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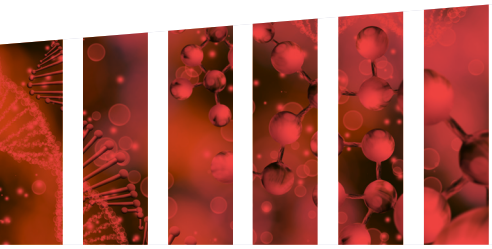

RHBG AS A BIOMARKER FOR CANCER & A DRUG TARGET TO INHIBIT CANCER PROLIFERATION

KEYWORDS

- Luminal
- Breast cancer
- Diagnosis
- RHBG
- Biomarker

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STATE OF THE ART

Breast cancer is the most common cancer in women. Due to the complexity and heterogeneity of breast cancer, clinical evolution is difficult to predict, and therapeutic and prophylactic treatments are not optimal. Devising novel and/or improved methods to diagnose and combat proliferative disorders, such as breast cancer, is therefore of key importance. Avoiding overtreatment in patients who only benefit from a modest therapeutic effect, while suffering from toxic side effects is also critical. Individual treatment optimization can be aided by improved methods to distinguish proliferative disease subtypes, such as for breast cancer, luminal and basal breast cancer.

THE INVENTION

The inventors have identified a transmembrane ammonium transporter protein from the Rhesus family, the Rhesus B glycoprotein (RHBG), whose expression level is predictive of cancer. RHBG constitutes thereby a promising biomarker for luminal breast tumour. This biomarker has potential applications in diagnosis, prognosis and monitoring (companion diagnostic) of luminal breast cancer and the patent application family covers the related methods.
The inventors furthermore evidenced that inhibition of RHBG expression in luminal breast cancer cells decreased proliferation of the cells. This makes RHBG an interesting therapeutic target as well for treatment of breast cancer.

KEY ADVANTAGES OF THE TECHNOLOGY

- RHBG is a new biomarker for luminal breast cancer tumors.
- RHBG is a new drug target for the development of treatments to inhibit luminal breast cancer proliferation.
- Clinical studies of the prognostic value of RHBG expression in breast cancers could provide further insights about the behaviour and treatment of RHBG expressing tumors.
- RHBG could be used as prognostic (Disease-Free and Overall Survival - DFS and OS) and predictive marker.

POTENTIAL APPLICATIONS

- Oncology
- Diagnosis
- Prognosis
- Companion diagnostic
- Breast cancer drug discovery

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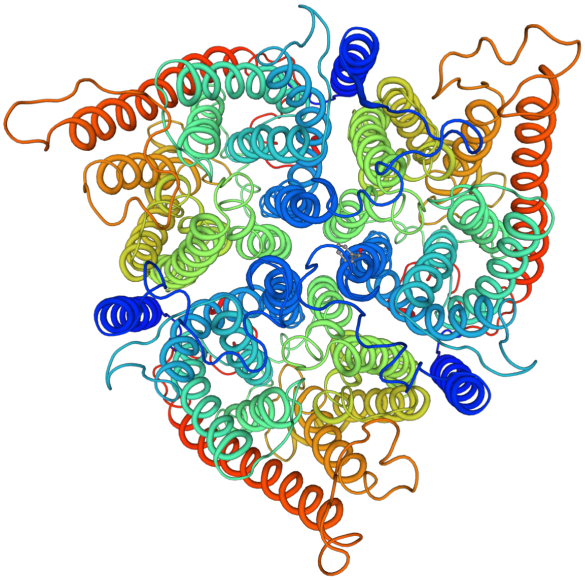

Fig.1: Ammonium transporter Rh type B

THE TEAM

The laboratory studies the translocation of ions and other solutes across cell membranes. Ammonium is ubiquitous in nature and has a general importance. It is a principal nitrogen source for micro-organisms and plants, and a cytotoxic metabolite of most animal cells. The research projects conducted in the Biology of Membrane Transport laboratory apply a global approach to characterize ammonium transport proteins of the Mep-Amt-Rh family at the molecular level and explore their roles in single-cell and whole-organism pathophysiology. For these purposes, mice, mammalian cell lines and yeast cells are used as models. Defects in mammalian Rhesus factors are related to a number of pathologies including red blood cells, kidney function and male fertility disorders. Ongoing studies in the laboratory are seeking to identify new connections linking Rhesus factors dysfunction and human diseases, with a specific concern for a potential role of these proteins in ammonium homeostasis and pH regulation of physiological fluids.

THE INVENTORS

Dr. Anna Maria Marini played a pioneering role in the discovery of ammonium transport systems defining a novel protein family termed Mep-Amt-Rh, and in the elucidation of the long-sought-for physiological function of Rhesus (Rh) factors in mammals (Marini et al., 1994, EMBO J.; Marini et al., 2000, Nature Genetics; Biver et al., 2008, Nature). She leads the laboratory where the research at the origin of the invention was performed and the development of the corresponding technology is currently under progress.

Dr. Ahmad Merhi conducts research in the field of structure-function analysis and regulation of transporters and in molecular oncology. Within Marini's team, he designed and performed the experiments reported in the invention.

RELEVANT PUBLICATIONS

> The Metabolic Waste Ammonium Regulates mTORC2 and mTORC1 Signaling, Merhi A., Delrée P., Marini A. M., Sci Rep. 2017;7:44602. Published 2017 Mar 17.

> Wnt/β-Catenin Signaling Regulates the Expression of the Ammonium Permease Gene RHBG in Human Cancer Cells, Merhi A., De Mees C., Abdo R., Alberola J. V., Marini A. M. PLoS One. 2015;10(6):e0128683. Published 2015 Jun 1.

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