

Invasion of peri-implant tissues by peri-implant pathogens: How close are *in vitro* models?

Invasión de tejidos periimplantarios por patógenos periimplantarios: ¿Qué tan cerca están los modelos *in vitro*?

Daniel Betancur.¹

Camilo Ulloa.¹

Affiliations:

¹Universidad de Concepción, Department of Surgical Stomatology, Periodontology Discipline and Postgraduate Program in Periodontology, School of Dentistry, Concepción, Chile.

Corresponding author: Daniel Betancur.
Roosevelt 1550, Concepción, Chile.
E-mail: danielbeta.c@gmail.com

In the biomedical area, implant infections are the most common and severe complication associated with the use of biomaterials. In many pathologies, the presence of pathogens and the infections could be resolved by the host immune system and/or antimicrobial therapy. However, the periodontal and peri-implant pathologies fit into the dysbiosis model of disease, where the recovery of the biological balance is necessary to maintain the health state, and antimicrobial treatment together with the host immune response alone is not sufficient, as the disease is the product of the imbalance between the bacteria and the host (dysbiosis), where the same bacteria present in health can now produce an infection.¹

The characteristic of the site where the implants are installed allow contact between these devices and the bloodstream, mucosal membrane, skin in some case, among other tissues. As such a depressed immune area is formed, defined in the literature as a “*locus minoris resistentiae*” (LMR), by the loss of the indemnity of the body barriers and the presence of a foreign material. In the case of dental implants, this LMR considers the collagen fiber disposition, the loss of the original “junctional epithelium”, the surface treatment of the implant in contact with the tissues and the type of connection. This predisposes the implant to be colonized by bacteria, with the subsequent invasion of the peri-implant tissues.²

The risk of infection in dental implant is very high, due to the invasiveness of surgery in some case, the permanent presence of implant in the body, the contact with mucosal membranes, co-morbidities and critical state of the patients, which in a high number of cases are older adults, and by the proximity to critical sites like the brain and the heart.²

The adhesion of bacteria to the implant surface could be reversible by non-specific forces (electrostatic, hydrophilic and hydrophobic interactions) on a surface not covered with host protein, or irreversible due to specific forces in a surface covered with host protein, like collagen, bone sialoprotein, fibronectin among others.

In this context, the majority of *in vitro* studies are limited, because they are not predictive regarding the behavior of bacteria towards the surface, inasmuch as the interactions between bacteria and implant surfaces depend of the type of bacteria, species, diversity, cellular cycle phase of the bacteria, etc., and generally these studies use a small number of

Cite as:

Betancur D & Ulloa C.

Invasion of peri-implant tissues by peri-implant pathogens: How close are *in vitro* models?

J Oral Res 2020; S1(1):4-6.

[Doi:10.17126/joralres.2020.024](https://doi.org/10.17126/joralres.2020.024)

microorganisms compared with that present in the peri-implant sulcus/pocket.³

In this stage, the invasion process happens like a race for the surface of the implant between the bacteria and the host cells. The term “*race for the surface*” was coined in 1987, and it refers to competition between the host cells and contaminant bacteria to occupy the implant surface.

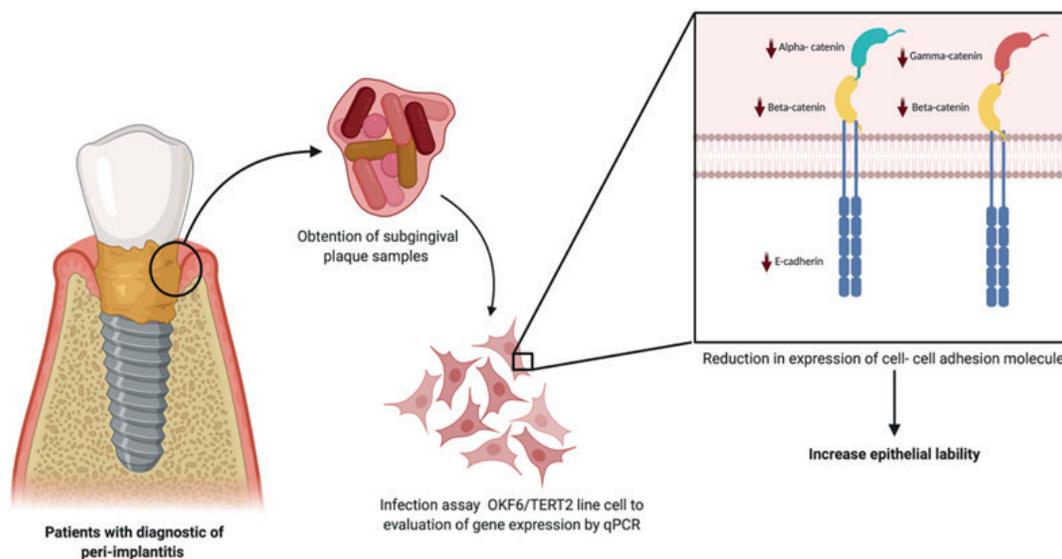
However, this race is always run with the microorganisms having an advantage, as they manage to quickly bind to the surface of the implant compared to the host cells which take much longer to do so. This phenomenon is not completely understood because the *in vitro* models in use just consider one cellular type and

evaluate very short periods of time with respect to the clinical reality.⁴

Once the biofilm is established on the surface of the implant, the bacteria manage to evade the host's immune response, using the small spaces on the rough surface where they cannot be phagocytized, a process known as exclusion of professional phagocytes.

In addition, they can invade nonimmune cells such as osteoblasts and remain dormant inside these for a long time, protected from the effect of antibiotics and inducing apoptotic pathways in these cells to later egress into the environment and replicate once again (partly explaining why implant infections are often recurrent after therapy).¹⁻⁵

Figure 1. Model of the effect of peri-implant bacteria in oral epithelial keratiocytes OKF6/TERT2, to measure for example the expression of cell-cell adhesion molecules by qPCR. Showing a decrease in the expression of catenins family in comparison with sample from healthy patients. ($p < 0.01$ using comparative quantitation by the $2^{-(\Delta\Delta CT)}$ method for quantitative real-time polymerase chain reaction data analysis). Graphics are not showed in this article.



Results from our group showed that in infection tests of human oral epithelial cells (OKF6/TERT²) with clinical isolates derived from patients with peri-implantitis, these bacteria induce a lower expression of cell-cell adhesion molecules such those in the catenin family.

An increase in the lability of the epithelium that favors the invasion of microorganisms derived from the peri-implant biofilm to deeper tissues also adds to the LMR (Figure 1). *In vitro* models that consider a greater number

of variables such as cell types, infection times, and a well-characterized bacterial inoculum are necessary to better understand the invasion mechanisms in peri-implant infections.

The changes in the epithelium barrier must be better studied in order to ascertain the role of epithelial cells in the colonization process of the implant surface and in the passage of bacteria from the peri-implant sulcus to the subepithelial connective tissue.

Acknowledgements: This study was funded by Proyecto RED1170658, CONICYT-Chile.

REFERENCES.

1. Arciola CR, Campoccia D, Ehrlich GD, Montanaro L. Biofilm-based implant infections in orthopaedics. *Adv Exp Med Biol.* 2015;830, 29–46.
2. Arciola CR, Campoccia D, Montanaro L. Implant infections: adhesion, biofilm formation and immune evasion. *Nat Rev Microbiol.* 2018;16(7):397-409.
3. Nguyen VT, Chia TW, Turner MS, Fegan N, Dykes GA. Quantification of acid-base interactions based on contact angle measurement allows XDLVO predictions to attachment of *Campylobacter jejuni* but not *Salmonella*. *J Microbiol Methods.* 2011;86, 89–96.
4. Subbiahdoss G, Kuijjer R, Grijpma DW, van der Mei HC, Busscher HJ. Microbial biofilm growth vs. tissue integration: "the race for the surface" experimentally studied. *Acta Biomater.* 2009;5(5):1399-1404.
5. Veerachamy S, Yarlagadda T, Manivasagam G, Yarlagadda PK. Bacterial adherence and biofilm formation on medical implants: A review. *Proc Inst Mech Eng H.* 2014;228(10):1083-99.