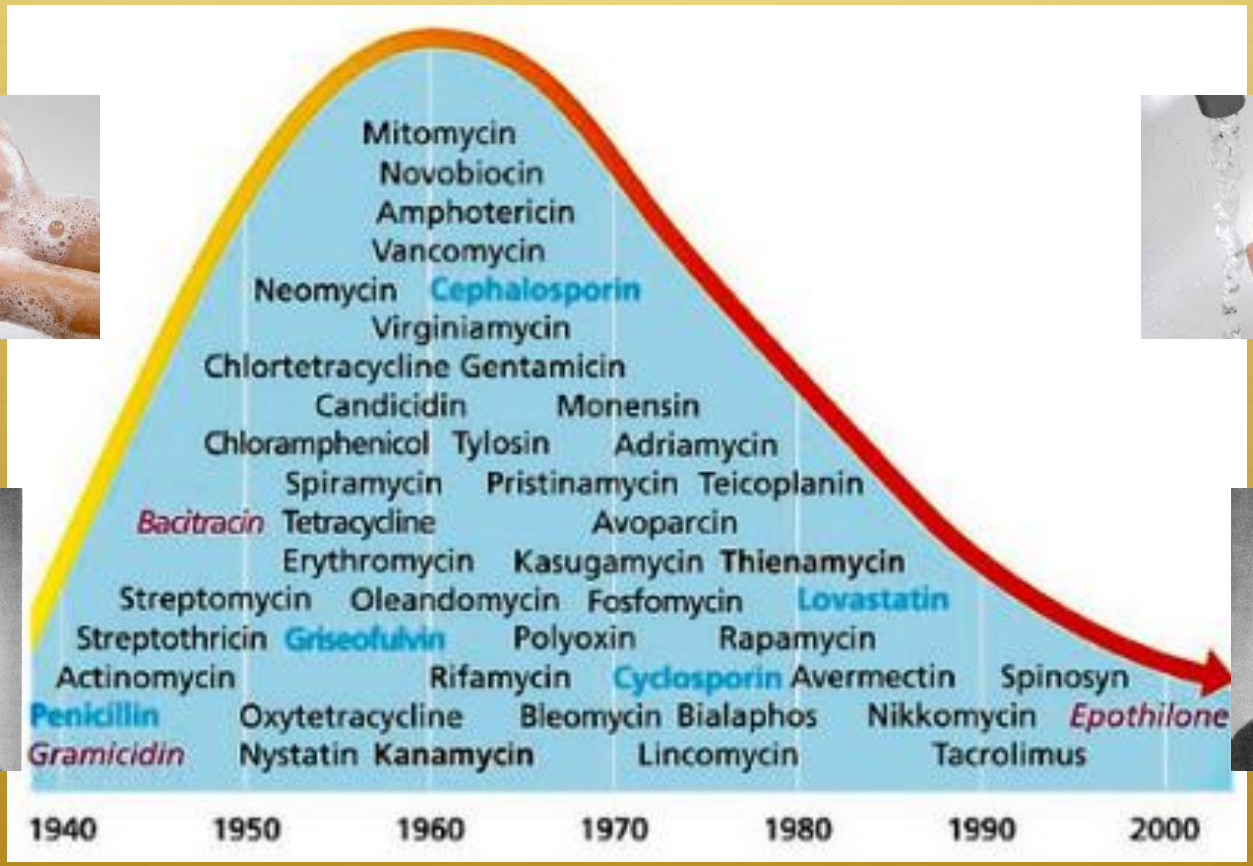


Antibiyotik Kullanımı ve Direnç Gelişme Süreci



Semmelweis’dan Semmelweis’a





Tüberküloz

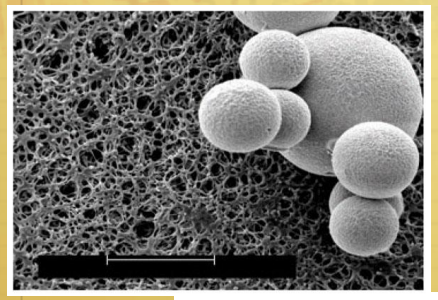
- Dünya nüfusunun üçte biri taşıyıcı
- Bunların arasından her yıl 9 milyon yeni hasta ortaya çıkıyor
- 3 milyon kişi (günde 5.000 kişi) yaşamını yitiriyor
- Gelişmekte olan ülkelerde önlenebilir ölümlerin %25'ini tüberküloz oluşturuyor
- İlaç direnci hızla artıyor
- Tüm enfeksiyon hastalıklarının tanısı için dünyada yıllık kişi başına yapılan harcama 1 doların altında

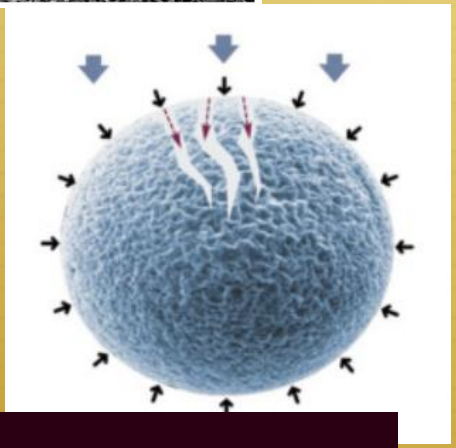
Kısıtlı Laboratuvar Koşulları

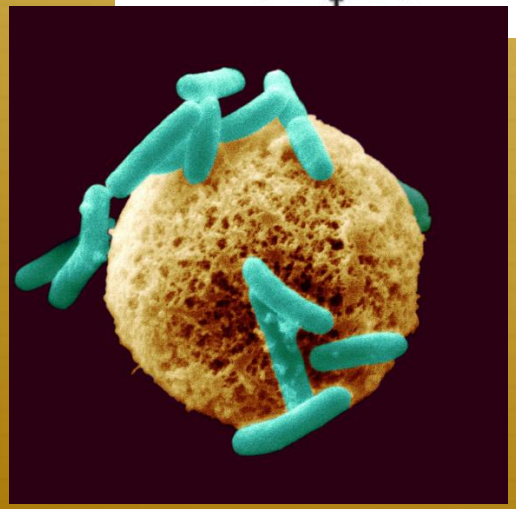
Uganda'da bir laboratuvar

Hindistan'da bir laboratuvar

Decomics







- Dekontaminasyon işlemi için örneğe çok fazla sıvı eklenmesi gerektiğinden, seyrelmiş örnekteki mikobakterileri yoğunlaştırma için santrifüj gerekmektedir.
- Decomics yönteminde dekontaminasyon ve nötralizasyon için eklenen sıvılar emici boncuklar tarafından emildiği için, santrifüj gereksinimi ortadan kalkmıştır.

DECOMICS

Örnek kabı ve dekontaminasyon sıvısı

Nötralizasyon sıvısı

Emici boncuklar

Decomics

Santrifüj gerektirmediği için dünyada laboratuvar olanakları en kısıtlı yörelerde dahi kullanılabilir.
Örnek işleme süresini 45 dakikadan 23 dakikaya indirmektedir.

Örnek kaba konur

Karıştırılır

10 dakika beklenir

Boncuk paketi açılır

Emici boncuklar eklenir

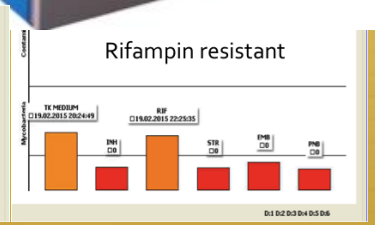
Karıştırılır
5 dakika beklenir

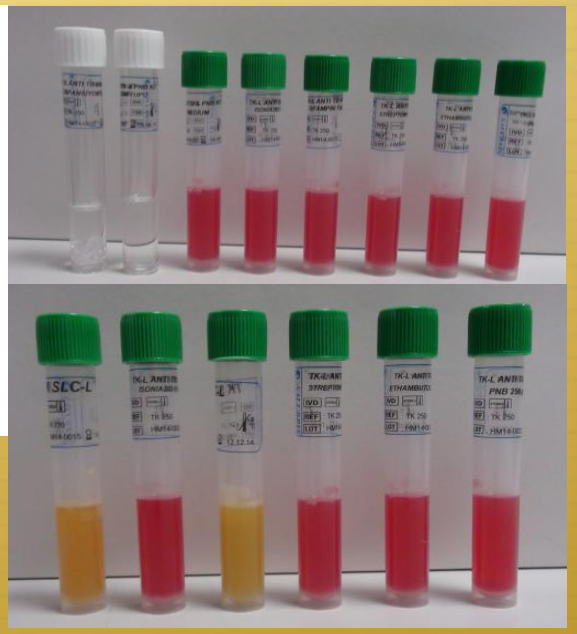
Nötralizasyon sıvısı eklenir

3 dakika sonra hazır olan örnekten ekim yapılır

TK Besiyeri ile Hızlı Kültür ve Duyarlılık Testi

Uninoculated Mycobacteria Contamination





UNITAID

2014

TUBERCULOSIS

Diagnostics Technology and Market Landscape

3RD EDITION

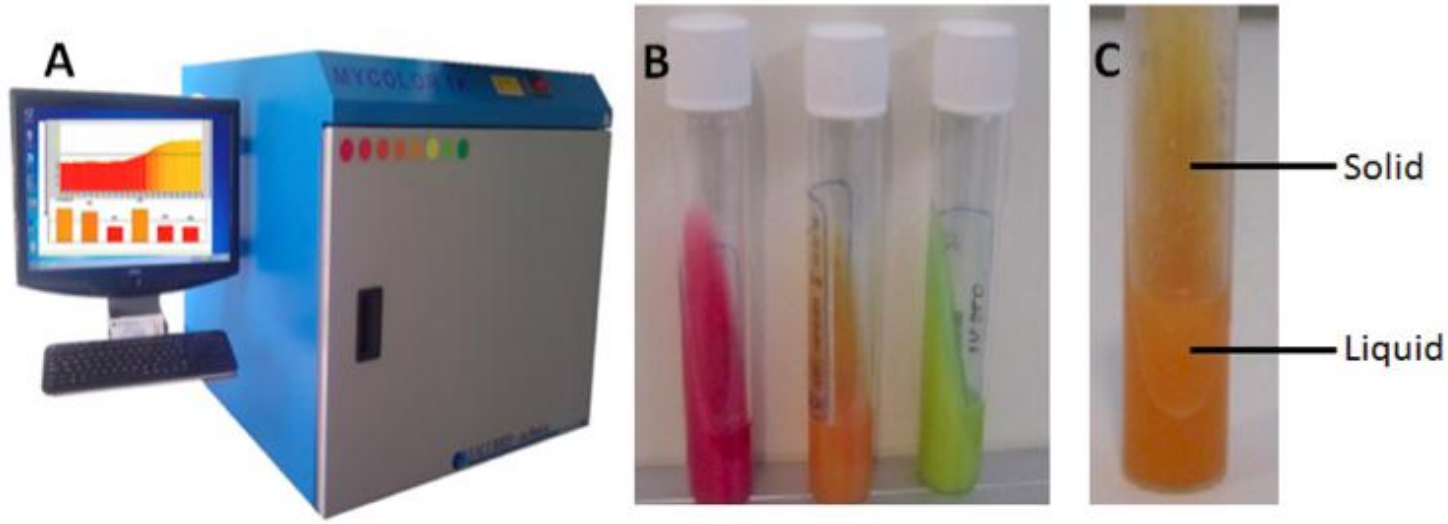
World Health Organization

For rapid processing of sputum for culture, Salubris Inc. (USA) offers Decomics®, a product that is both CE-IVD marked and US FDA (510k) cleared, and marketed since 2012. This is used to decontaminate and concentrate specimens for culture-based testing from a variety of common specimen types without the need for a centrifuge. The test uses absorbent beads and reagents to liquefy, decontaminate and neutralize samples in less than 25 minutes. A variety of commercial vendors, including Becton, Dickinson and Company (hereafter BD; USA) and Hardy Diagnostics (USA), also offer kits to decontaminate sputum samples for culture, employing derivatives of the N-acetyl cysteine and NaOH methods commonly used to prepare sputum specimens prior to culture.

http://unitaid.org/images/marketdynamics/publications/UNITAID_TB_Diagnostics_Landscape_3rd-edition.pdf

Salubris Inc. offers a series of products that also perform with automated TB culture (Figure 14). They manufacture: TK MEDIUM® SLC; a biphasic, culture medium that can be incubated and automatically monitored in the MYCOLOR TK® instrument (Figure 14); and TK MEDIUM SLC-L, a liquid formulation.

Figure 14. A: MYCOLOR TK automated incubator; B: TK colorimetric media with changes from red to orange (mycobacterial positive culture) red to green (contaminated culture); C: biphasic format of TK media with both solid and liquid media



Source: Images reproduced with permission from Salubris Inc.

TK MEDIUM® is an egg-based solid medium similar to L-J.[92] Unlike the liquid media used in other automated platforms, the TK media do not require any additives, creating a simplified workflow and reducing risk of contamination.[92] The media contain dyes that react upon the growth of microorganisms (Figure 14).[93] Upon mycobacterial growth, the original red colour turns orange and then yellow. The colour change is indicated before colonies are visible on the agar, improving the time to detection. Contamination by fungi or Gram-negative bacteria produces a green pigment; some Gram-negative bacteria can produce orange/yellow. The TK SLC medium is biphasic having both solid and liquid media (Figure 14). The TK

assessment between this system and the other liquid systems has not been performed, but recently a new liquid medium, TK SLC Liquid®, was compared to MGIT.[94] Overall, the performance of both media was similar, but MGIT™ had a faster median time to result, 7.7 days as compared to 15.1. Contamination was much more prevalent in the MGIT™ tubes (13.7%) compared to TK SLC Liquid (1.3%), which may be due to the preparation steps prior to inoculation of MGIT.

Çiftci and Karakeçe *BMC Infectious Diseases* 2014, **14**:130
http://www.biomedcentral.com/1471-2334/14/130

BMC
Infectious Diseases

RESEARCH ARTICLE Open Access

Comparative evaluation of TK SLC-L, a rapid liquid mycobacterial culture medium, with the MGIT system

İhsan Hakkı Çiftci* and Engin Karakeçe

UNITAID

2015

TUBERCULOSIS

Diagnostics Technology and Market Landscape

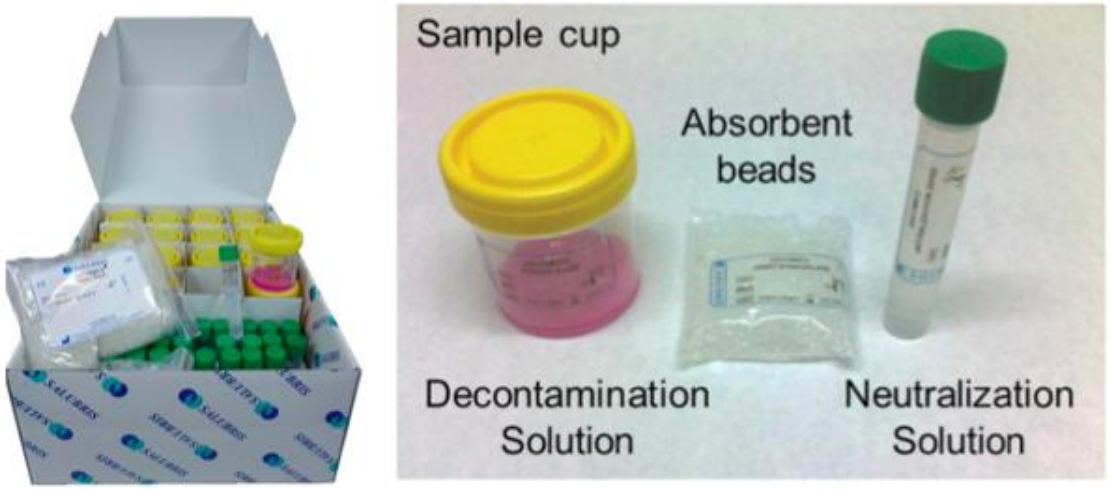
4TH EDITION

World Health Organization

4.2.4. *Culture-based tools for the diagnosis of TB and DST*

There is little to report in terms of new product information from developers regarding culture-based diagnosis of TB. Salubris Inc. (USA) no longer supplies the biphasic TK MEDIUM® SLC for use in its MYCOLOR TK® automated culture system. The company now offers the TK MEDIUM® SLC-L, a liquid media that is now housed in a plastic tube to limit risks of mishandling. A consistent issue with the conventional decontamination method of sodium hydroxide and N-acetyl cysteine (NaOH-NALC) is the risk of incomplete decontamination or overexposure to reagents killing the MTB cells. The NaOH-NALC method also requires centrifugation that can limit processivity rate and incorrect use of this can result in infection risks via aerolisation. The Decomics® kit (Figure 9) uses absorbent beads and reagents to liquefy, decontaminate and neutralize samples in less than 25 minutes without requiring a centrifuge or NaOH-NALC.

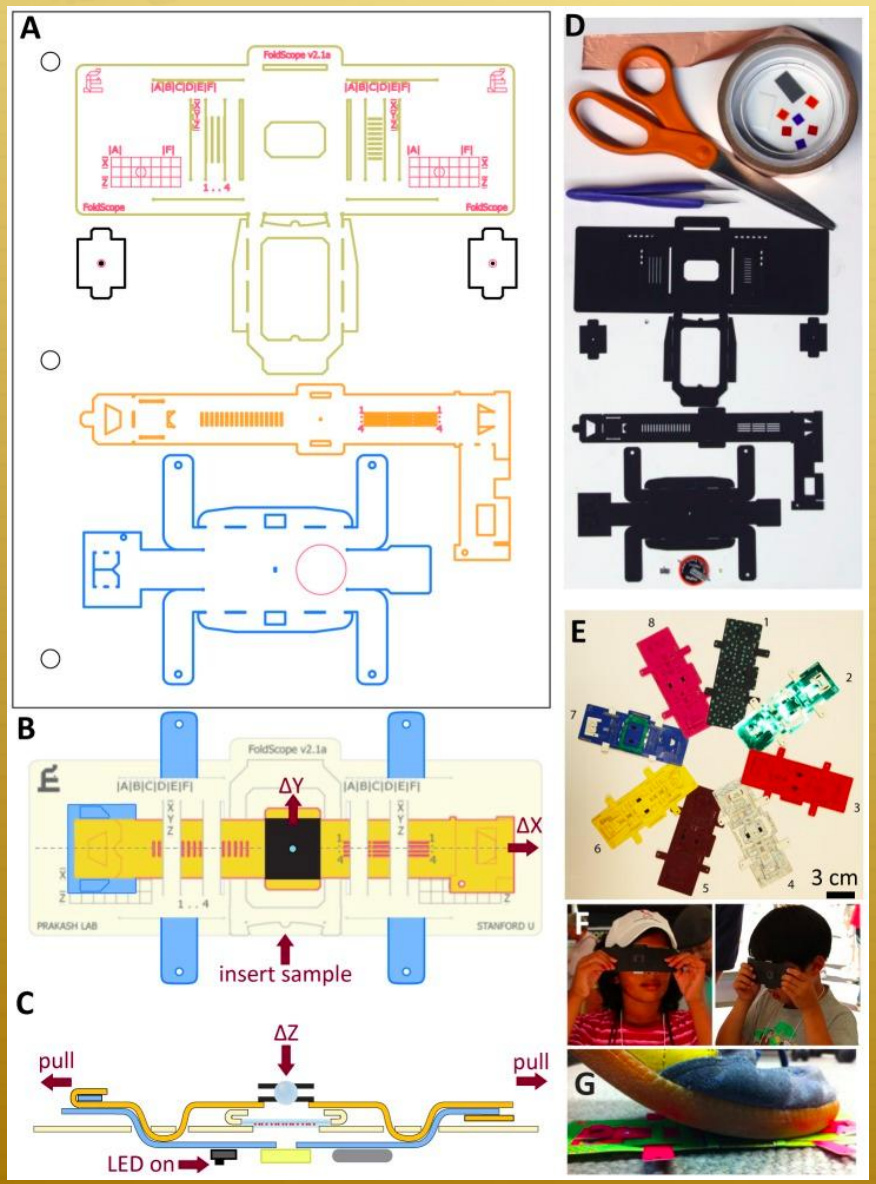
Figure 9. Decomics® kit from Salubris Inc.: individual components including sample cup, decontamination solution, beads and neutralization solution



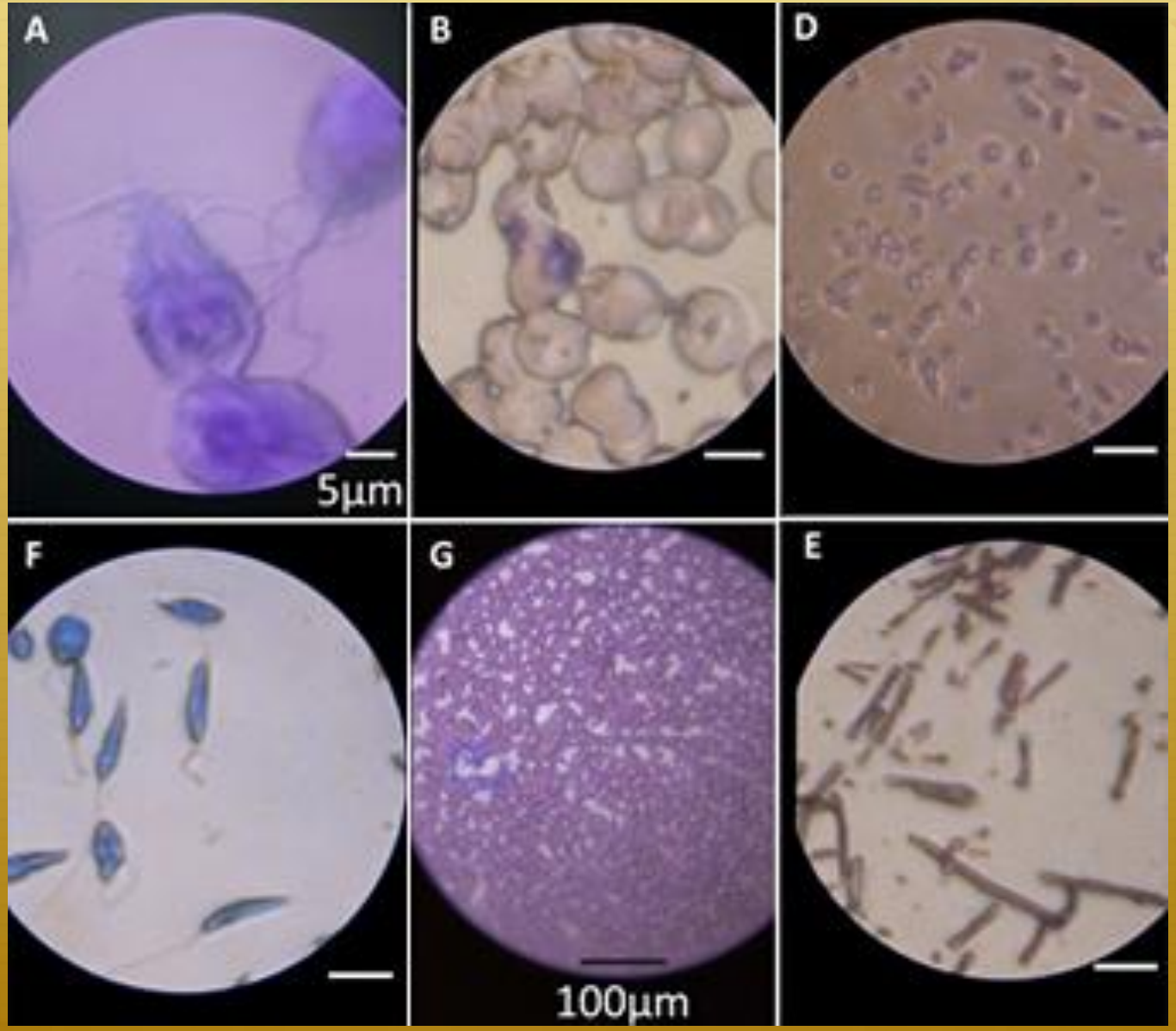
Source: Image reproduced with permission from Salubris Inc.

A recent evaluation of the TK MEDIUM® SLC-L and Decomics® beads was performed in India with 500 specimens with comparison to NaOH-NALC processing and L-J culture. The authors noted an improved performance of MTB diagnosis from the liquid media versus L-J (130 MTB vs 110 MTB) and with an earlier median time to detection (12 days vs 30). Rates of contaminated culture were reduced from 7% observed with the NaOH-NALC method to only 2% with Decomics®. This kit also reduced the median time for specimen processing to approximately 23 minutes as compared to NaOH-NALC, which took 45 minutes. The Decomics® product is CE-IVD marked and US FDA (510k) cleared. Current pricing of this product is unknown.

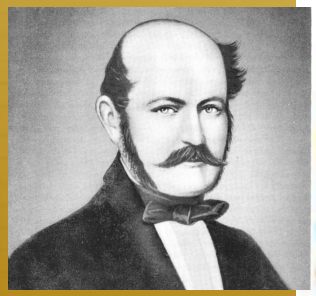
Foldoskop (Origamik mikroskop)

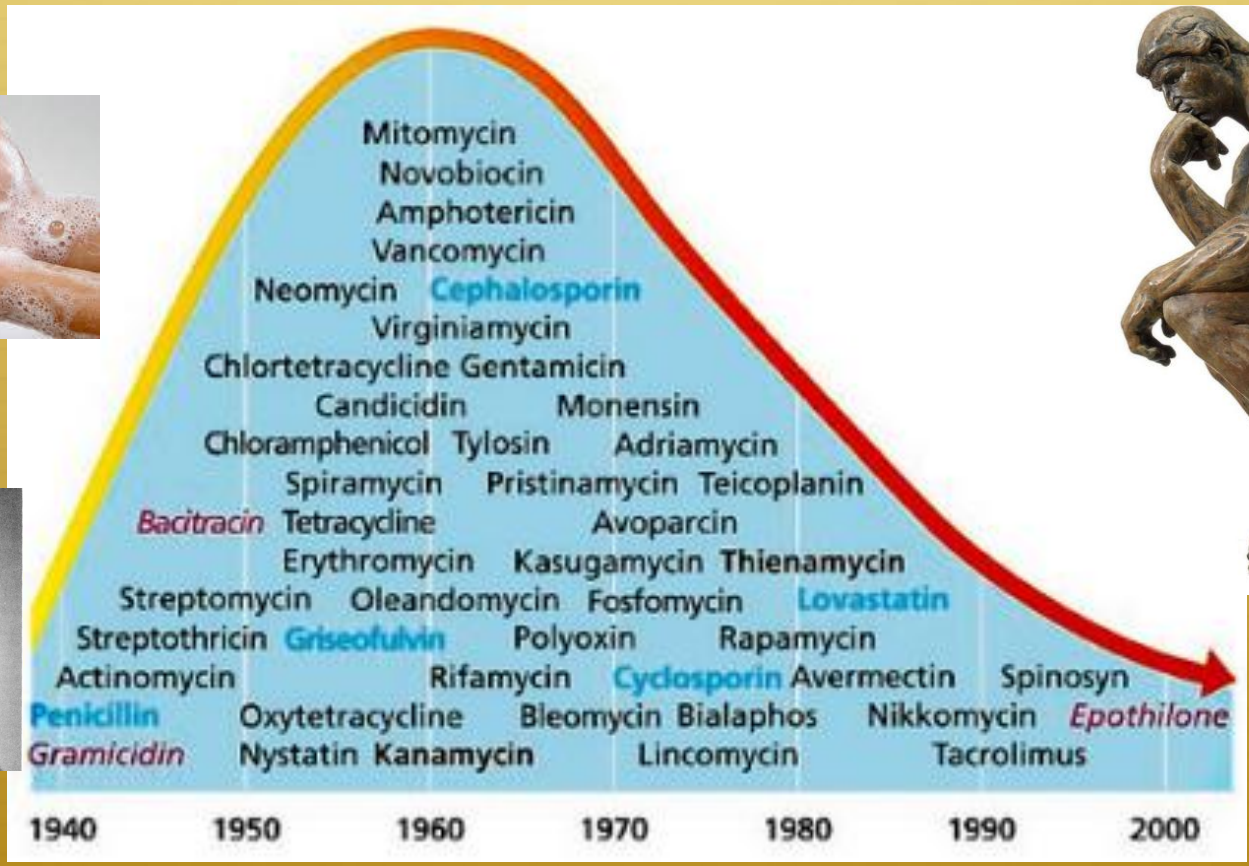


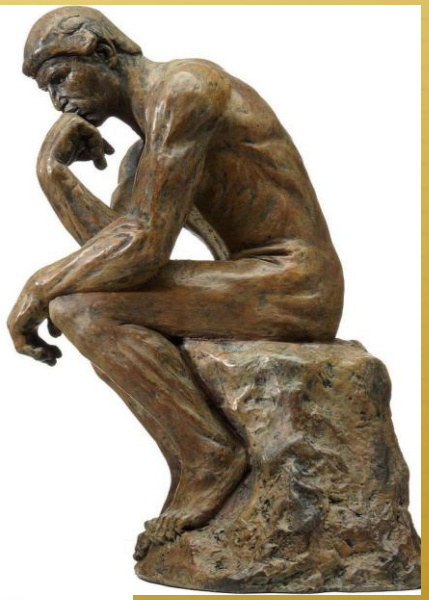
Foldoskop Görüntüleri



Peki Şimdi Ne Yapacağız???

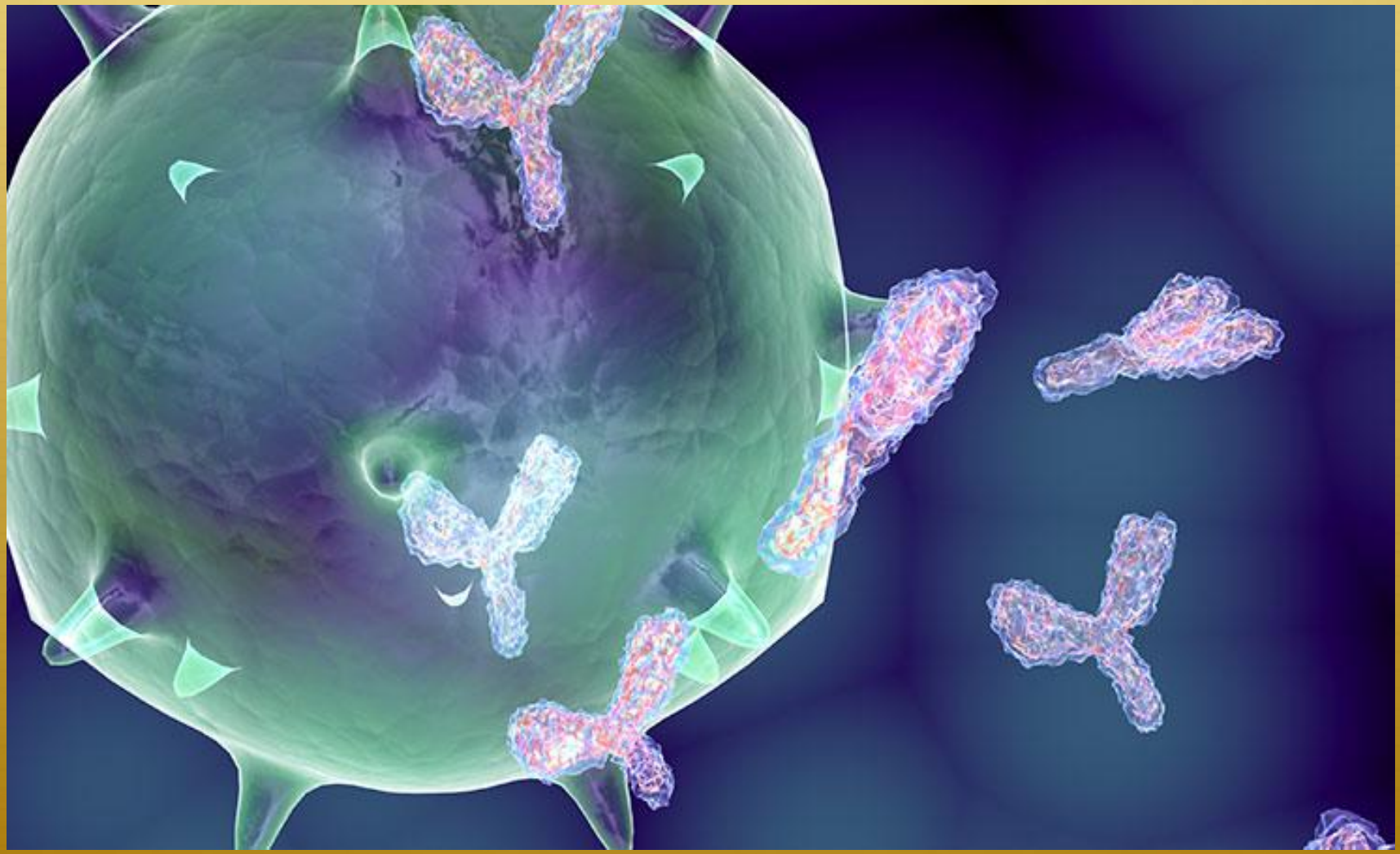




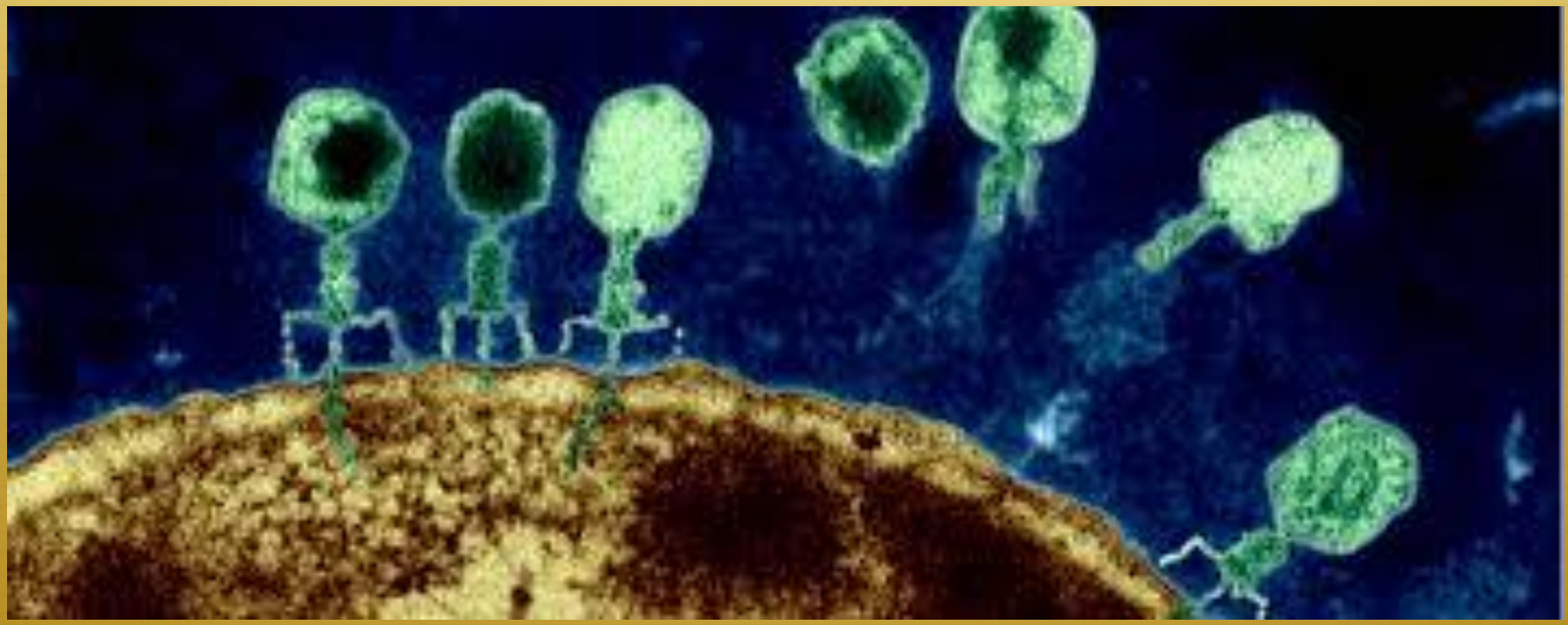


Tüm Genom İncelemesi ve Biyoinformatik ile Yeni Antibiyotik Hedeflerinin Belirlenmesi?

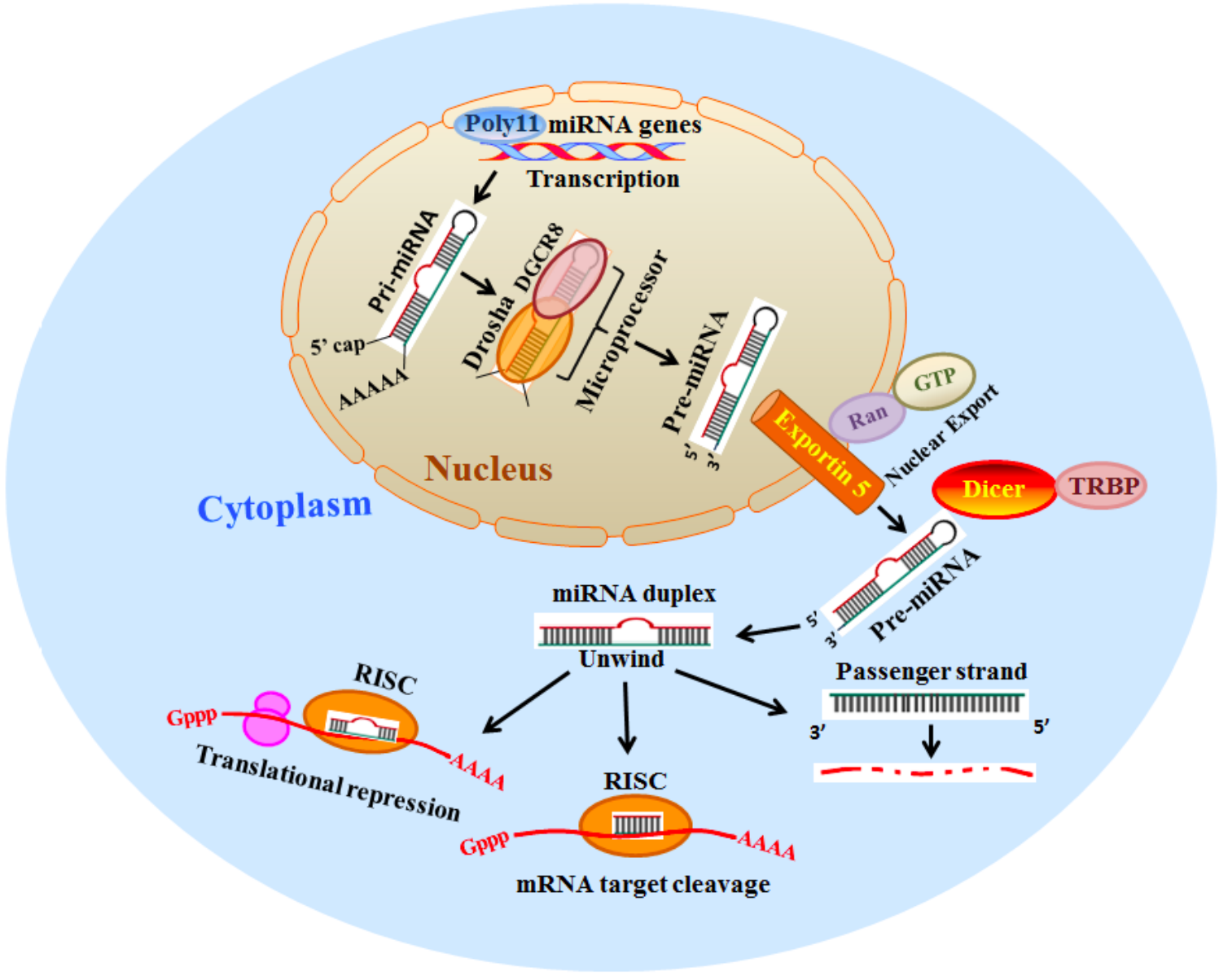
Monoklonal Antikor Tedavisi?



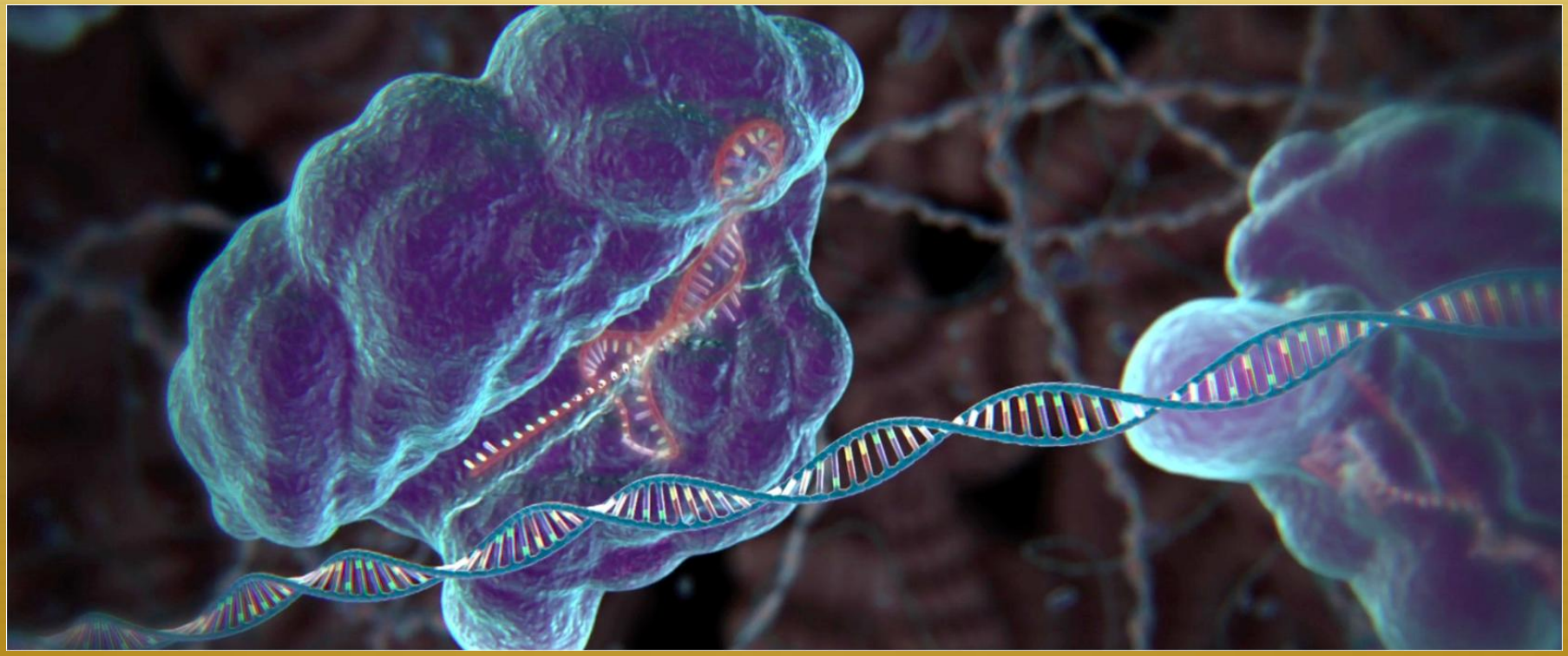
Faj Tedavisi?



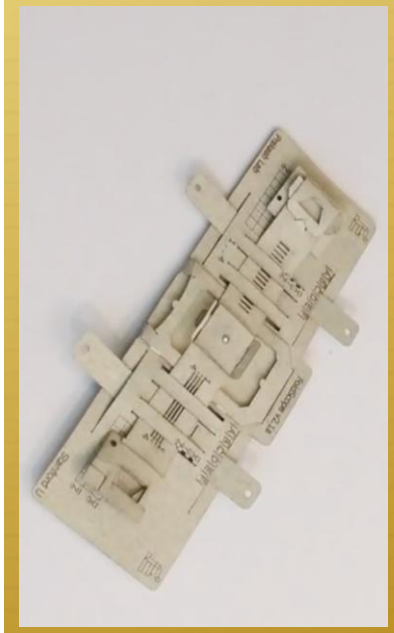
mikroRNA ile gen susturma?



Crispr / CAS Sistemi ile Gen Modifikasyonu?



Teşekkürler



Karikatürist
Eren Özdemir
8 Yaşında