



Stony Brook
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The Use of Bioactive Proteins and Peptides to Promote Osseointegration and Success of Dental Implants: A Systematic Review

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Introduction:

- Failure of osseointegration and peri-implantitis are common causes of implant failure (Kochar et al., 2022).
- Literature has proposed ways to mitigate these processes.
- The use of biological proteins and peptides have shown promising results.
- Benefits of proteins and peptides include biocompatibility, ease of synthesis, high antibacterial activity, and bone forming properties (Jurczak et al., 2020).

Objective:

- Summarization of the major biological proteins and peptides to promote the success of dental implants.

Methods:

- Keyword searches into google scholar, pubmed, and MEDLINE (2012-2021) *implant, osseointegration, peri-implantitis, proteins and peptides, extracellular matrix, growth factors, antimicrobial peptides*.
- 4,906 results, records were screened according to PRISMA 2020 flow chart.
- Inclusion criteria: studies that tested the effects of biological proteins/peptides on interactions between host cells and medical implant surfaces/materials *in vitro* and *in vivo*.

Results

- 105 studies to be reviewed.
- Four categories:
 - 1) Extracellular matrix components
 - 2) Growth Factors
 - 3) Antimicrobial Peptides
 - 4) Miscellaneous

Mechanisms for using proteins/peptides in implantology:

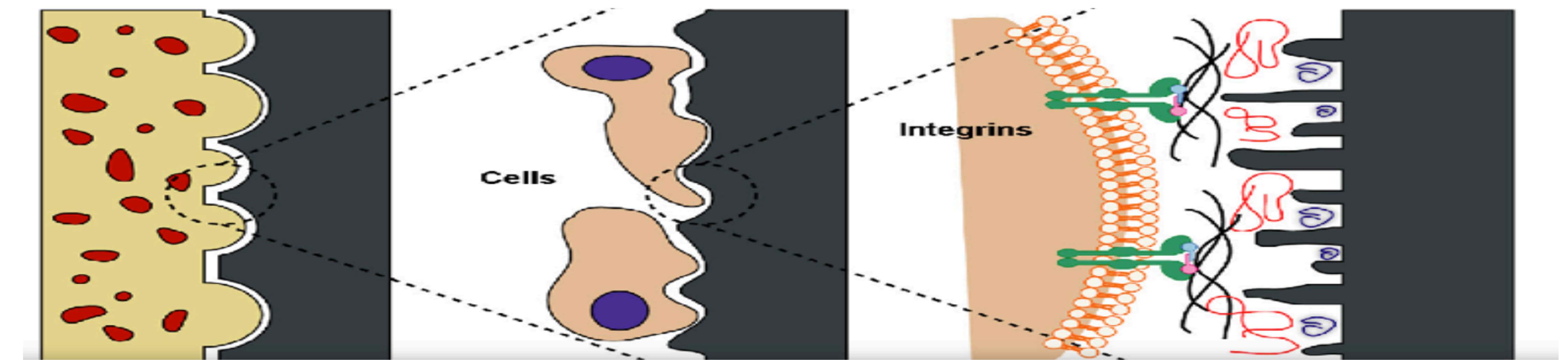
1. Coatings
2. Release systems
3. Local injections
4. Systemic administration

Extracellular Matrix Components

- Molecules of this class are collagen, fibronectin, elastin, laminins, and SIBLING proteins.
- Mechanism involves interaction with integrins (Geißler et al., 2000).
- Peptides derived from larger proteins are beneficial due to their higher specificity and lower immunogenicity (Reyes et al., 2007; Gomar et al., 2007).

Growth Factors

- Biologic molecules secreted to affect cellular growth (Stone et al., 2022).
- Roles in the body include regulation of inflammation, angiogenesis, and growth.



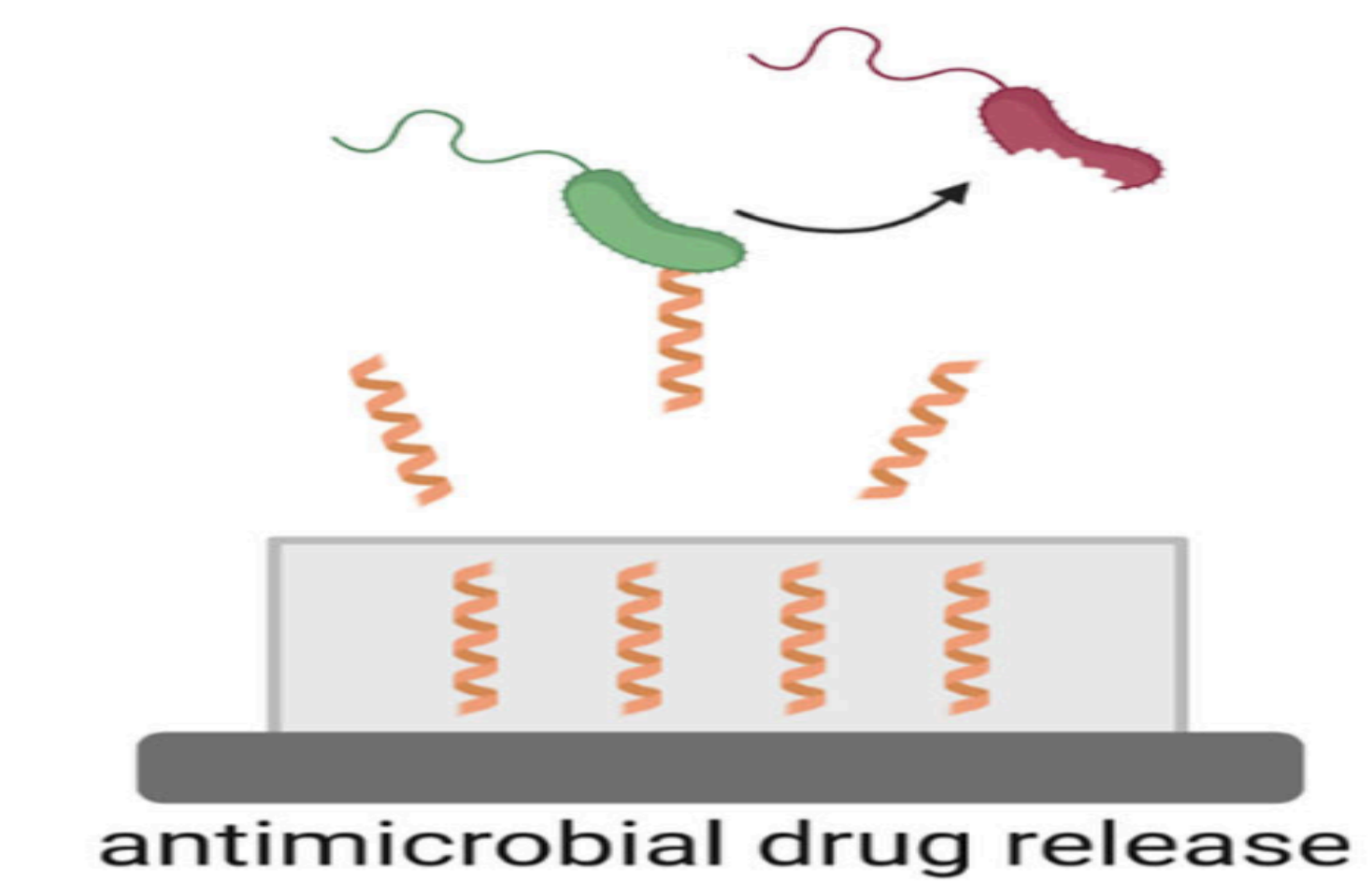
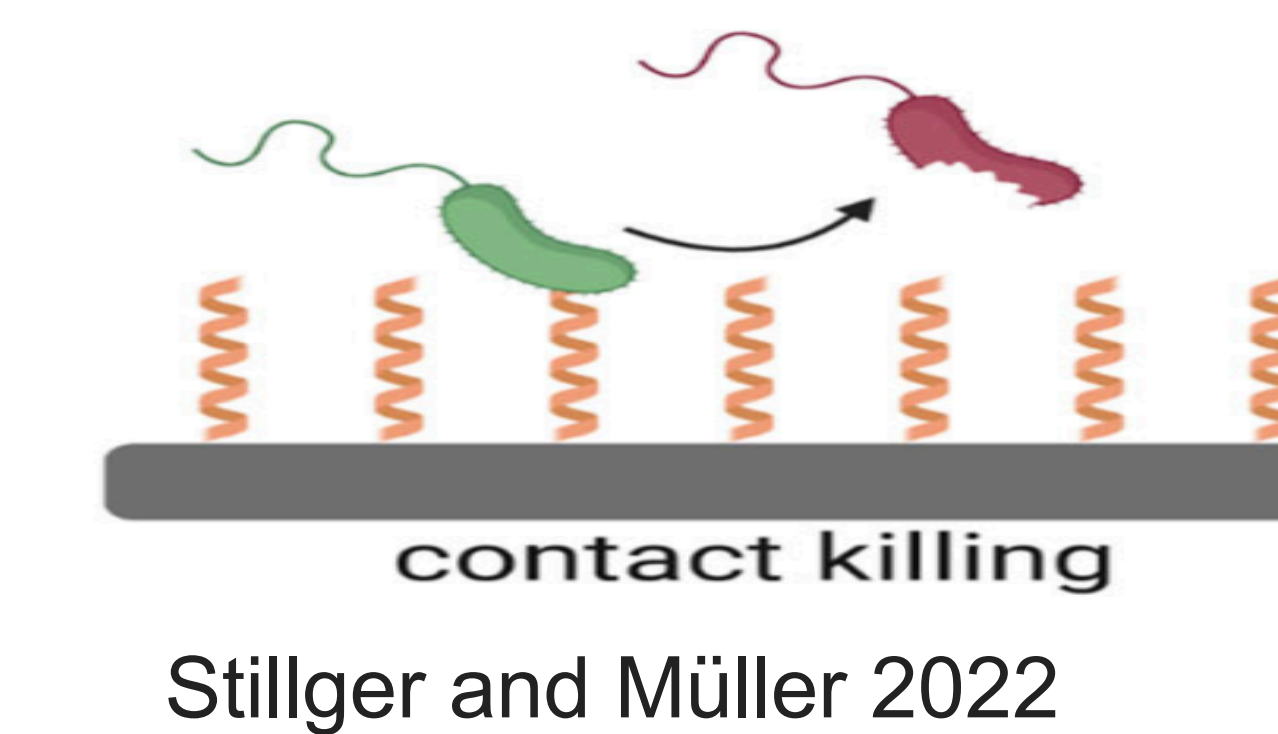
Gittens et al., 2014

Molecules	Outcomes
Collagen, Fibronectin, Laminins, Elastin, Osteopontin (OPN), Bone Sialoprotein (BSP), Dentin-Matrix Protein-1	↑osteogenesis, cellular proliferation, cellular adhesion and attachment, and mineralization

Molecules	Outcomes
Bone Morphogenic Proteins (BMPs), Fibroblast Growth Factor-2 (FGF-2), Vascular Endothelial Growth Factor (VEGF), Osteogenic Growth Peptide (OGP)	↑osteogenesis and bone remodeling, ↑wound healing and neovascularization, antibacterial activity, ↓inflammation

Antimicrobial Peptides (AMPs)

- AMPs can kill bacteria residing in biofilm, antibiotic resistant bacteria, and bacteria in the peri-implant tissues (Hancock and Sahl 2006; Riool et al., 2017).
- Significant AMP families include human beta defensins, histatins, and cathelicidins.
- Outcomes of studies include decreased bacterial load and improved osseointegration.



Miscellaneous

- Include peptides derived from animals, anchorage proteins, antibodies, and hormones.

Molecule	Outcomes
Silk Fibroin	↑osteogenesis, ↓inflammation
Mussel-inspired peptides	↑antimicrobial activity, ↑osteogenesis.
Titanium-binding peptides (TiBPs)	↑osteogenesis, ↑binding to Ti, ↑retention of antimicrobial challenge
Albumin	resistance to hydrogen peroxide, corrosion resistance
Sclerostin antibodies	↑osteogenesis, ↑bone mineral density, ↑cementogenesis
DKK-1 antibodies	↑bone formation and repair
Parathyroid hormone	↑osteogenesis, ↑VEGF
Growth Hormone	↑bone formation, ↑bone repair
Melatonin	↑osteogenesis, ↓inflammation, ↑protein adsorption
7ND	↓inflammation, ↓bone resorption, no effect

Discussion

- Mechanisms involve promoting bone formation, cellular proliferation, anchorage to implant surface, antimicrobial activity.
- Optimal molecule(s)?
- Consider adverse effects, optimal dosage, duration of treatment, drug interactions, etc.
- Plausible solution: combination that can yield bone formation, high attachment to implant surface, and antimicrobial activity.

Conclusion

- the use bioactive molecules under the category of proteins and peptides are efficient at promoting implant success.
- More research is needed in human clinical trials in order to determine the optimal molecule, combination of molecules, and practical application for clinicians to utilize them in practice.