

# ESMO/BIG CURRICULUM IN TRANSLATIONAL RESEARCH IN BREAST CANCER

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The European Society for Medical Oncology (ESMO) and Breast International Group (BIG) recognised an existing gap in the formal educational criteria for medical professionals involved in translational research activities in breast cancer. The aim of this document is to support and better coordinate the training of medical personnel by emphasising the basic subjects to be considered within standardised curriculum.

Trainees should understand that translational research is a multidisciplinary team effort.

Trainees should understand that there is a variety of topics in translational research in breast cancer and the projects therefore could be managed differently.

The writing committee of this curriculum strongly advises that teaching faculty has a strong practical experience in the topic.

This curriculum targets professionals from all disciplines involved in translational research activities. The goal for the trainees is to introduce them to advances and pitfalls in translational research and to facilitate the involvement in translational research.

The core committee acknowledged the importance of functional imaging for translational research but felt that it would be beyond the scope of this program to cover this area. The committee would instead propose a separate program focusing on functional imaging.

## INTRODUCTION

## KNOWLEDGE

## LEARNING OBJECTIVE(S)

### Biology of cancer

Biology of cancer refers to molecular processes that lead to malignant transformation, cancer progression, and treatment resistance.

- Signal transduction
- Genetics and epigenetics
- DNA damage repair
- Invasion and homing
- Proliferation and metastasis
- Hormones and cancer transformation
- Cancer immunity
- Tumour stroma
- Cancer heterogeneity
- Stem cell hypothesis
- Angiogenesis
- Cancer cell metabolism
- Circulating disease

The trainee has to understand the biological impact of the most common molecular alterations observed in cancer.

### How to design a biomarker project?

Biomarker project is a study that aims to define the clinical outcome associated with a biological variable.

- Institutional requirements and rules in conducting translational research  
*Logistic, legal, ethical and other issues*
- Hypothesis generating vs. hypothesis driven projects
- How to get funding for translational research projects?  
*How to write a grant?*

At the end of training, the fellow should be able to design a biomarker project and to understand its impact and limitations.

### Biosamples collection and processing

Biosamples are specimens derived from tissues or liquids for biomarker research.

- Fitness for research purpose of biosamples
- Storage and biobanking
- Sample processing and preanalytical steps (extraction, quantification, qualification, morphological characterisation, tissue microarray)

The trainee should be able to define the threats and opportunities related to sample processing.

## Molecular techniques and analysis

Molecular techniques refer to tools that allow quantification of biological variable.

- Standard package in molecular laboratory  
*Cell culture, cell proliferation/viability assays, cell cycle analysis, apoptosis assays, Western/Northern/Southern Blot, Immunoprecipitation, pCR/qPCR, RNA interference (siRNA, shRNA), transfection and re-expression, cloning, (Sanger) sequencing, protein/RNA/DNA extraction, quantification and quality assessment*
- Functional validation
- Gene expression arrays
- Copy number arrays and SNP arrays
- Epigenetics
- Next generation sequencing
- Protein assays beyond IHC
- Metabolomics
- Cell culture
- Mouse models
- High-throughput interference technologies
- Circulating markers including circulating tumour cells
- Flow-cytometry
- Other

The trainee should be able to describe the techniques and understand their potentials and limits.

## Research in pathology

Pathology is a panel of technologies that allow assessing biological variables *in situ*.

- The standard package in pathology
- New techniques in pathology research

The trainee should be able to describe the main techniques in pathology and to understand their potentials and limitations.

## Publicly available tools and data

Data that are available from online resources may serve to correlate biological and clinical variables.

- Publicly available tools and data

The trainee should know about main online resources where data are stored and should be able to discriminate the biases related to the use of these data.

## Statistics and bioanalysis

Statistics and bioanalysis are a panel of methods to define if research hypothesis is valid.

- Statistical analysis plan
- Correlative analysis
- Outcome endpoints
- Pitfalls in statistical analysis

The trainee should understand the main statistical tests and pitfalls in statistical analysis.

## INTRODUCTION

## KNOWLEDGE

## LEARNING OBJECTIVE(S)

### Validation

Validation refers to the method of confirming preliminary data.

- Validation strategy
- Independent validation cohorts
- Validation of molecular assays
- Reverse translation back into clinical trials

The trainee should understand the importance of well designed validation studies and the importance of predefined hypotheses.

### How to report results in translational research?

Reporting of results is essential to disseminate novel findings/knowledge according to standardised criteria.

- REMARK guideline

The trainee should be able to write a paper reporting on biostudies. The trainee should be able to cite the main criteria from REMARK guideline.

### Target validation

Target validation refers to research approach with aim of defining whether a molecular process could be targeted for therapeutic purpose.

- Target validation

The trainee should be able to design a study that aims in validating a target.

### Early drug development

Early drug development refers to studies that aim to define preliminary toxicity, efficacy and treatment dose.

- Definition of DLT, MTD, and OBD
- Integration of late toxicities in decision for recommended doses
- Monitoring of drug safety
- Conventional and innovative design of phase I
- Dose finding step of phase I
- Principles of dose modifications in combination trials
- Goals and design of extension phase
- Basic principles and definition in pharmacokinetics
- How to explore pharmacodynamic endpoints
- Logistics and resource management in early drug development
- Basic principles in molecular screening
- Biomarker analyses in phase I

The trainee should be able to design a phase I trial.