IN VITRO METHOD FOR PREDICTING THE BIOCOMPATIBILITY OF MEDICAL IMPLANTS

DESCRIPTION OF THE INVENTION

Researchers at the Universitat Jaume I of Castelló (UJI), the University of the Basque Country (EHU/UPV) and the Center for Cooperative Research in Biosciences (CIC bioGUNE) have developed and patented a new *in vitro* method for predicting the biocompatibility of materials to be used in the manufacture of medical implants, such as joint and dental prostheses, valves and stents, among others. The invention consists in an accelerated test of the biocompatibility of materials that makes it possible to rule out those with poorer prospects of success during the *in vitro* phase. As a result, the costly investments required to perform unnecessary *in vivo* trials are avoided and the new materials can be tested in the clinical phase sooner.

The new method is based on the detection of a group of proteins linked to the inflammatory reaction. The novelty of this methodology lies in the fact that a robust correlation has been established between the protein profile obtained in *in vitro* tests and that acquired by means of *in vivo* trials, which are, by definition, more reliable.

The success of an implant depends on its biological integration within the organism. The aim is to achieve this integration in the shortest possible time, which means preventing the immune reaction from getting out of control in terms of both intensity and time (chronicity) and, ultimately, that no foreign body reaction and implant rejection take place. Hence, the implants must be manufactured with materials that have been shown to be compatible with living tissues, that is, with proven biocompatibility.

The problem is that all the candidate materials have to undergo a number of complicated tests before they can be approved for use as medical implants. Such testing ranges from *in vitro* assays to determine their cytotoxicity to *in vivo* trials with the prototypes that have displayed good properties in the *in vitro* assays. They also have to be submitted to preclinical studies as well as clinical trials in humans. All this is a long, very costly process.

In many cases, although the *in vitro* cytotoxicity and cell proliferation trials yield good results, what eventually happens is that the material being tested fails to display a good level of biocompatibility in the *in vivo* tests. In such cases, the *in vivo* assays are a complete waste of time and resources, and they also involve the death of a significant number of animals.

What if we could predict or forecast the biocompatibility of the new materials in the *in vitro* phase, so as to be able to rule out the less promising candidates and save on costs?

This is exactly what is proposed with this technology. The researchers have identified a profile of protein markers, related with the immune response, which can be analysed in an isolated *in vitro* biological sample. The presence of this protein above a certain reference level indicates a lack of *in vivo* biocompatibility. Thus, and thanks to this *in vitro* / *in vivo* correlation, the new method uses the determination and quantification of those markers in *in vitro* samples to predict or forecast the biocompatibility of biomaterials/implants, joint and dental prostheses, catheters, etc.

SECTORS FOR COMMERCIAL APPLICATION

The technology is useful for three sectors:

1. Manufacturers of medical prostheses, and more especially firms dedicated to the manufacture of dental implants and hip and knee replacement prostheses, and, in general, any companies that make materials designed to be in contact with bone.

2. R&D centres. All those groups that perform *in vitro* and *in vivo* trials applied to the development of new biomaterials in order to determine their biocompatibility.

The application of this technology in these two sectors would allow new materials to be developed for prostheses or regenerative medicine at a lower cost and in less time. It would enable firms and research centres to increase their productivity related to the search for new biocompatible materials. By offering an indication of the biocompatibility of the materials being developed, it becomes possible to rule out those with few chances of success at an early stage, thereby saving the costs of conducting *in vivo* trials.

3. Healthcare sector, and more particularly dental clinics, hospitals and other players involved in the placement of prostheses. Application in this sector would be at patient level. Based on the results of a simple

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blood test, the patient would be given detailed information about whether he or she is likely to suffer complications in joint replacement surgery.

TECHNICAL ADVANTAGES AND COMMERCIAL BENEFITS

Thus, the advantages of this technology are:

- It is a fast reliable *in vitro* method that compares well with the results obtained at the *in vivo* level.
- It speeds up the development and reduces the costs of materials for the manufacture of medical implants to a notable extent, since it makes it possible to rule out the materials that display a lower degree of *in vitro* biocompatibility, and consequently avoid the need for costly *in vivo* trials.
- It also allows personalised pre-implantation diagnoses to be reached for individual patients in order to determine the likelihood of an implant being rejected by the body and, accordingly, prescribe the type of prosthesis with the greatest prospects of success.
- It also allows the number of animals used in experimentation to be reduced.

The main innovative aspect of this method is that it is based on an analysis of the peptide profile which has been proved to have a robust correlation between the *in vitro* results and the biocompatibility exhibited by the material under *in vivo* conditions. None of the accelerated tests based on protein developed to date have shown evidence of such a correlation, without which it is not possible to match the results obtained *in vitro* with what will later happen with the material implanted inside the body.

STAGE OF DEVELOPMENT OF THE TECHNOLOGY

The method has been validated and a prototype kit is available.

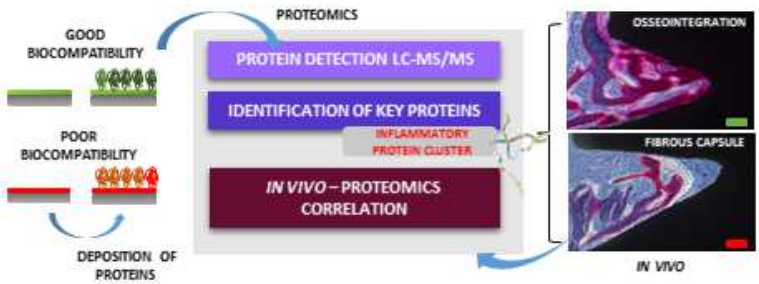
INDUSTRIAL PROPERTY RIGHTS

This invention is protected by means of a Spanish patent with reference number P201631682 filed on 12/23/2016.

COLLABORATION SOUGHT

- Licence agreement for use, manufacture or commercialisation.
- Development of applications.

RELATED IMAGES



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