Overcoming Drug Resistance in Breast Cancer using High Throughput Combination Screenings

Mary-Ann Jallad[1,2], Pilar Ayuda-Duràn[1], Robert Hanes[1], Jorrit Enserink[1] and Kjetil Taskén[2]

[1]Department of Molecular Cell Biology, Institute for Cancer Research, Oslo University Hospital, Oslo, Norway

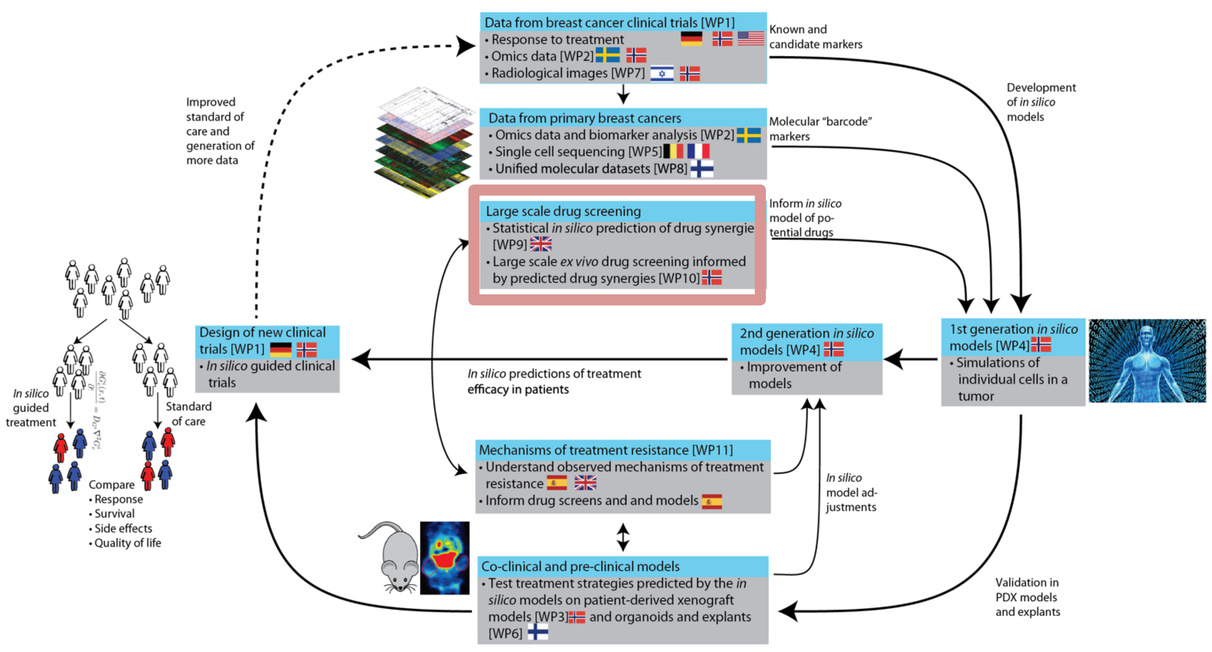
[2]Department of Cancer Immunology, Institute for Cancer Research, Oslo University Hospital, Oslo, Norway

RESCUER

RESistance Under Combinatorial Treatment in ER+ and ER- Breast Cancer

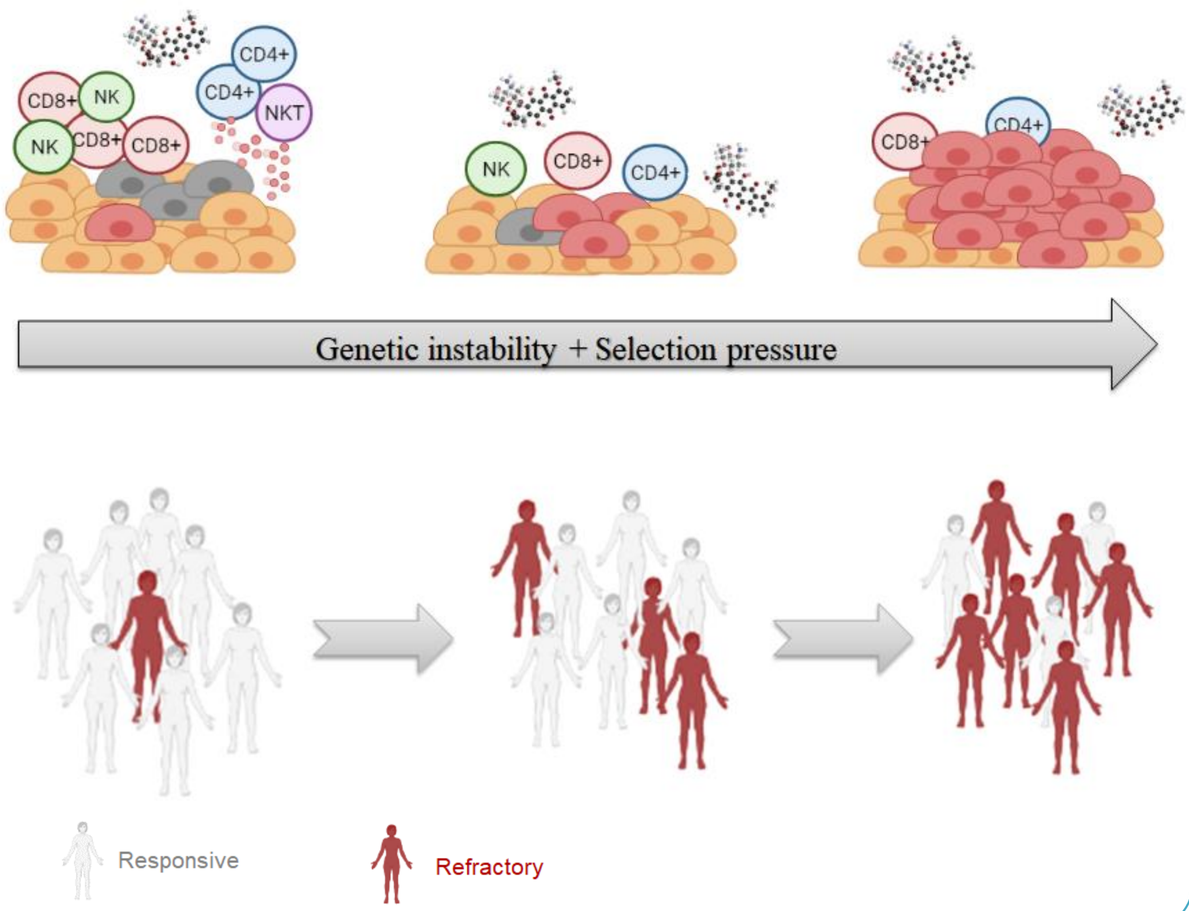
Overview

RESCUER is a consortium of fifteen organizations from ten different countries that aims to identify novel characterization methods for breast cancer drug resistance and new knowledge on effective combinatorial treatments. To this end, RESCUER brings together a multidisciplinary combination of partners (clinical, scientific, technical, industry) who express diverse exploitation interests, aimed at bringing results to actual use in several different areas and generating a wider impact within and beyond the core project objectives. The work is divided into thirteen inter-related packages that function together to fulfill RESCUER's aims.



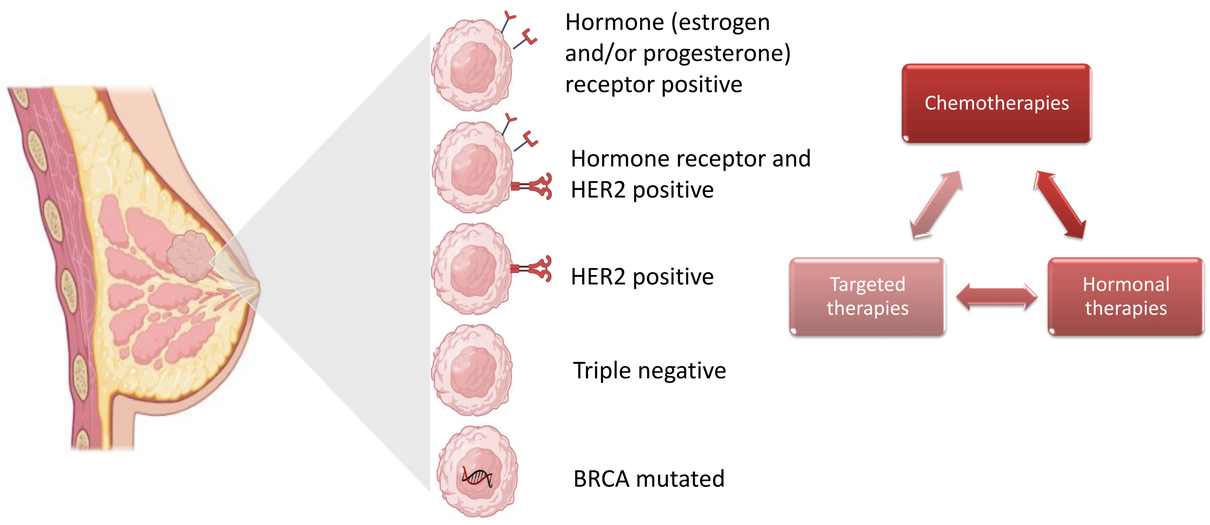
Introduction

Despite the various breast cancer treatments currently available, a subpopulation of cancer patients does not respond to treatment. More importantly, the resistance gets increasingly significant during the course of treatment, thus further reducing the chances of a progression free survival. This is mainly caused by the genetic instability of cancer cells coupled with the pressure exerted by both the immune system and the drugs used which select for resistant variants that are harder to treat. These variants use multiple evasion mechanisms to resist killing by either drugs or the immune system. Hence the importance of combination therapies that allows targeting several of these resistance mechanisms simultaneously.



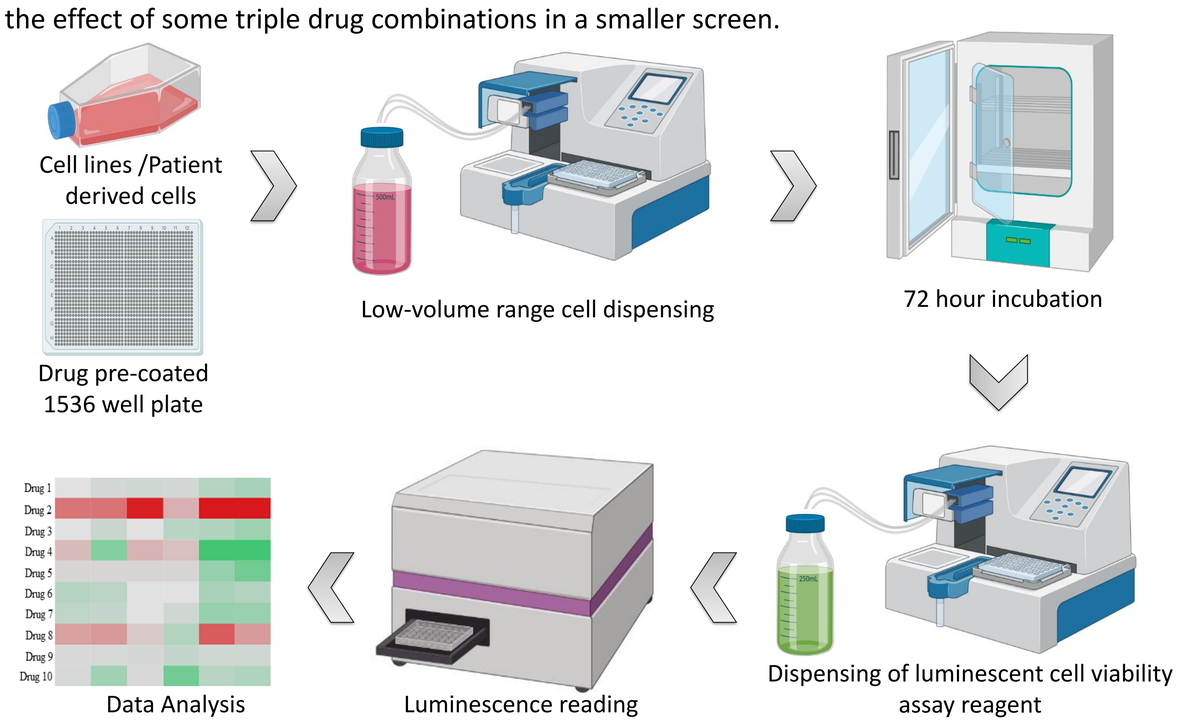
Objective

The aim of our work package is to explore new treatment options for the various breast cancer subtypes through conduction of large-scale screening and identification of synergizing drugs.



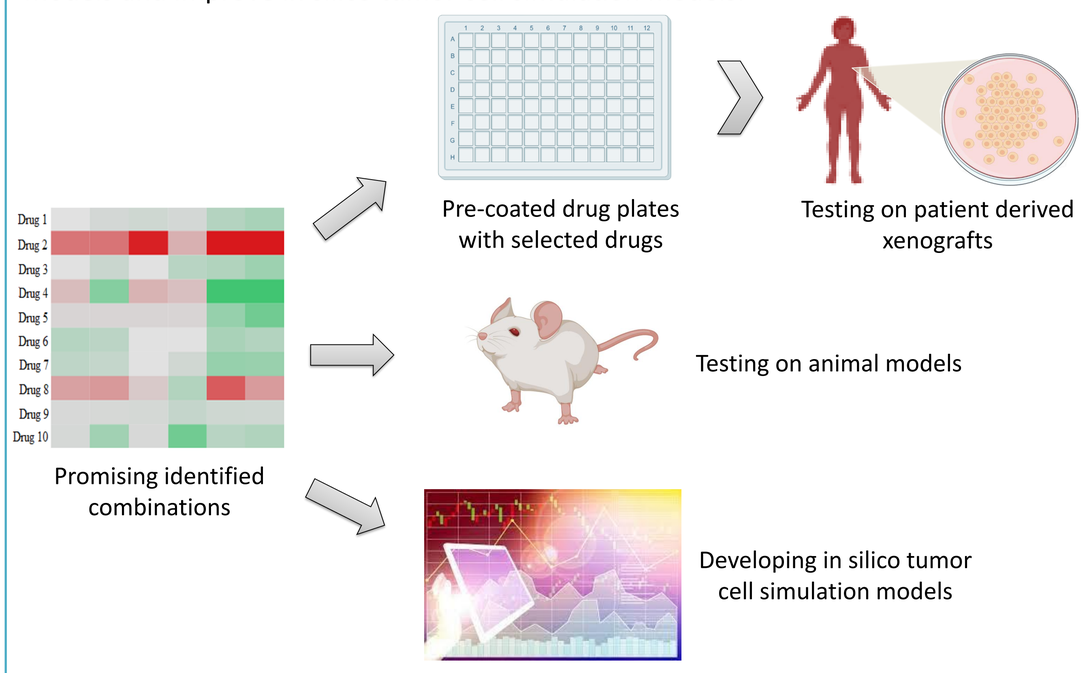
Experimental Protocol

Large-scale drug sensitivity screening allows the simultaneous testing of a multitude of drug combinations. This is especially important in a highly active research field where the number of new candidate therapeutic compounds is constantly on the rise. For this purpose, we designed a library of 64 drugs which we first tested as single therapies on 12 cell lines representing the different breast cancer sub-types. Accordingly, 53 drugs were selected for the combination drug screen which will be performed on at least 20 breast cancer cell lines. In addition, we explored the effect of some triple drug combinations in a smaller screen.



Application

After the identification of selected promising combination therapies, a smaller scale screening will be designed to validate the results on patient derived xenogafts using the same experimental protocol. In addition, the generated data will guide in vivo experiments on animal models and improve in silico tumor cell simulation models.



Acknowlegements

- The RESCUER project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant agreement No. 847912.
- This communication reflects only the author's view and the EC is not responsible for any use that may be made of the information it contains.