

Antimikrobiyaller ve sinyal molekülleri

2

Antimikrobiyallerin altın çağı

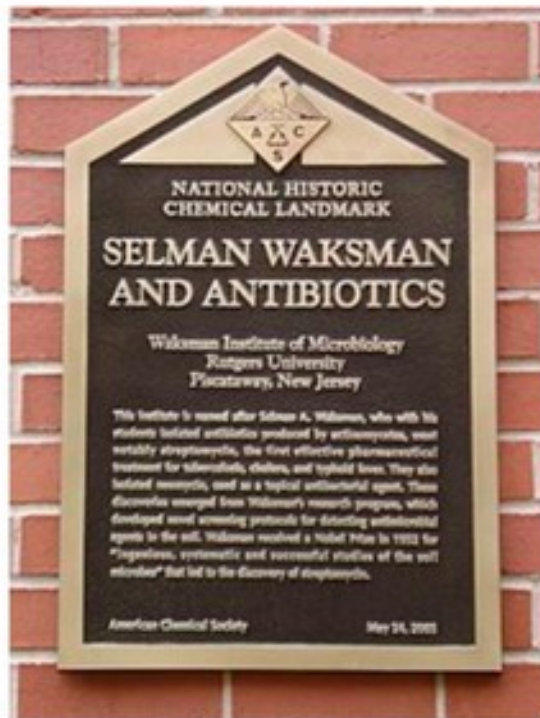
Sömürülen mucize

Antibiyotik "işi" eskisi kadar karlı değil...



aktinomisin
klavasin
streptomisin
grisein
neomisin
frasidin
kandisidin
kandinin

...

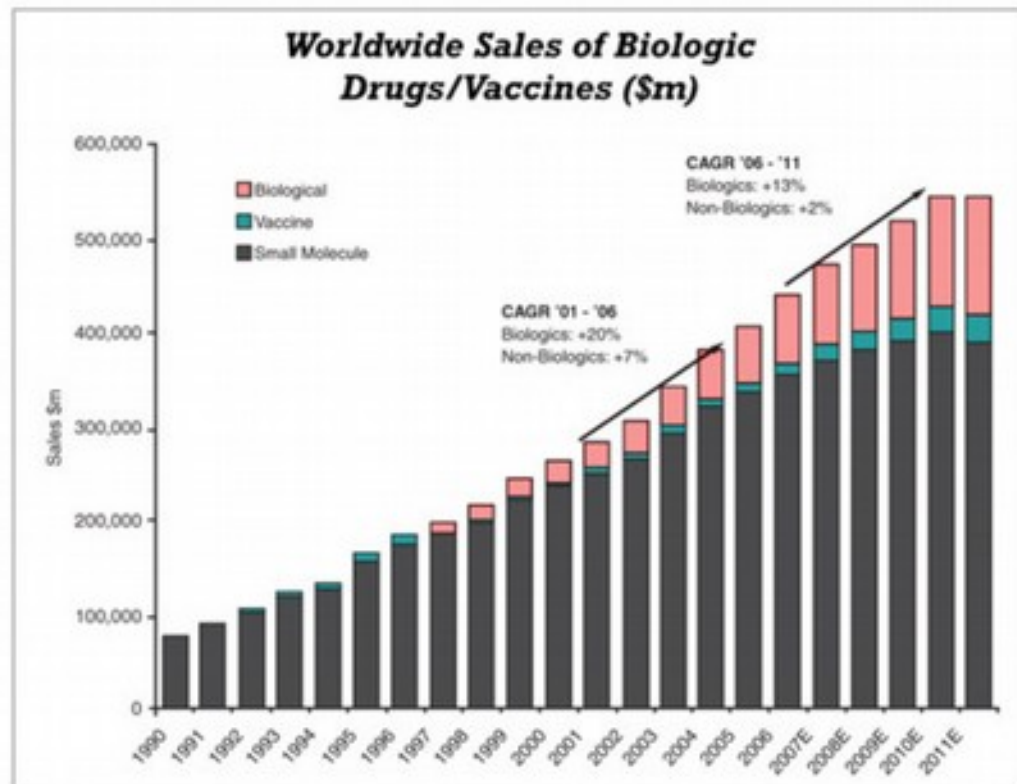


..



Üretilen antimikrobiyallerin çok büyük kısmı, tarım ve hayvancılık sektöründe tüketiliyor.
- beşeri ilaç olarak yasaklananlar dahil!

Allen, H.K., Stanton, T.B., 2014. Altered Egos: Antibiotic Effects on Food Animal Microbiomes. Annual Review of Microbiology 68, 297-315. doi:10.1146/annurev-micro-091213-113052
Hogging It!: Estimates of Antimicrobial Abuse in Livestock (2001) [WWW Document], n.d. . Union of Concerned Scientists. URL http://www.ucsusa.org/food_and_agriculture/our-failing-food-system/industrial-agriculture/hogging-it-estimates-of.html (accessed 11.6.16).

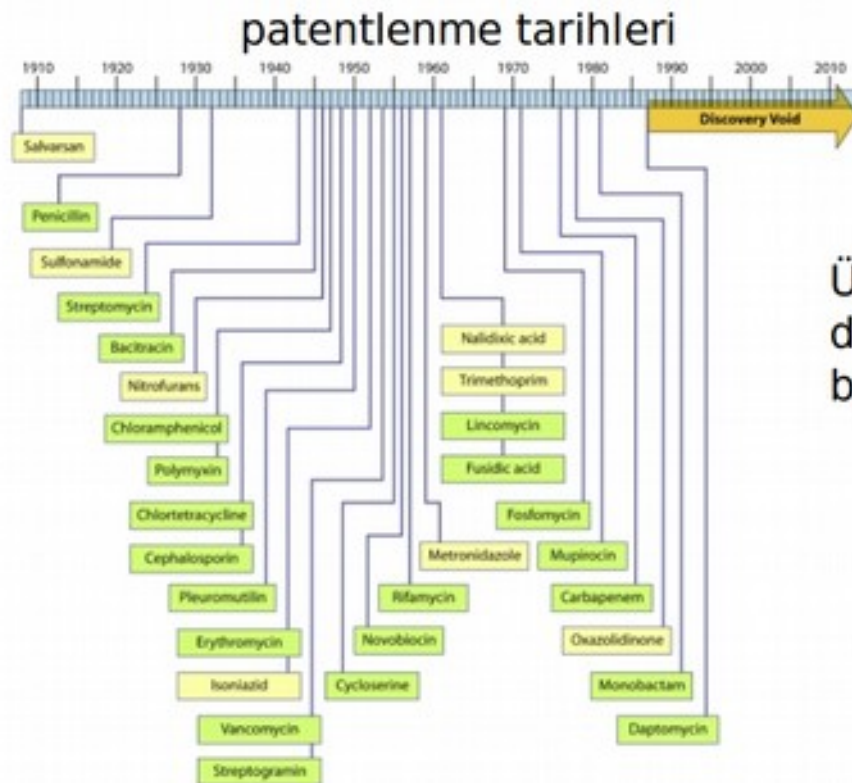


Source: Lehman Brothers PharmaPipelines estimates

Cikletten
ucuz
antibiyotikler...

http://www.bio-itworld.com/biologic_drugs/

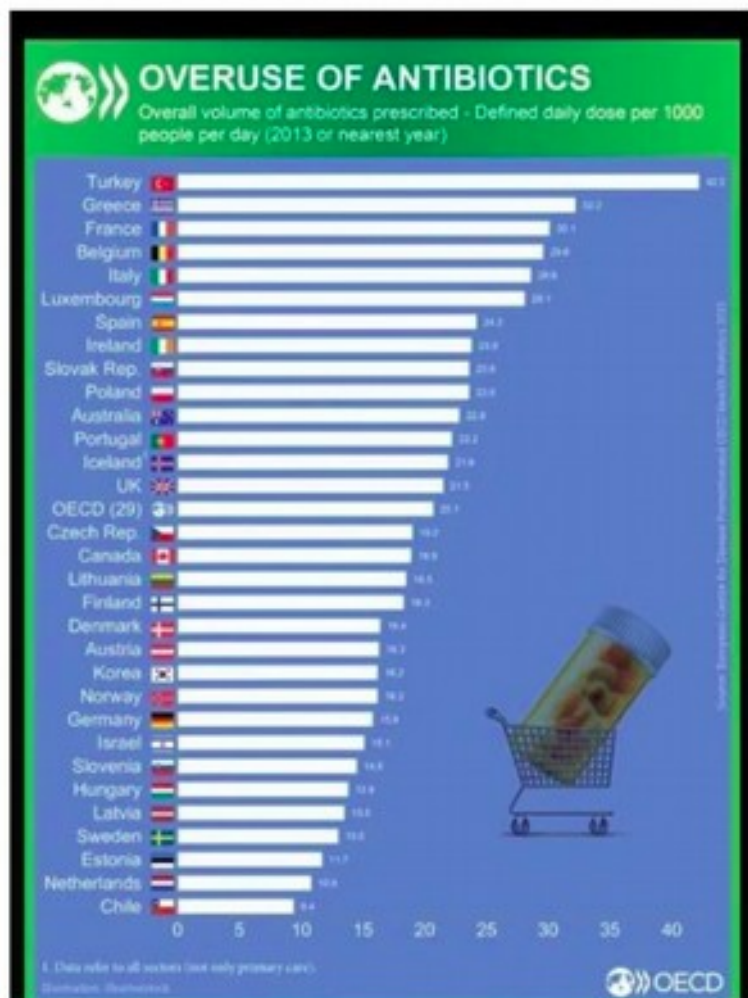
yeni sınıflar vs sınıf modifikasyonu



Büyük Farma

Üretkenlik olasılığı düşük olan doğal kaynaklardan yeni madde bulma olasılığına karşı...

...mevcut maddelerin hedefe yönelik olarak türevlendirilmesi: sentetik kimya!

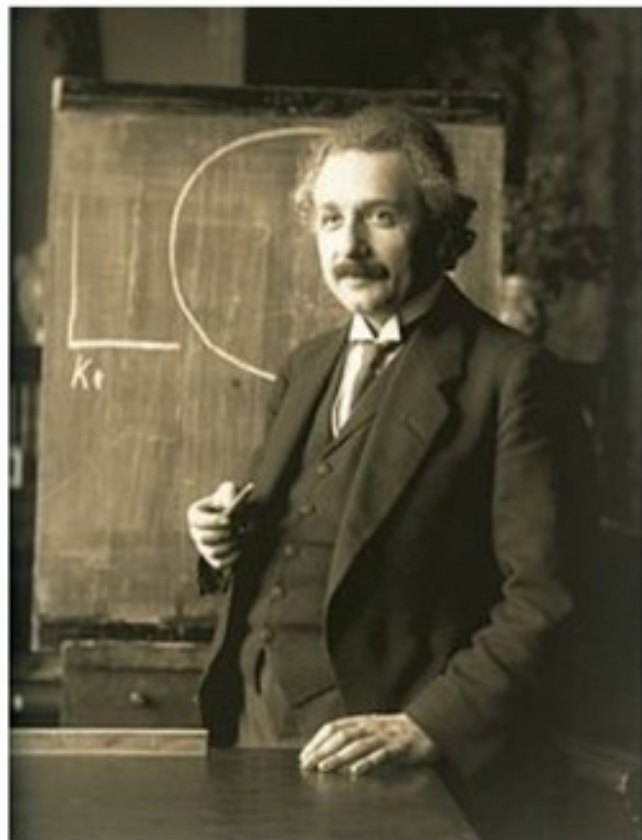


Sosyal
medyada
Türkiye :)

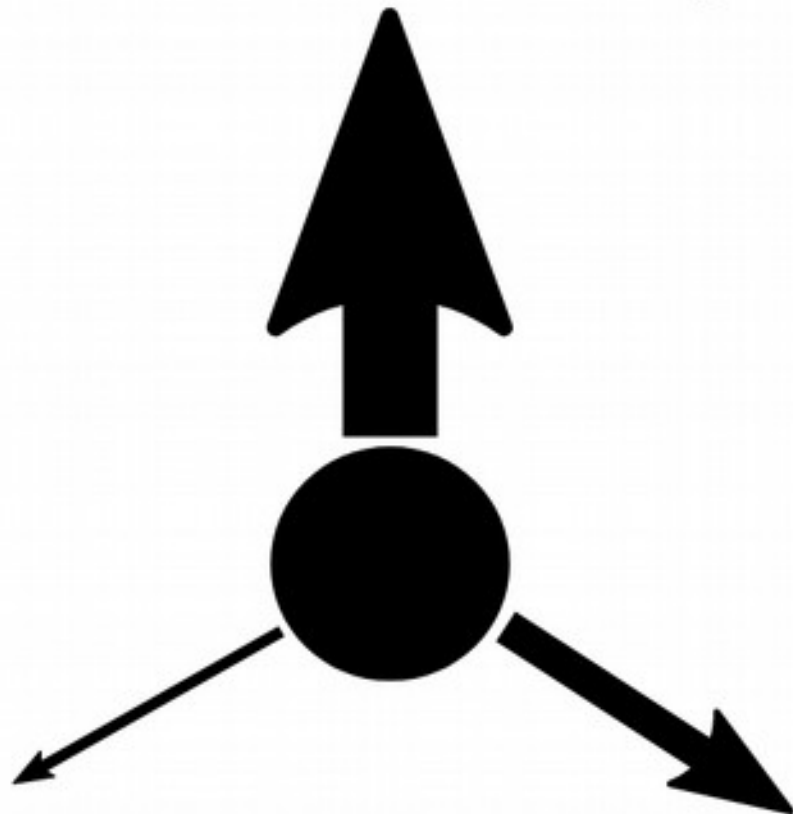
Antibiyotik sonrası çağ geliyor mu?

http://güncel_durum_için_tıklayınız.html

I know not with what weapons
World War III will be fought, but
World War IV will be fought with
sticks and stones.



sentetik kimya



doğal kaynaklar

sentetik biyoloji

Paulander, W., Maisnier-Patin, S. & Andersson, D. I. The fitness cost of Streptomycin resistance depends on rpsL mutation, carbon source and RpoS (σ^S). Genetics 183, 539–546 (2009)

Sm^R *Salmonella enterica* suşlarında rpsL K42N ya da P90S substitüsyonları artmış üreme hızına sahip!

*Aslında, σ^S (RpoS) aracılı stres yanıtı gerçekleşmeyen bu hücreler durağan faza GİREMİYOR
 \Rightarrow hayatta kalmak için bu yanıt önemli!

rpsL \leftrightarrow rpoS EPISTATİK ilişkisi

Yu, J., Wu, J., Francis, K. P., Purchio, T. F. & Kadurugamuwa, J. L.
Monitoring in vivo fitness of rifampicin-resistant *Staphylococcus aureus*
mutants in a mouse biofilm infection model. *J. Antimicrob.*
Chemother. 55, 528–534 (2005)

rpoB mutasyonları \rightarrow Rif^R *S. aureus* hücreleri

Çoğu mutant fare biyofilm modellerinde azalmış "fitness" a sahip

Foucalt, M. L., Courvalin, P. & Grillot-Courvalin, C. Fitness cost of VanA-type vancomycin resistance in methicillin-resistant *Staphylococcus aureus*. *Antimicrob. Agents Chemother.* 53, 2354–2359 (2009)

MRSA'lar da van A induksiyonu \rightarrow üreme hızında %
20-38 azalma

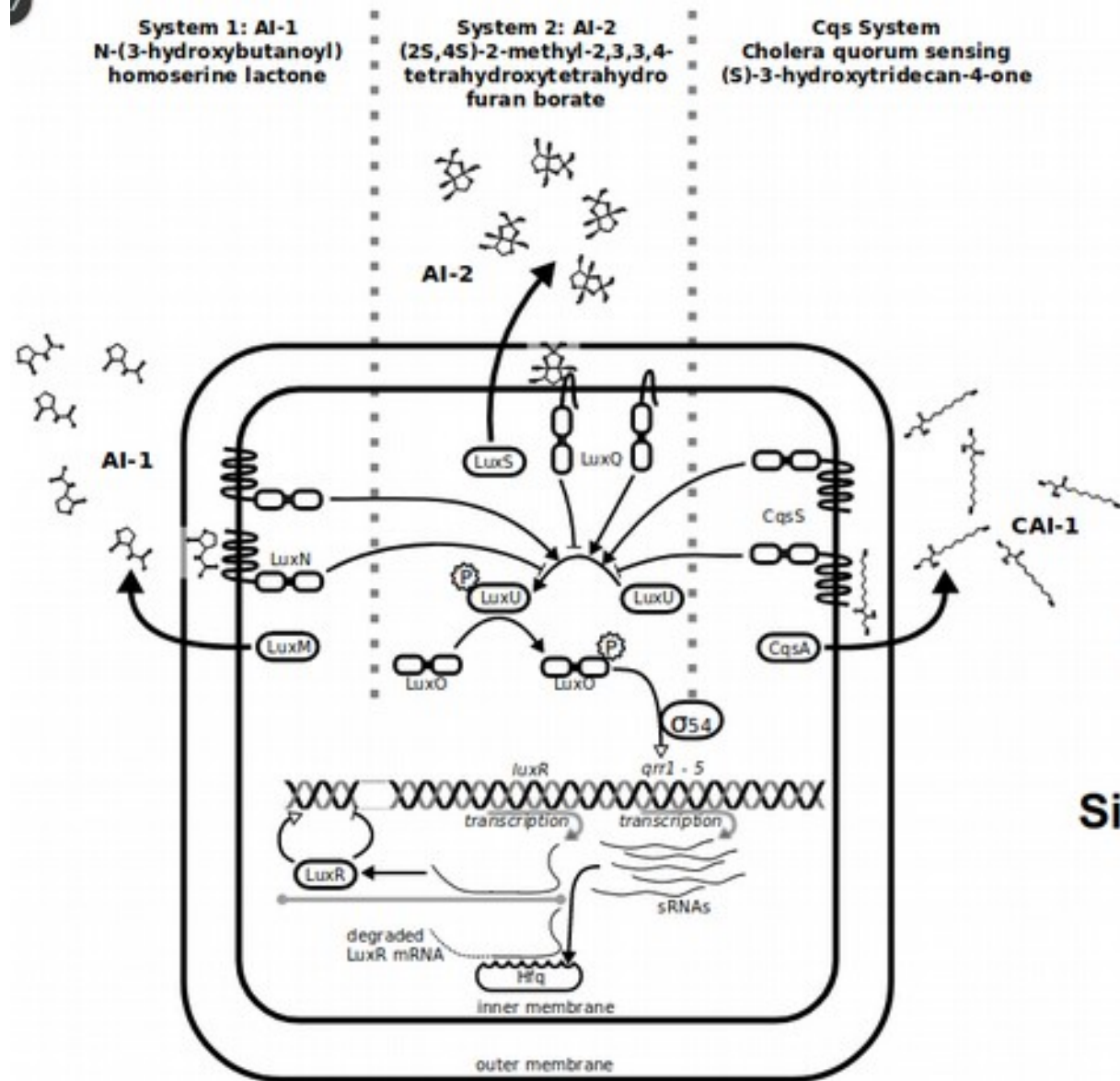
(vanA induksiyonu olmayan durumlarda yalnızca % 0.04-0.3
düzeyinde)

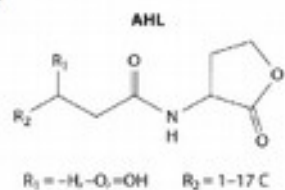
Macvanin, M., Johanson, U., Ehrenberg, M. & Hughes, D. Fusidic acid-resistant EF-G perturbs the accumulation of ppGpp. Mol. Microbiol. 37, 98–107 (2000)

Elongasyon faktörü G'yi kodlayan *fusA* mutasyonları →
Fus^R S. enterica

ppGpp düzeyleri etkilenmekte

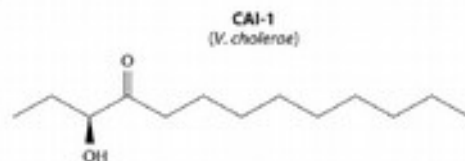
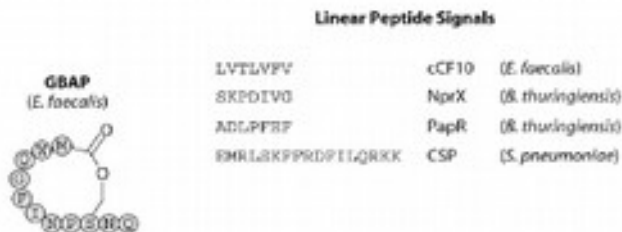
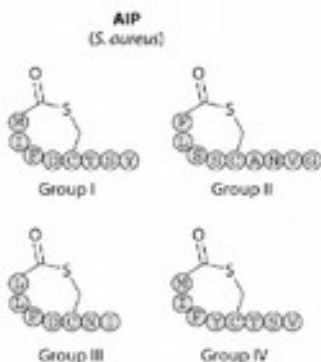
Bu PLEİTROPİK etki nedeni ile, bakteri farklı ortamlara uyum sağlamakta güçlük çekmekte!



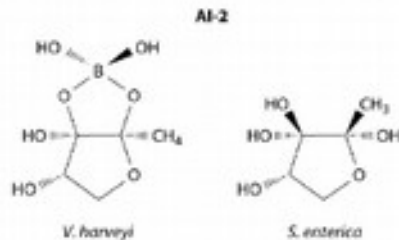
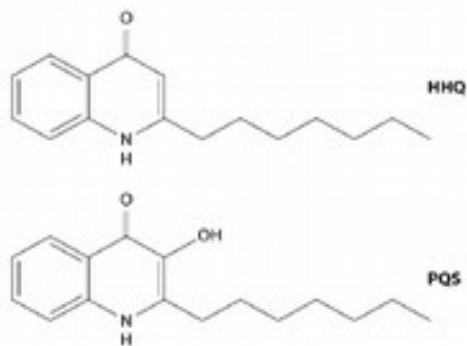


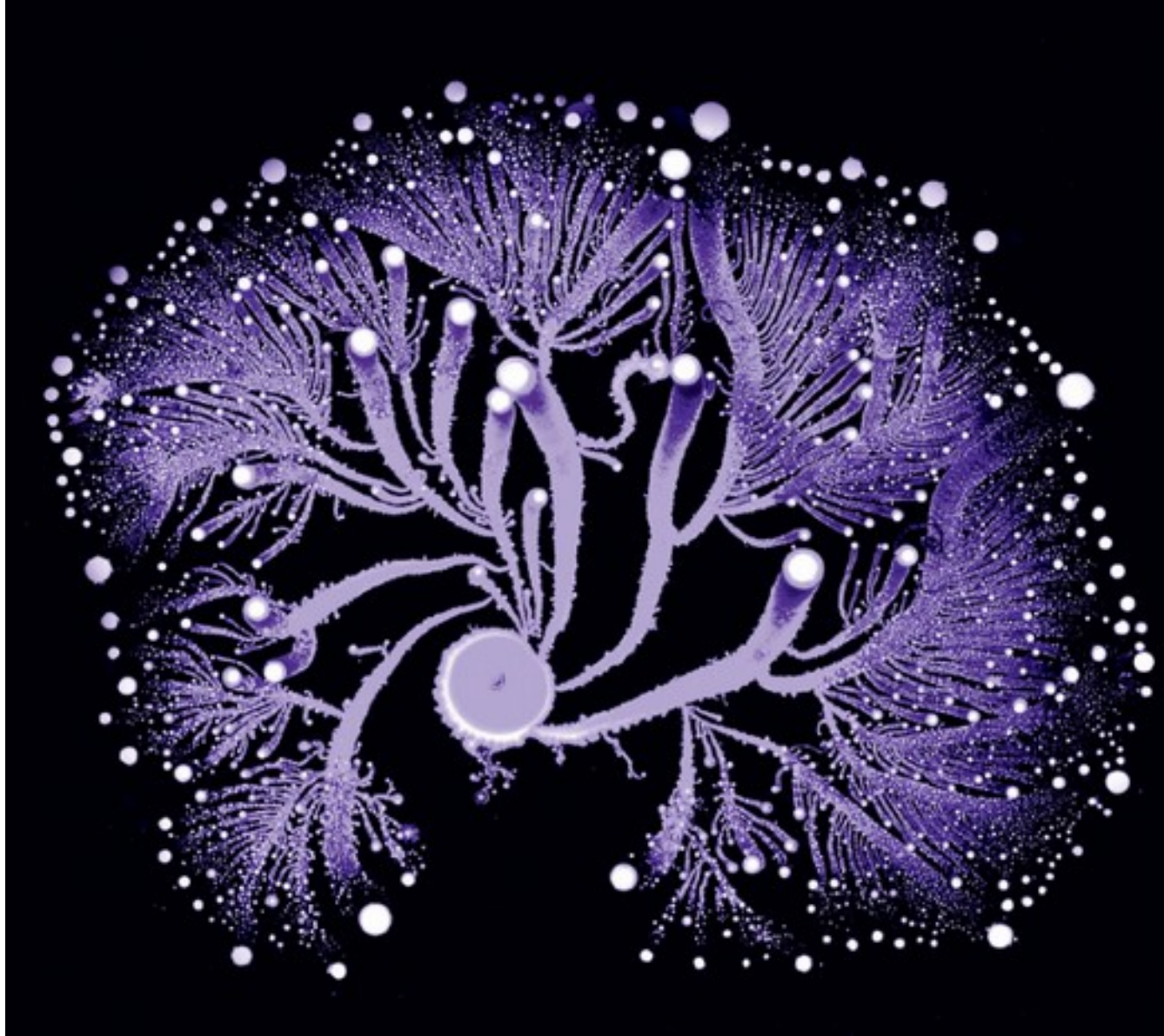
Classes of autoinducers

(not an exhaustive list)



2-alkyl-4-quinolone Family (*P. aeruginosa*)





1. Sirota-Madi A, Olender T, Helman Y, Ingham C, Brainis I, Roth D, et al. Genome sequence of the pattern forming *Paenibacillus vortex* bacterium reveals potential for thriving in complex environments. BMC Genomics. 2010 Dec 17;11(1):710.

Social IQ

