3rd Meeting of the International Consensus Meeting
8-10 of May, 2025 Istanbul

Is there a role for the use of proteolytic enzymes to treat orthopedic infections?

Débora Coraça-Huber, Nicholas J. Norton, Bingyun Li, Elena De Vecchi, Guillermo Bonilla, Holger Rohde and Kordo Saeed

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Débora Coraça-Huber, Austria

Nicholas Norton, UK

Bingyun Li,, USA

Elena De Vecchi, Italy

Guillermo Bonilla, Colombia

Holger Rohde, Germany

Kordo Saeed, UK

Why is this topic important?

1) **Challeneges to treat biofilm infections**
2) **Inability of the host immune systems to effectively clear them**
3) **Phenotypic antibiotic resistance.**
4) **…**

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CONSENSUS STATEMENT ARTICLE | Free Access

2018 international consensus meeting on musculoskeletal infection: Summary from the biofilm workgroup and consensus on biofilm related musculoskeletal infections

Kordo Saeed, Alex C. McLaren, Edward M. Schwarz, Valentin Antoci, William V. Arnold, Antonia F. Chen, Martin Clauss, Jaime Esteban, Vanya Gant, Edward Hendershot, Noreen Hickok ... See all authors

First published: 22 January 2019 | https://doi.org/10.1002/jor.24229

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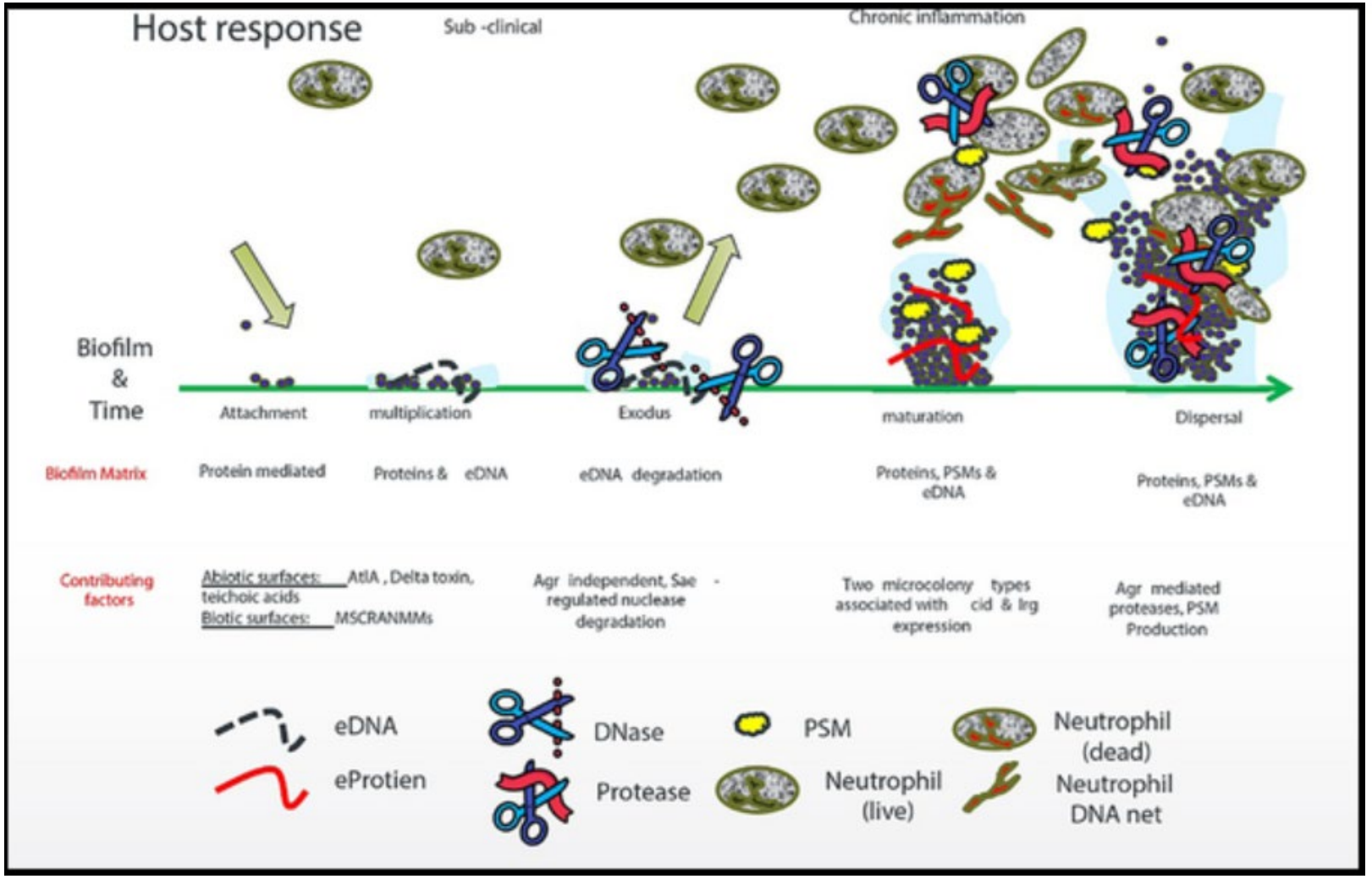
CONSENSUS | Free Access

Bacterial toxins in musculoskeletal infections

Kordo Saeed, Parham Sendi, William V. Arnold, Thomas W. Bauer, Débora C. Coraça-Huber, Antonia F. Chen, Hyonmin Choe, John L. Daiss, Michelle Ghert, Noreen J. Hickok, Kohei Nishitani, Bryan D. Springer, Paul Stoodley, Thomas P. Sculco, Barry D. Brause, Javad Parvizi, Alex C. McLaren, Edward M. Schwarz

First published: 07 April 2020 | https://doi.org/10.1002/jor.24683

Paradigm of establishment of Staphylococcus aureus Peri – prosthetic joint infection



Saeed K, et al. J Orthop Res. 2021 Feb;39(2):240-250. doi: 10.1002/jor.24683. Epub 2020 Apr 14. PMID: 32255540; PMCID: PMC7541548.

To address this

Databases Searched: PubMed, Medline & Embase

Search Results yielded 694 publications

Two of the coauthors went through title and abstract and scored inclusion or exclusion, discrepant results were adjudicated by a third person.

Thirty-one articles were reviewed,

Of which 26 articles was finally deemed to be suitable,

Caspases : proteases playing a crucial role in apoptosis and inflammation. The executioners of cell death

Urokinase

Dispersin B, an enzyme active against PNAG, and DNase I are able to inhibit biofilm formation, detach preformed biofilms and sensitize bacteria to be killed by other antimicrobials

Dispersin B followed by a protease (proteinase K or trypsin)

Serratiopeptidase (SPEP), a proteolytic enzyme produced by the enterobacteria Serratia E15

Phage derived enzymes e.g. LysECD, XZ.700, ply2638, lysostaphin, M23LST(L)_SH3b2638A(M23) and CHAPGH15_SH3bALE1 (GH15), as well as the DA7 polysaccharide depolymerase etc

Major Limitations:

Heterogenous data

Pre-clinical studies

Concern about release of planktonic bacterial → BSI and other seeding infections

Most studies are on Staphylococcal biofilms

Effect varies between the clinical isolates tested

Question:

- Is there a role for the use of proteolytic enzymes to treat orthopedic infections?

❖Response:

No. While enzymatic therapies have demonstrated effects against implant related biofilms in pre-clinical models, their safety and efficacy needs to be demonstrated in the clinical scenario. Thus, clinical trials are necessary to clarify the translational potential of proteolytic enzymes to treat orthopedic infections

Level of Evidence: Weak

❖**Vote:**

Agree	**n=39; 87%**
Disagree	**0**
Abstain	**n=6; 13%**