Kits for modulation of anti-rejection therapies and early detection of neurodegenerative diseases

UNIVERSITÀ DEGLI STUDI FIRENZE

INVENTORS: Prof.ssa Gabriella Caminati
Prof. Piero Procacci
Prof. Stefano Menichetti
Dott. Laura Marsili
Dott. Maria Raffaella Martina

STATUS PATENT: Granted

N° PRIORITY: 102019000025066

GRANTED ON: 15 December 2021

PATENT FAMILY: PCT WO2021124269A1

The Technology (1/3)

The patented technology is the result of an elaborate multidisciplinary research project of physical, organic and computational chemistry, and consists of a nanofunctionalized device that enables the quantitative determination of a specific biomarker, the FKBP12 protein, involved in many diseases. Quantification of this protein in the blood enables efficient monitoring of the postoperative course of transplant patients, modulation of proper drug administration in autoimmune diseases as well as early detection of neurodegenerative diseases such as Parkinson's and Alzheimer’s. The patented technology enables efficient and low-cost monitoring of the operative course after organ transplantation. In fact, FKB12 constitutes an excellent pharmacological target for dose monitoring of immunosuppressive drugs, both in the context of organ transplantation and in the context of therapy of autoimmune diseases such as Chron's disease, Lupus, and rheumatoid arthritis. Direct determination of the concentration of FKBP12 in the blood allows efficient modulation of 'immunosuppressive activity in post-transplant therapies in order to limit side effects, overdoses, and acute rejection phenomena.

The Technology (2/3)

FKBP12 plays a primary role in therapies for autoimmune syndromes. Indeed, inhibition of FKP12 with immunosuppressive drugs (such as FK506) leads to the formation of a ternary complex with Calcineurin, resulting in the arrest of the immune response. The determination of FKBP12 may therefore prove to be of decisive importance in therapies involving the use of immunosuppressive drugs such as autoimmune hepatitis, rheumatoid arthritis, Chron's disease, and multiple sclerosis. FK506 despite being among the most potent immunosuppressant drugs used in antirejection therapies and autoimmune diseases induces major overdose effects such as development of skin tumors, lymphomas, or serious infections. As suggested by the Food and Drug Administration [Immune monitoring post liver transplant, World J Transplant. 2014 Mar 24; 4(1): 30-39.], in anti-rejection therapies or for autoimmune diseases, the dosing of immunosuppressive drugs should not be modulated by assessing the concentration of the drug in the blood, a methodology currently used, but by quantification with uninhibited FKBP12.The unavailability of rapid and reliable assays for FKBP12 has so far prevented this molecule from being used as a sentinel in the post-transplant course or treatment of autoimmune diseases when using immunosuppressive drugs.

The Technology (3/3)

The proposed device fills this gap by offering operational simplicity combined with high sensitivity that allows its direct use in hospital, clinical or analytical laboratory settings. More importantly, the use of the sensor kit for early diagnosis of neurodegeneration is outlined. Currently, diagnosis is based on symptomatology alone or on invasive, expensive tests, available only in specialized centers and in any case capable of detecting only already severely compromised situations.The invention differs in its lower cost, ease of use, accuracy, rapidity and specificity of the results obtained. The patented kit is equipped with a nanosensor that enables direct analysis of biological samples and makes it possible to detect early stages of NDs and thus anticipating the initiation of therapies suitable for their treatment. Many clinical trials of potential drug candidates for the treatment of NDs have failed precisely because conducted on patients now at too advanced a stage of the disease. The device thus lends itself to be used for campaigns to prevent neurodegeneration by preventive screening of the population in the risk range due to age or genetic familiarity and thus detect and intervene at the early stage of neurodegeneration. In fact, the rapid development of medical research activity will lead to the use of less invasive sampling methods such as nasal swabs, or expiratory condensate, which will certainly encourage a positive population response to a screening campaign.

The Inventors

Gabriella Caminati received her Ph.D. in chemical sciences in 1990. Since 1993 she has been a postdoctoral fellow at Columbia University of New York (USA) and Ecole Normale Supérieure de Lyon (France) and a visiting scientist at the Max-Planck Institut fur Biophysickalische Chemie in Göttingen (Germany). Since 2000 he has been a researcher in the Department of Chemistry at the University of Florence where he teaches the Chemistry-Physics of Organized Molecular Systems Course. His main research interests in the field of Physical Chemistry are in the characterization of surface and nanosystems, the study of biomimetic systems and the fabrication of nanostructured devices such as sensors, electro-optical devices and photovoltaic cells.

Piero Procacci is Professor of Physical Chemistry at the University of Florence since 2001, with multi-year working experiences at IBM corporation in Kingston (NY), Columbia university in New York (USA) and Ecole Normale Supérieure de Lyon (France), Piero Procacci has developed his research in the field of computational chemistry, initially in the study of spectroscopic properties of solid materials, liquids or glassy materials, later specializing in the development of algorithms for the simulation of complex systems, finally devoting himself in recent years to topics in the biological field with a focus on drug design through advanced simulation techniques, developing molecular didynamics codes for the prediction on HPC platforms of drug-receptor dissociation constants. Piero Procacci has authored about 130 papers in international journals with an h-index of 40 (google-scholar).

Stefano Menichetti is Full Professor of Organic Chemistry at the Department of Chemistry 'Ugo Schiff' since 2005. Main research interest is the development of stereocontrolled, catalytic and environmentally sustainable synthetic methodologies for the preparation of new molecules with applications in pharmaceutical chemistry and materials science. Author of more than 160 publications in international peer-reviewed journals (iH = 30, total citations 3006) and three patents.

Industrial Application

The patented invention satisfies at least three possible competing technological needs, which are independent of each other since they are located in different areas of the life science field.

The first area of application of the invention is in the area of post-transplant anti-rejection therapies, specifically in the instrumentation to aid the health care provider in the proper dosing and modulation of anti-rejection therapies, with a view to limiting their possible side effects, overdoses, and other undesirable complications.

The second technological need met by the patented invention relates to techniques for the early diagnosis of neurodegenerative diseases (ND), which currently lacks methodologies and techniques capable of combining (i) accuracy, (ii) rapidity, and (iii) specificity of results.

A third field of application concerns, by extension, the treatment of all those diseases in which the ability to directly determine the level of FKBP12 protein concentration in the blood can contribute to the proper administration of therapies that include immunosuppressive drugs.

Future developments

- TRL 4
- Patent available for exclusive or nonexclusive license
- Inventors are available for research, development, and consulting activities

Further info

Ufficio di Trasferimento Tecnologico, Università degli Studi di Firenze

Sede: Piazza S. Marco 4 – 50121 Firenze

Sito web: www.unifi.it

E-mail: brevetti@unifi.it

Further info:

Ufficio Regionale di Trasferimento Tecnologico

Sede: Via Luigi Carlo Farini, 8 50121 Firenze (FI)

E-mail: urtt@regione.toscana.it

UNIVERSITÀ DEGLI STUDI FIRENZE

REGIONE TOSCANA

urtt Ufficio Regionale di Trasferimento Tecnologico