Molecular view and MMP inhibition in dental restoration

Héber Silva[a,b], Rúben Chaves[a,b], Mario Polido[a], Ana Azul[a], Krasimira Petrova[b], Jorge Caldeira[a,b]

a) CiiEM, Instituto Superior de Ciências da Saúde Egas Moniz, Campus Universitário, Quinta da Granja, Monte de Caparica, 2829-511 Caparica, Portugal.

b) RequiMte, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Monte de Caparica, 2829-516 Caparica, Portugal.

Email: jcaldeira@egasmoniz.edu.pt

In the latter years, dental restoration techniques have suffered great advances and improvement. Nevertheless the durability of the resin-dentin bond is prone to fail after a certain period of time. There are several identifiable reasons for dental restorative failure, and here we focus in the presence of Matrix Metalloproteinases (MMP) in the hybrid resin-dentin layer a have collagenolytic and gelatinolytic activity and can degrade the dentinal collagen fibers bound to the resin.[2] These are the main attachment point of the polymeric resins that are used.

In this work we analyzed the ultrastructure of the dentin layer through Atomic Force Microscopy in different steps of the dental restoration. About 50 new polymerizable monomer that have been synthesized and their in sillico MMP inhibitory activity tested in order to select the most promising resin monomers that can potentially inhibit MMPs and therefore prolonging the durability of the dental restoration. Their in sillico MMP inhibitory activity has been measured for 5 different MMPs, namely MMP-1, -8 and -13 which are collagenases and MMP-2 and -9 which are gelatinases. AFM imaging revealed that the acid treatment and posterior washing with sodium hypochlorite exposed the dentinal tubules (figure 1).

These dentinal tubules are responsible for the diffusion of MMPs through the dentin, creating a direct path between MMPs and the hybrid layer. Through the use of docking software, namely Molegro and FlexX Leadit (figure 2), some compounds have revealed promising results and need to be studied further.

Future work involves the in vitro determination of the inhibitory capacity of the monomers that showed the most promising results and also the optimization of these newly synthesized monomers, improving their inhibitory capacity. The topographic evaluation of the dentin layer with these new compounds will be accessed through AFM.

This work is supported by Fundação para a Ciência e Tecnologia

PTDC/SAU/BMA/122444/2010, including grants to Rúben Chaves and Héber Silva.

[1] Breschi, L; et all., Dent Mater, **24(1)**,(2008) pp.90-101.

[2] Liu, Y., et all,J Dent Res, **90(8)**,(2011) pp.953-68.

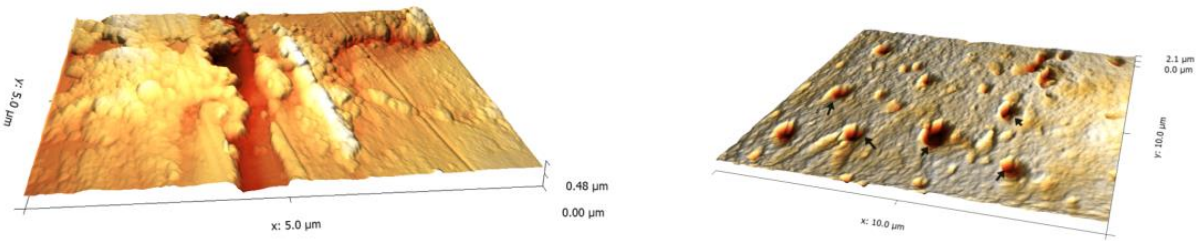

Figure1. AFM image of exposed dentinal tubules after acid treatment (left). and sodium hypochlorite cleaning procedure (right).

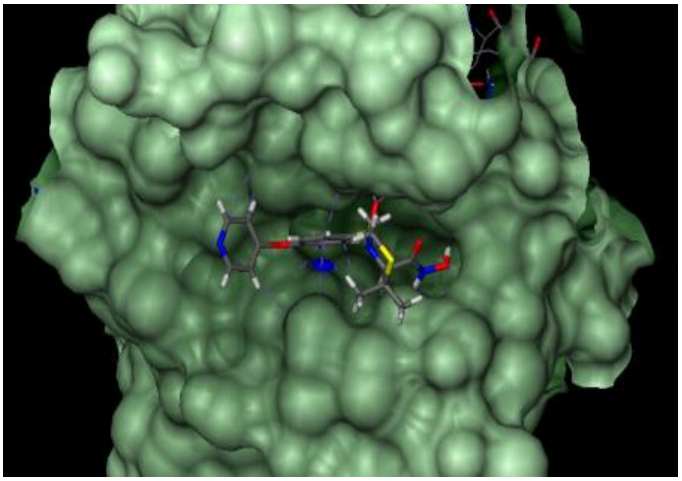

Figure 2. Docking between MMP-1 and synthesized monomers using FlexX.