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Periodontal disease: molecular visualization through computer modeling and 3D printing

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Project Purpose:
- To teach others about Periodontal Disease using 3D models to enhance understanding.
- My interest in periodontal disease began three years ago, when I started working in a periodontic dental office, but did not understand what truly was causing the disease.

Periodontal Disease:
- Bacteria can burrow under the gums, adhere to teeth, and form pockets called subgingival crevices depleting gum tissue.
- Jawbone can be destroyed and lost from periodontal bacteria attributing to the loss of teeth.
- Presently periodontal therapy relies on non-surgical and surgical techniques to remove bacteria from the mouth.
  - Antibiotics are currently secondary support to therapy but no primary therapy has been found.

Project Focus: Two prominent periodontal bacterial species: T. denticola and P. gingivalis (highlighted on this poster).

3D Visualization:
- Located in the College of Pharmacy, molecules were printed using 3D Systems: Z-650 3D printer.
- Powder-based 3D molecules are printed in layers.
- Molecular structures are found online through the public resource: Research Collaboratory for Structural Bioinformatics: Protein Data Bank.
- Identified was the crystal structure of Gingipain R (RgpB) that is secreted by P. gingivalis.

Mechanism:
- Plaque build-up on the tooth (left) contains numerous bacterial species, prominently including P. gingivalis, that migrate underneath the gingival tissue. Infected gum tissue is characterized by excess inflammation that progresses over time to cause jawbone loss. Bone loss is shown in the tooth diagram by the green osteoclasts eating away at the yellow-colored jawbone beneath it. This process occurs by P. gingivalis stimulating the activation of lipopolysaccharides (LPS) and secretion of gingipains. Activating LPS allows for the secretion of cytokines (IL-8-72 and IL-877) from leukocytes and epithelial cells that are a part of the inflammatory response. Gingipain R (RgpB) is an important cysteine proteinase. RgpB cleaves IL-8-72 and IL-877 rendering them more active. The more active forms are known as truncated forms that can recruit additional neutrophils (large purple squares above) and further tissue destruction over time. Increased neutrophil activity can be accompanied with increased chemotactic activity over time that leads to a decrease in the body’s immune reaction to the tissue inflammation that allows periodontal bacteria to survive in the mouth. This causes jawbone destruction and eventually the loosening of teeth.

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Future:
- Drug-design to combat early stage periodontal disease caused specifically by P. gingivalis.

2010 Developments
- Eight different benzamidine analog inhibitors were analyzed by their 3D structures to see which had the most potential for drug-design against P. gingivalis.

2015 Developments
- Polyphenol enriched extracts from the plant Rumex acetosa L. have strong interactions within the RgpB binding cavity, interfering with the adhesion of P. gingivalis.
- Epicatechin-3-O-gallate-(4R-8)-epicatechin-3-O-gallate10 is the extract molecule shown in 3D and 2D, to have a high specificity that could be a strategy for early prevention of periodontal adhesion.

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