RESPONSIFY

towards individualising cancer therapy

RESPONSIFY Expertise

GBG Forschungs GmbH –
German Breast Group, Frankfurt (D)
Prof. Dr. Sibylle Loibl, Prof. Dr. Gunter v. Minckwitz

CHARITE Universitätsmedizin Berlin,
Institute of Pathology, Berlin (D)
Prof. Dr. Carsten Denkert

DNAVision SA (B)
Dr. Sebastien Massart

DIAXONHIT (F), Paris
Dr. Pascale Beurdeley-Fehlbaum

Institute de cancérology Gustave Roussy, Paris (F)
Prof. Dr. Fabrice André

Institute Jules Bordet, Brussels (B)
Prof. Dr. Christos Sotiriou

Karolinska Institutet
Cancer Center Karolinska, Stockholm (S)
Prof. Dr. Barbro Linderholm

Sividon Diagnostics GmbH, Cologne (D)
PD Dr. Ralf Kronwett

tp21 GmbH, Berlin (D)
Dr. Petra Zalud

University of Basel,
Institute of Pharmaceutical Medicine (CH)
PD Dr. Matthias Schwenkglenks, Dr. Patricia Blank

University College London – Cancer Institute (UK)
Prof. Dr. Charles Swanton, Dr. Maria Antonietta Cerone

For more information please contact

Prof. Dr. med. Carsten Denkert
CHARITE, Institute of Pathology (D)

Prof. Dr. med. Sibylle Loibl
GBG Forschungs GmbH – German Breast Group (D)

The Collaborative Project RESPONSIFY has received funding from the European Community's Seventh Framework Programme under grant agreement FP7 HEALTH 2011-278659.
Neither the European Commission nor any person acting behalf of the Commission is responsible for the use which might be made of the information provided on this website.

Concept & Realisation tp21 GmbH · Design by pigurdesign

www.responsify-fp7.eu

Genome-based biomarkers leading to validated molecular diagnostic tests for response prediction in breast cancer

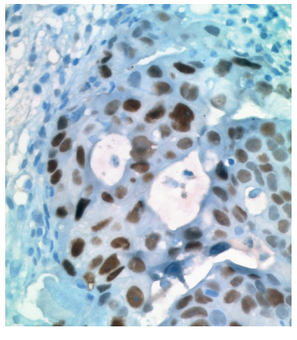
Towards individualising cancer therapy

Breast cancer is the main research focus of RESPONSIFY because it is the most common cancer in women worldwide with more than 1.1 million women newly diagnosed annually, accounting for 14% of all female cancer deaths. In Europe, approximately 463,000 women show new cases of breast cancer each year. While the disease is curable in early stages, about 50% of patients present with stage II or III tumours.

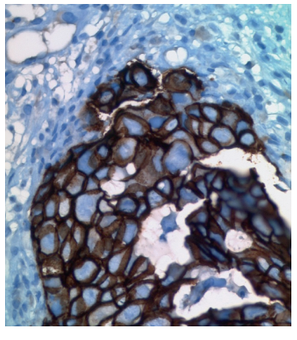
Today almost all women are candidates for different systemic therapies (endocrine-, trastuzumab-, chemotherapy), so that suitable and validated predictive assays are urgently needed to optimise clinical outcomes and minimize unnecessary toxicity.

To date, the response rate to breast cancer therapy is approximately 20-40 %. The RESPONSIFY researchers aim to increase this rate considerably by the development of validated biomarker approaches.

The main goal is the development **of new available biomarker tests**, which can indicate whether and how a specific treatment affects an individual patient. This approach to a more **"personalised medicine"** will facilitate response prediction and select patients to a specific treatment from non-responders.



Nuclear expression of estrogen receptors in luminal breast cancer



HER2 positive breast cancer is characterized by strong membranous overexpression of HER2

The RESPONSIFY project aims to get breast cancer therapy more tailored to individual patients. Translated into clinical practice, this will help physicians to make decisions and avoid ineffective treatments.

The main aim is the development of new standardised biomarker tests. Biomarker tests can indicate whether and how a specific treatment affects an individual patient and therefore facilitate response prediction and select those responding from those not responding to a specific treatment.

A major focus of RESPONSIFY is the investigation of the interaction of tumour cells with the immune system. We are able to show that tumours with a high immune infiltrate have an increased response to neoadjuvant chemotherapy, and this finding can be validated by immunological gene signatures. This approach is particularly relevant considering the new clinical trials on immunotherapy that investigate immune checkpoint inhibitors in breast cancer. RESPONSIFY has evaluated the molecular targets of these inhibitors, which are linked to therapy response.

In addition, RESPONSIFY evaluates the role of mutations for the therapy of breast cancer. In particular mutations of the PIK3CA gene are relevant for resistance to combined anti-HER2 therapies.

With help of biomarker tests, physicians could evaluate the prognosis and determine the treatment strategy early on. By this approach, it is possible to start treatment already before surgery, in a so called neoadjuvant therapy, which can help to reduce the tumour burden before surgery and to evaluate response. The advantage of neoadjuvant therapy is that the effective response of the therapy on the tumour is immediately visible.

RESPONSIFY aims to establish strategies, which allow a faster translation of research results into clinical practice. Overall RESPONSIFY works towards the big challenge of individualising cancer therapy based on standardised biomarker assays that could be commercialised by the RESPONSIFY SMEs for use in clinical routine.

The RESPONSIFY scientists are working to identify new markers that allow more specifically targeted and patient-specific use of chemotherapy in breast cancer. In particular they identify groups of patients, in which the use of chemotherapy is expected to be particularly effective. By assessing health economic characteristics of these markers, an evidence base will be generated to sustain efficient decision making on novel test-treatment combinations in breast cancer management.

The aim of the RESPONSIFY project is to identify the conditions that determine which specific drug substances are effective in the treatment of breast cancer, including the substances trastuzumab, lapatinib and carboplatin.

In order to better observe the effects on the tumour, researchers administered the chemotherapy and aforementioned drug substances prior to surgically removing the tumour.

Neoadjuvant chemotherapy, in particular with carboplatin, is effective in patients with tumours in which many inflammatory cells can be found. This suggests that body's own defense system is capable of supporting and strengthening the effects of chemotherapy.

For anti-HER2 therapy, trastuzumab and lapatinib exhibit relatively weak effects in tumours exhibiting a mutation of the PIK3CA gene occurring in approximately 19 percent of cases.

RESPONSIFY
interdisciplinary research