

# Personalization of medical device interfaces: decreasing implant-related complications by modular coatings and immunoprofiling

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## Personalized medicine & medical devices

The organ/tissue function replacement using implantable medical devices has become a pillar of modern medicine with a considerable level of success. Cochlear, orthopedic and dental implants are some of the examples of implantable medical devices with more than several million implantations per year. However, such an increased volume of use has also brought about an increased level of complications. One such complication is infections around medical devices, particularly in hospital settings where a significant portion of infections called ‘nosocomial infections’ is closely related with implanted devices. Although there are certain indications such as smoking, presence of chronic systemic diseases and so on, there is no current method available to predict such medical complications.

One potential way to handle this problem follows the recent developments in personalized medicine. Currently in the field of oncology and in pharmaceutics in general, patient-specific precision medicine [1] techniques are taking hold. The most basic approaches are based on demographic correlations (such as lifestyle-related stratification of the therapies for improved efficacy), but more advanced techniques look at the gene expression level (such as determination of the expression of HER-2, a specific growth factor receptor which is the target of some breast cancer drugs). In the field of implantable devices, the personalization up to now has taken the form of application of additive manufacturing techniques for obtaining personalized implants with better anatomical fits for a given patient. Beyond this, with such techniques it is also possible to print personalized surgical instrumentations and personalized models for pre-operation decision making [2]. Accompanying such efforts, advances in imaging technologies have resulted in dedicated systems for personalized planning of implant positioning (such as tools that enable virtual implant positioning on 3D constructed images of the defect/damaged area). However, there is another important determinant of the success of implants, which is the immune response to the implanted material, as an implant is generally considered by the body as a foreign object [3]. The extent, intensity and the severity of such immune reactions are highly personalized also. Thus, it is equally important not only to create personalized interfaces between the implants and the host tissues in a patient specific, but also organ or tissue-specific manner.

## Ways of achieving personalization

Interface personalization can be achieved in several ways such as patient-specific modification of surface properties of implants including wettability, roughness, nano/microscale topography [4], chemistry and so on [5]. Another way to achieve interface personalization is the incorporation of delivery systems for cytokines that will regulate the implant microenvironment as a function of the expected immune response of the patient. This can be done by a single cytokine that is highly relevant for a given tissue [6] or via cytokine cocktails [7]. A third option is to

create patient-specific coatings on implant materials that will act as an optimized interface. Such coatings should be multifunctional [8] in the sense that they should not only provide an optimized microenvironment but they should also incorporate preventive measures such as antimicrobial properties [9]. This will mean surfaces that will provide amenable properties for the tissue-specific cell type to adhere and cover the implant surface to facilitate integration, and that can resolve the initial inflammation in a pro-regenerative manner to diminish adverse immune reactions and the associated collateral damage. Moreover, these surfaces should have the necessary components to prevent opportunistic bacterial, fungal and maybe even local viral infections.

Immunoprofiling can be achieved by the quantification of the soluble factors in the patient's blood, or by *in vitro* evaluation of the behavior of the isolated patient immune cells. However, in order to delve into the background of an individual's adaptive immune response to a given material, antibody-level information is necessary. For this end, use of mimotope variance analysis [10] provides a unique opportunity to not only determine the generic responses to new biomaterials, but also patient-specific response to biomaterials, which can guide the development of immune-compatible, patient-specific implant surfaces. Such immunoprofiling based pre-implantation and postimplantation diagnostics can improve the functional outcomes of different implants by aiding in the implant type selection and can also significantly decrease the implant-related complications.

The coupling of immunoprofiling with immunomodulatory surface modifications would provide us with an arsenal to resolve tissue replacement-related problems in a patient-specific manner without searching for new materials for each new situation. This will also broaden the capacities of the multiscale coatings from the resolution of the known complications to have immunomodulation in their vicinity and also protective solutions in conditions such as the ongoing COVID-19 outbreak.

#### Author contributions

NE Vrana: conception, first draft K Palm, P Lavalle: contribution to the the first draft, revision.

#### Financial & competing interests disclosure

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- **Example of application of mimotope variance analysis technology.**