Antifriz Protein: Anti-bakteriyel, Anti-biyofilm ve Antibiyotik sinerjizmi

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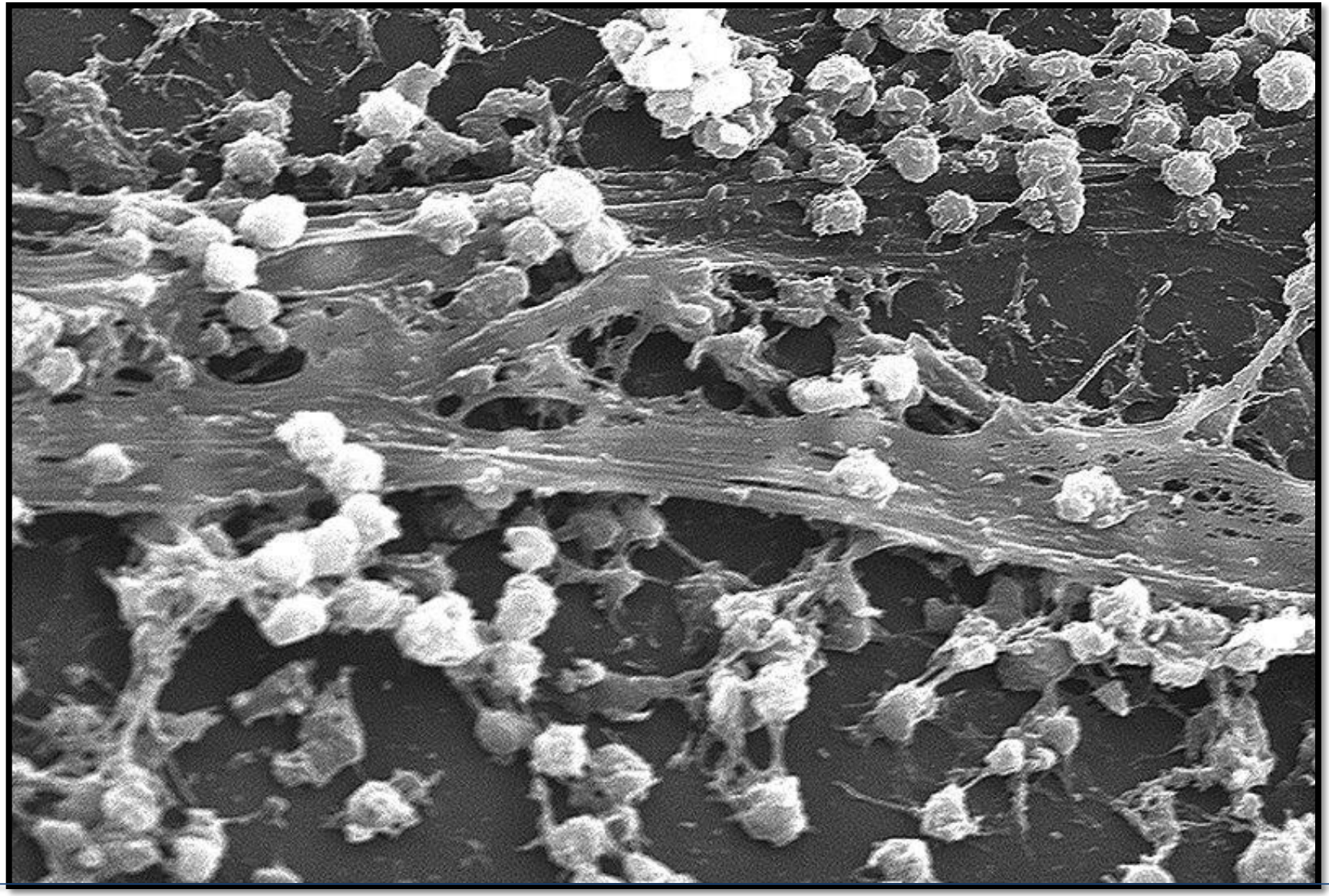
Biyofilm



J Clin Invest. 2010 Sep;120(9):3179-90. doi: 10.1172/JCI42868. Epub 2010 Aug 25.

Anaplasma phagocytophilum induces Ixodes scapularis ticks to express an antifreeze glycoprotein gene that enhances their survival in the cold.

Neelakanta G[1], Sultana H, Fish D, Anderson JF, Fikrig E.

Author information

Abstract

In the United States, Ixodes scapularis ticks overwinter in the Northeast and Upper Midwest and transmit the agent of human granulocytic anaplasmosis, Anaplasma phagocytophilum, among other pathogens. We now show that the presence of A. phagocytophilum in I. scapularis ticks increases their ability to survive in the cold. We identified an I. scapularis antifreeze glycoprotein, designated IAFGP, and demonstrated via RNAi knockdown studies the importance of IAFGP for the survival of I. scapularis ticks in a cold environment. Transfection studies also show that IAFGP increased the viability of yeast cells subjected to cold temperature. Remarkably, A. phagocytophilum induced the expression of iafgp, thereby increasing the cold tolerance and survival of I. scapularis. These data define a molecular basis for symbiosis between a human pathogenic bacterium and its arthropod vector and delineate what we believe to be a new pathway that may be targeted to alter the life cycle of this microbe and its invertebrate host.

Ixodes scapularis antifriz protein (IAFGP) ve sentetik peptit (P1)

IAFGP sekansı*

```
1   MTTLLRLTILIVAVAGVLG^SSKRAAR
27            AATPATAATPATPATAAT
45  PAI       AATPATAATPATAAT
63  PARKAR AATPATPATPATAATPATAAT
90  PARKAR AATAATPATPATAAT
111 PARKAR AATPATPATAATPATAAT
135 PARKAR AATPATPATAATPATAAT
159 PARKAR AATPATPATAATPATAAT
183 PARKAR AATPATPATAATAAT
204 PARKAR AATAATPATPATAAT
225 PARKAR AATPATAATAATPATAATAAA
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Peptit sekansı

P1:PARKARAATAATAATAATAATAAT

sP1: AAAAATATAAARRAAAAPTTAKT

(scrambled P1 peptide)

- Alanine-Alanine-Threonine (AAT) / Proline-Alanine-Threonine (PAT)
- Her bir Thr'ne β-D-galactosyl-(1→3)-α-N-acetyl-D-galactosamine
- 4 triplet fonksiyon için yeterli

**GirishNeelakanta, HameedaSulatana, Durland Fish, John F.Anderson, Erol Fikrig. Journal of Clinical Investigation. 2010*

Ixodes scapularis antifriz protein (IAFGP)

- **Amaç:**
  - Kateterle ilişkili enfeksiyonların önlenmesinde IAFGP etkinliği
  - İnsan ökaryotik hücrelerine toksik olup olmadığının araştırılması
  - Çeşitli antibiyotiklerle sinerjizmin test edilmesi

Protein moonlighting: The anti-virulance function of an anti-freeze protein

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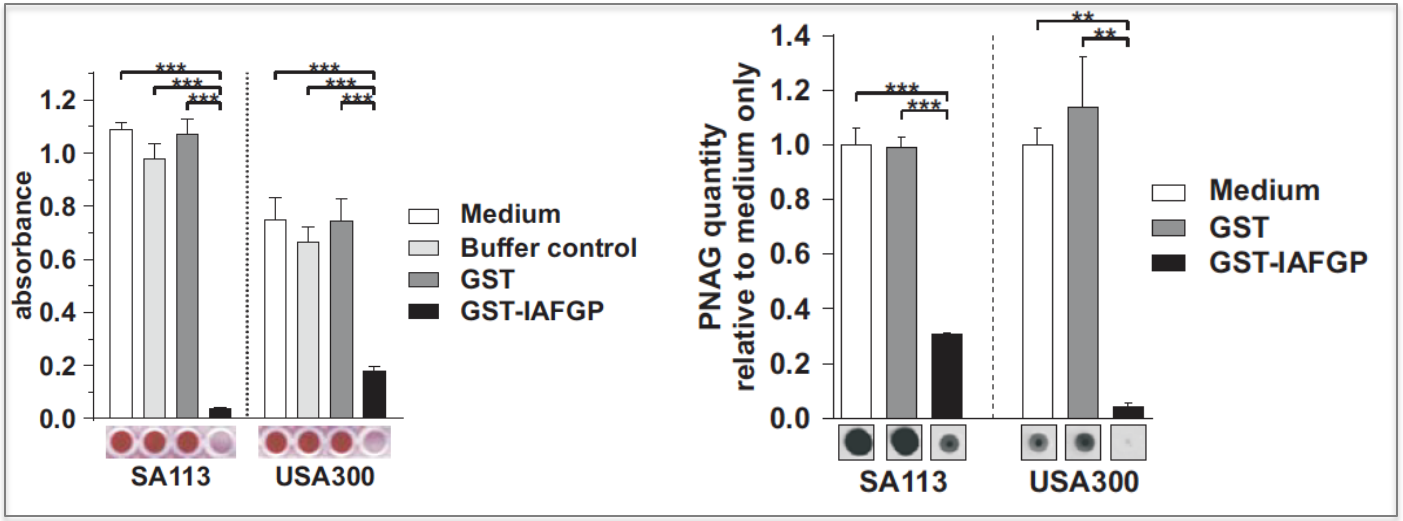
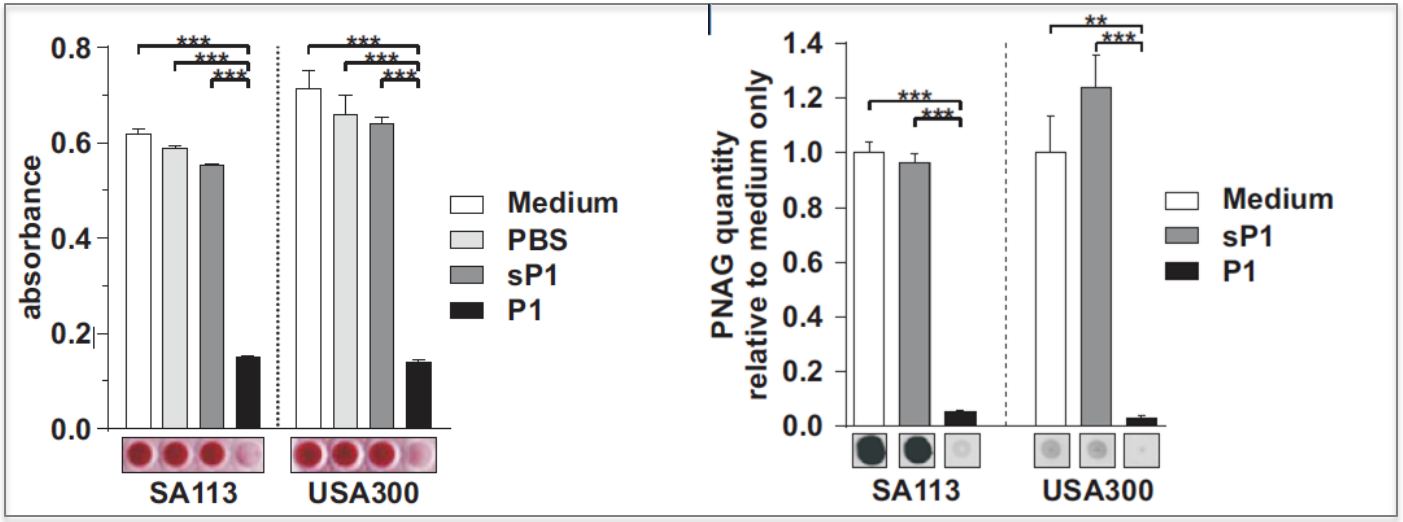
October 3th, 2014

IAFGP anti-biyofilm aktivite

IAFGP



P1



Martin Heisig , Nabil M. Abraham, Lei Liu, GirishNeelakanta , Sarah Mattessich, Hameeda Sultana, Zhengling Shang, Juliana Mastronunzio, Charlotte Killiam, Wendy Walker, Lynn Cooley, Richard A. Flavell, HerveAgaisse, and Erol Fikrig. Cell Reports 2014 in press.

IAFGP/P1
Fare Kateter İmplant Modeli

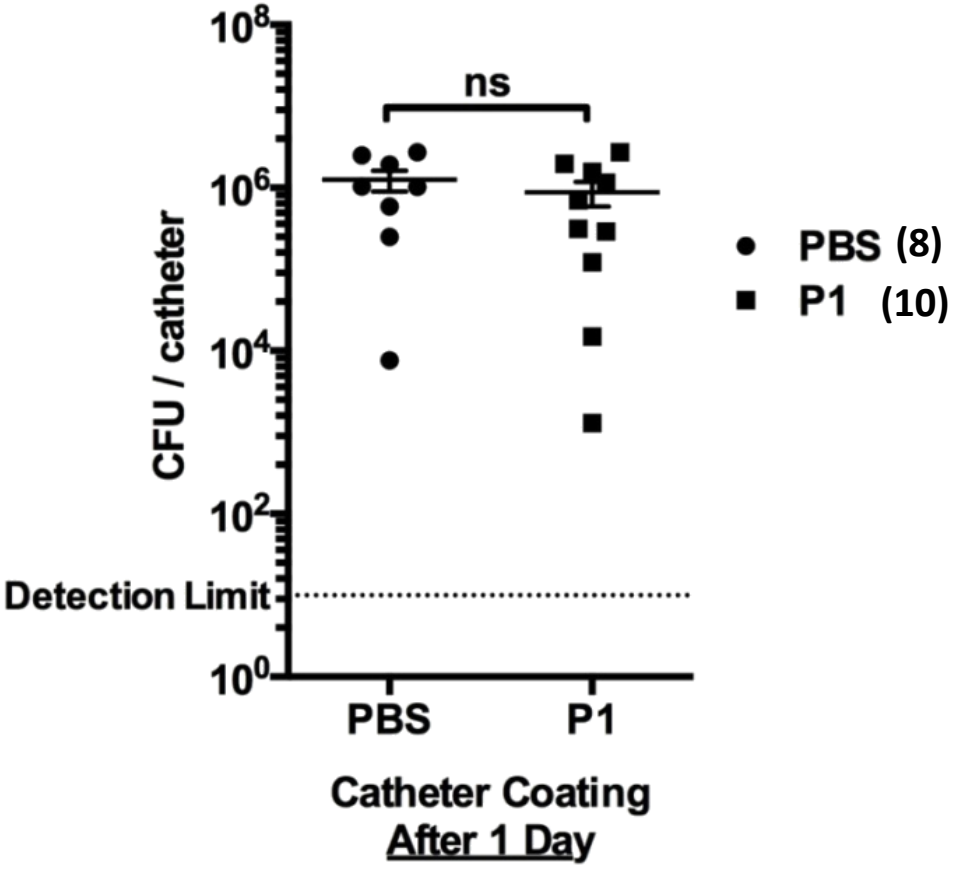
Amaç:

- Kateterle ilişkili enfeksiyonun önlenmesi

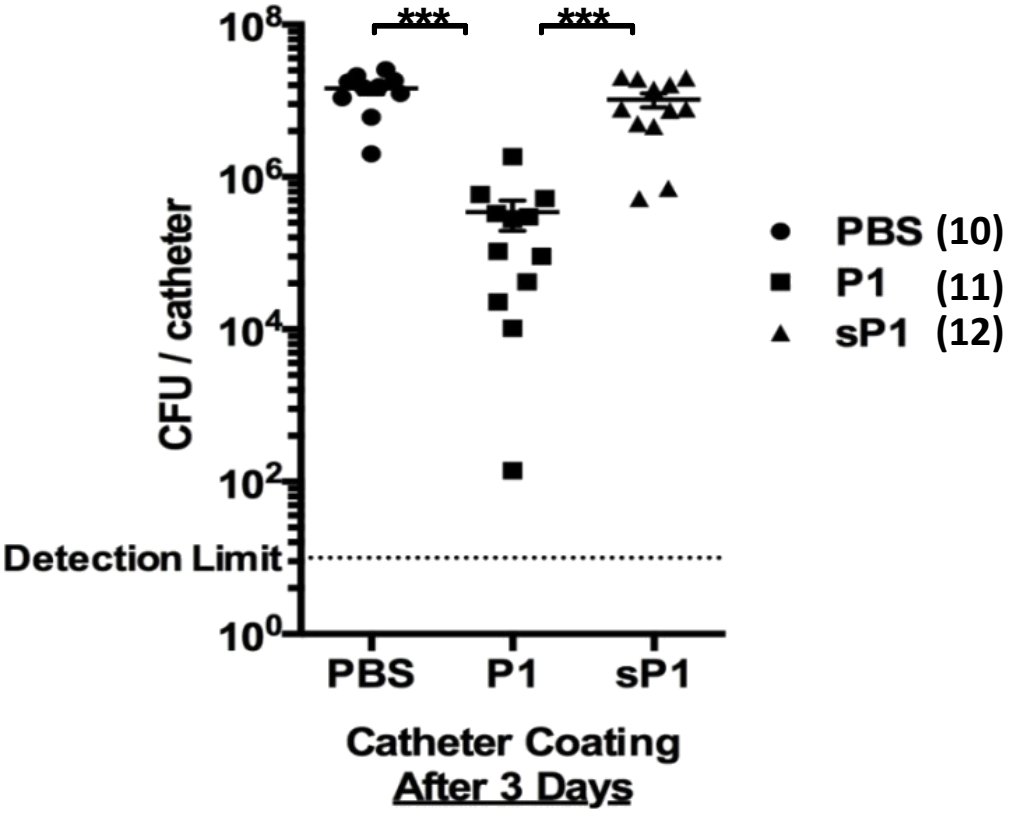
Yöntem:

- **Hayvan deney protokolü**
- **IFGP/P1, kontrol peptid ve PBS kaplı katater fare sırt bölgesine deri altına implante edildi.**
- **Kateter lümenine *S. aureus* enjekte edildi. 1, 3, 7. günlerde kateter çıkarılarak PBS içinde sonikasyon sonrası, seri dilüsyonlarda plak ekimi yapılarak bakteriyal CFU saptandı.**

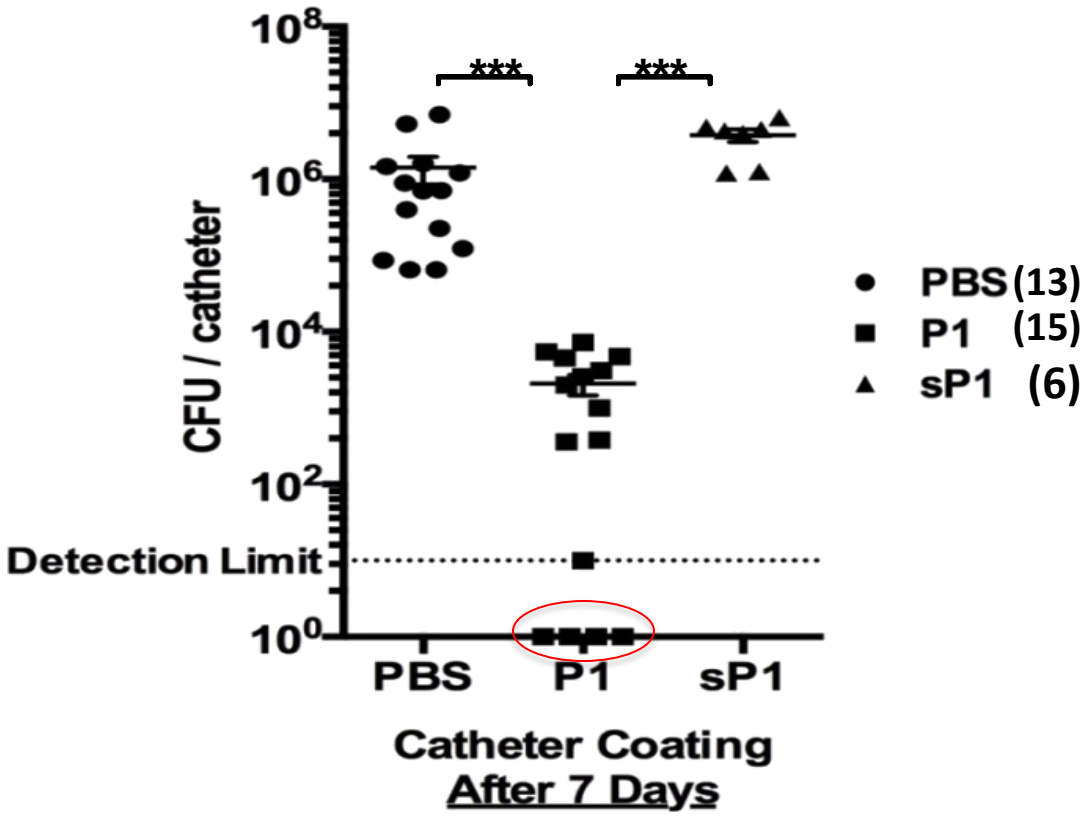
IAFGP/P1
Fare Kateter İmplant Modeli



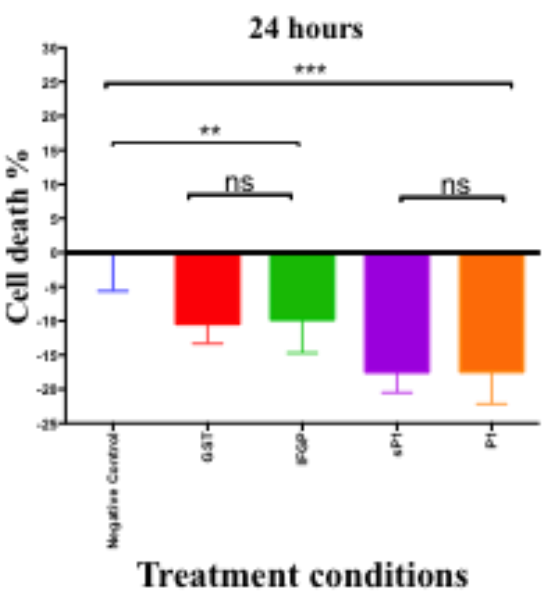
IAFGP/P1
Fare Kateter İmplant Modeli

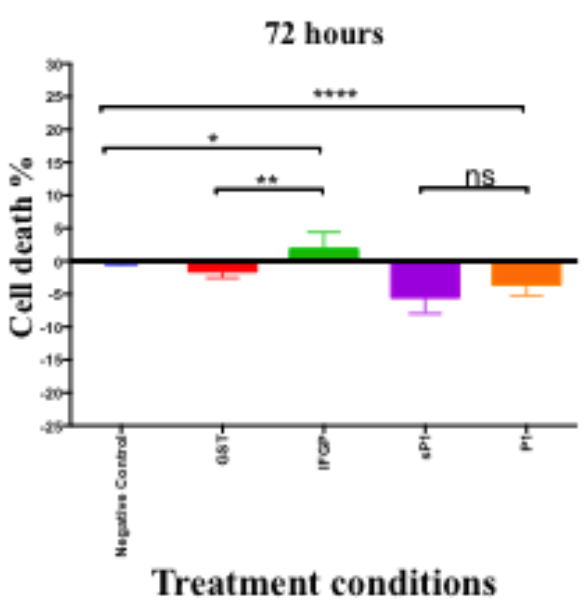


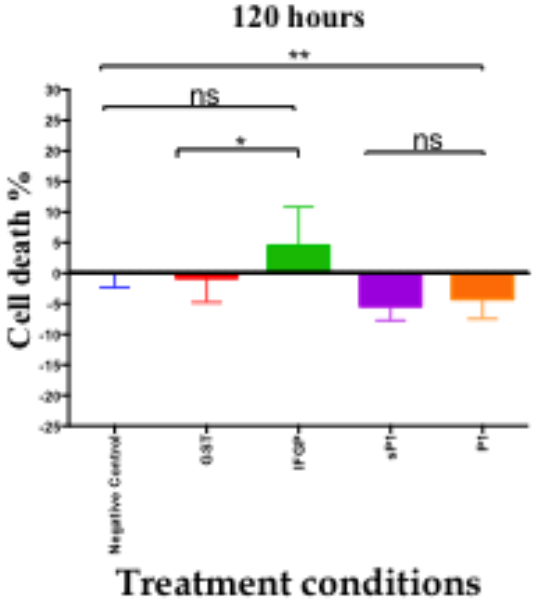
IAFGP/P1
Fare Kateter İmplant Modeli



IAFG ökaryotik hücre canlılığı üzerine etkisi



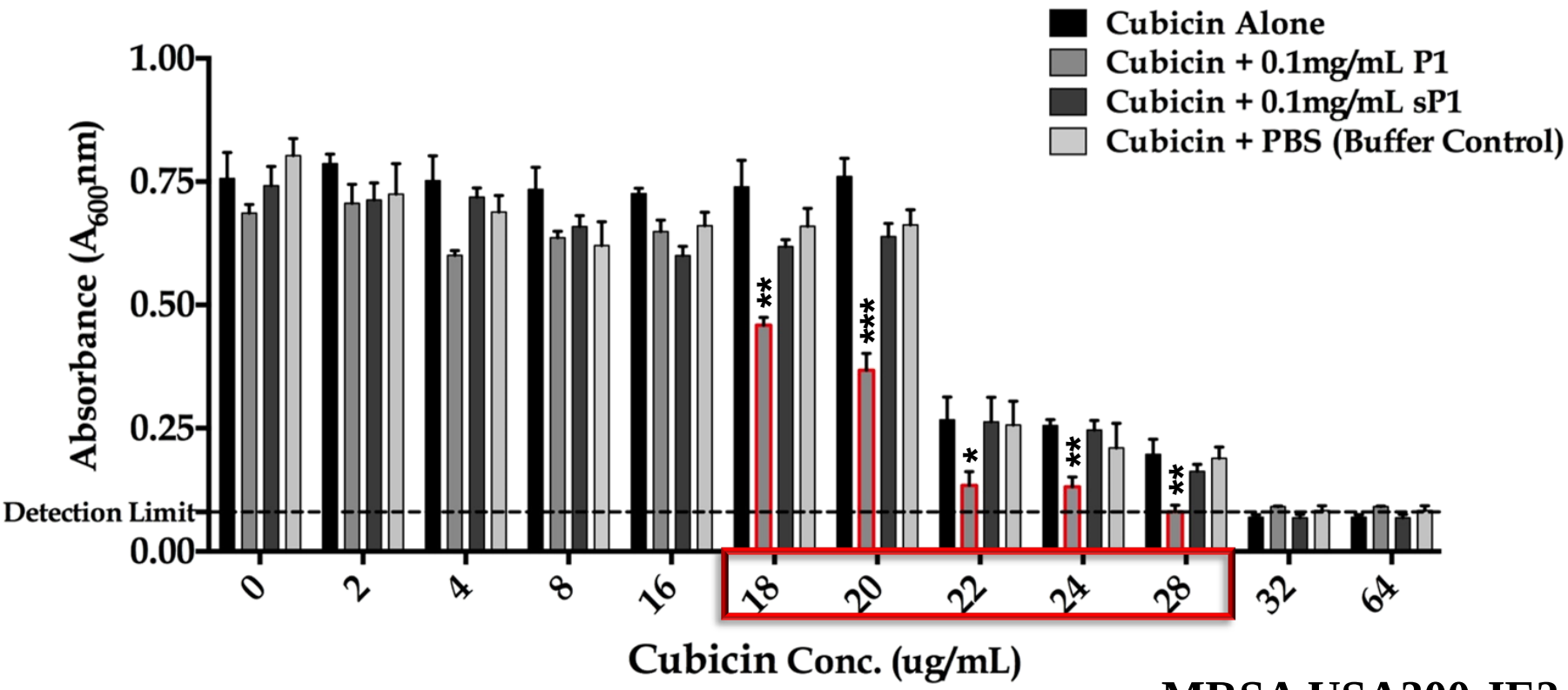




Sinerjistik aktivite

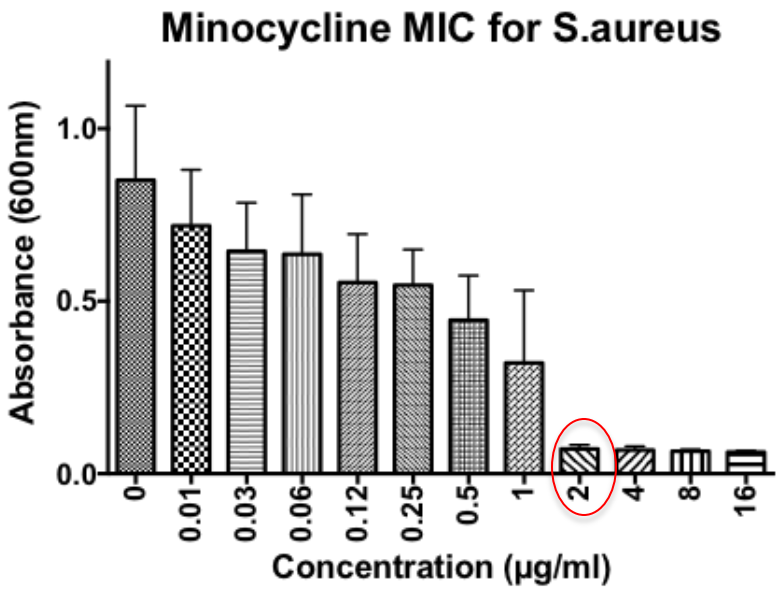
	Antibiyotik	Etki mekanizması	Sinerjizm
1	Gentamicin	*Aminoglycoside bakterisidal antibiyotik* Bakeriyal ribozom 30s alt birimine bağlanarak prt. sentez inhibitörü	✔
2	Ampicillin	*β-Lactam bakterisidal antibiyotik* Geridönüşümsüz transpeptidaz inhibitörü	✖
3	Penicillin G	*β-Lactam bakterisidal antibiyotik* Geridönüşümsüz transpeptidaz inhibitörü	✖
4	Oxacillin	*β-Lactam bakterisidal antibiyotik* Geridönüşümsüz transpeptidaz inhibitörü	✖
5	Ciprofloxacin	*2. Kuşak Fluoroquinolone bakterisidal antibiyotik* DNA gyrase, type II ve IV topoisomerase inhibisyonu	✔
6	Vancomycin	*Glycopeptide bakterisidal antibiyotik* Peptidoglycancrosslinking inhibisyonu; terminal D-Ala:D-Ala bağlanır	✖
7	Linezolid	*Sentetik oxazolidone sınıfı, bakteriyostatik antibiyotik* Protein sentez inhibisyonu; protein sentez başlangıç aşamasını inhibe eder	✖
8	**Daptomycin**	***Lipopeptide bakterisidal antibiyotik*** **Bakteriyal hücre memran fonsiyonunu bozar; membran depolarizasyonu**	✔
9	**Minocycline**	**Semi sentetik Tetracycline, bakteriyostatik antibiyotik** **Ribozom 30s; Protein sentezi inhibisyonu**	✔

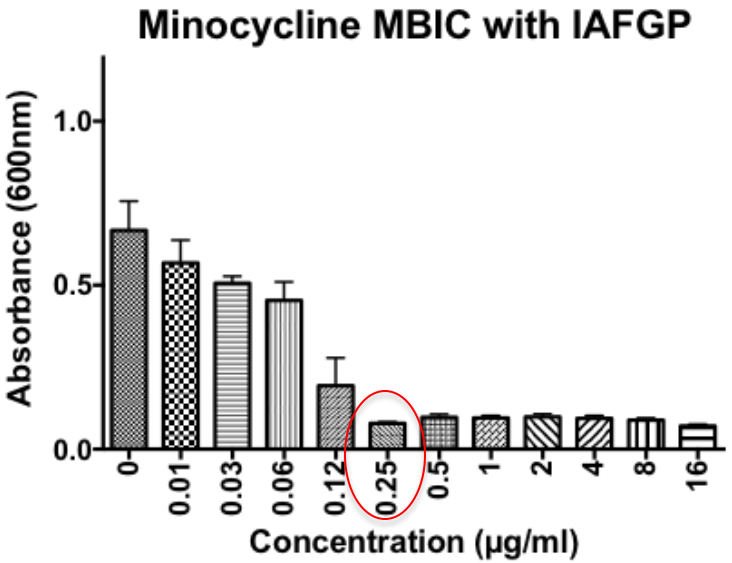
Daptomycin

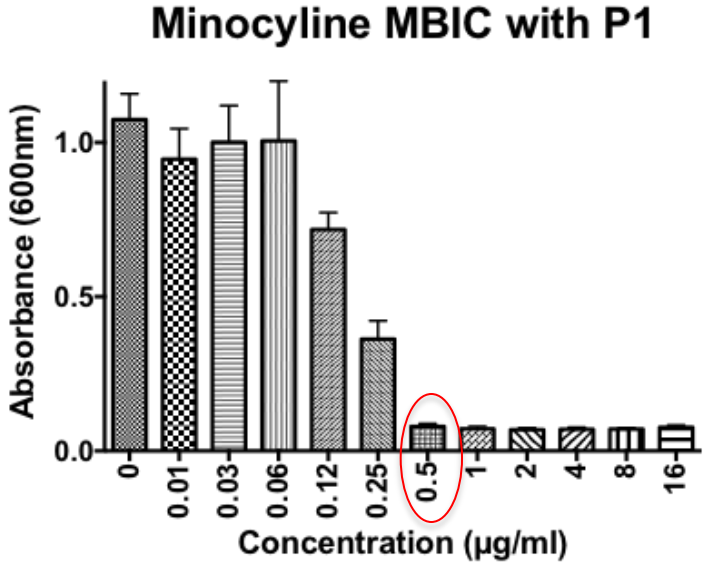


MRSA USA300 JE2

Minocycline







Sonuç

- ***Ixodesscapularis*** **antifriz protein (IAFGP) MRSA ve MSSA karşı anti-virulans etkinlikte bir ajandır**
- **IAFGP ve P1 biyofilm formasyonunu bozar**
- **Kataterde biyofilm formasyonunda ve bakteri adheransında azalmaya yol açar**
- **IAFGP ve P1 *S. aureus* karşı Gentamicin, Ciprofloxacin, Daptomycin ve Minocycline ile sinerjik aktivite gösterir**
- **Toksik değildir**
- **Kateterle ilişkili enfeksiyonların tedavisinde yeni bir seçenektir**