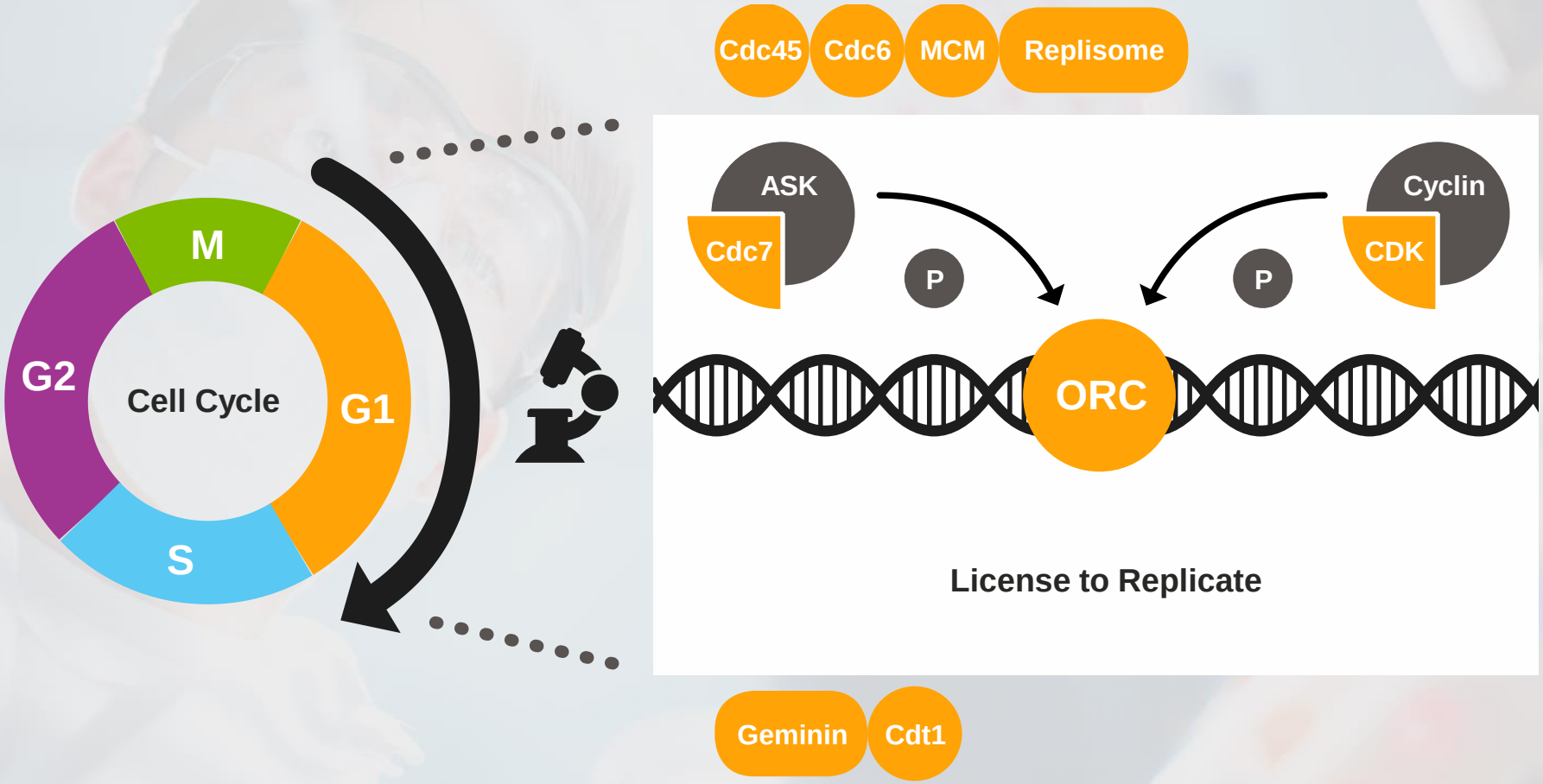
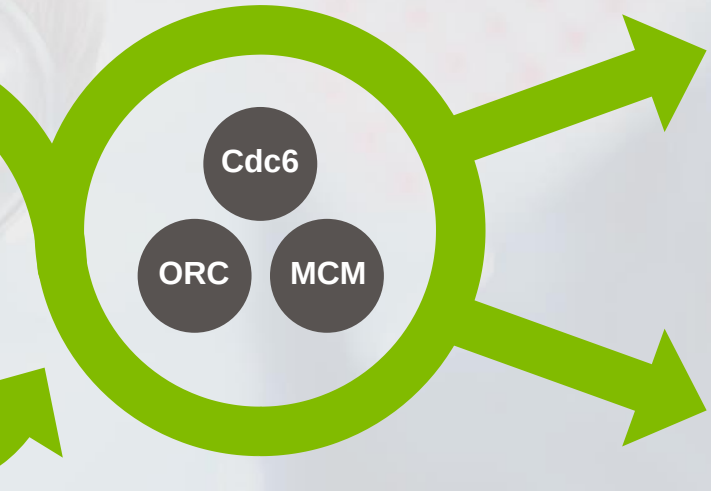
The Cell **Cycle** Cancer Test

The **DNA** Replication Initiation Machinery



Three Ways Out of Cycle

quiescence



differentiation

senescence

Introduction

DNA replication initiation proteins in tissue maintenance and cancer

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DNA replication initiation proteins in tissue maintenance and cancer

From bench to bedside – new tests for cancer detection and prognosis

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Requirement for Prognostic and Predictive Markers in Breast cancer

50% of patients who receive loco-regional treatment will never relapse, whereas the remainder will die of metastatic disease

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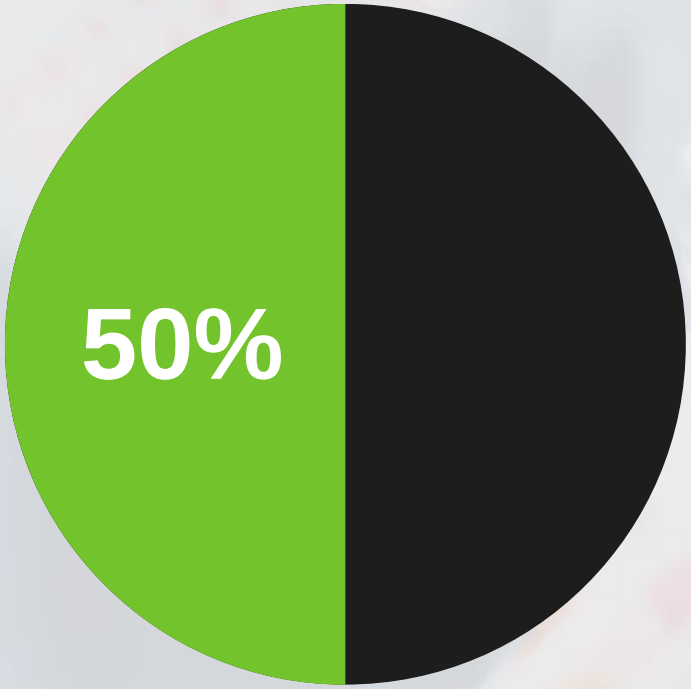
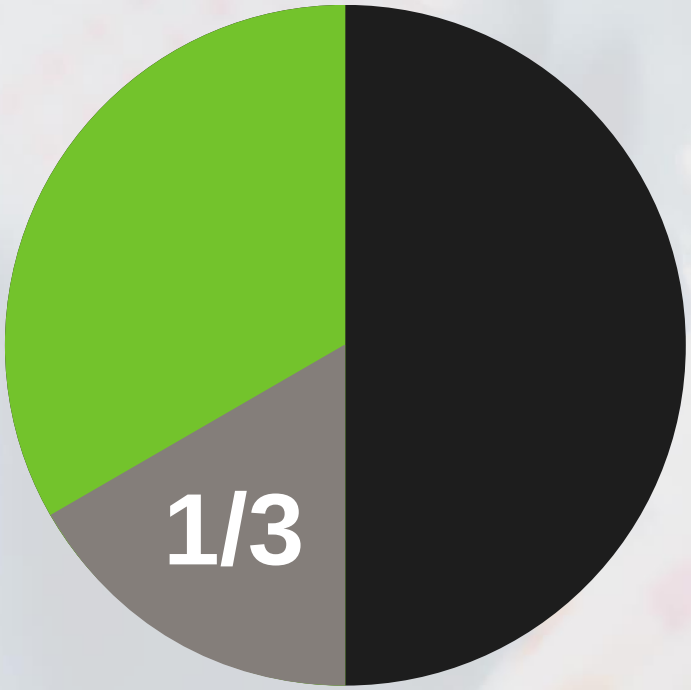


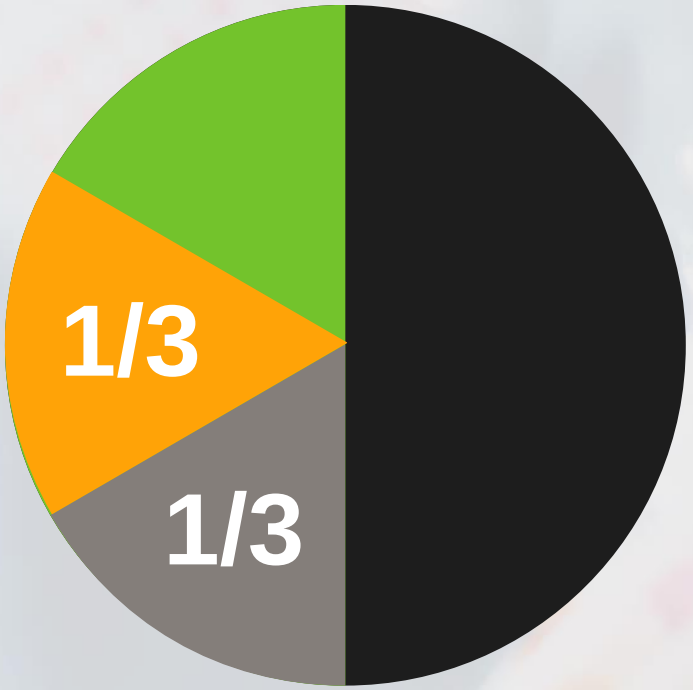
Requirement for Prognostic and Predictive Markers in Breast cancer

1/3 of patients who are node-negative will experience relapse

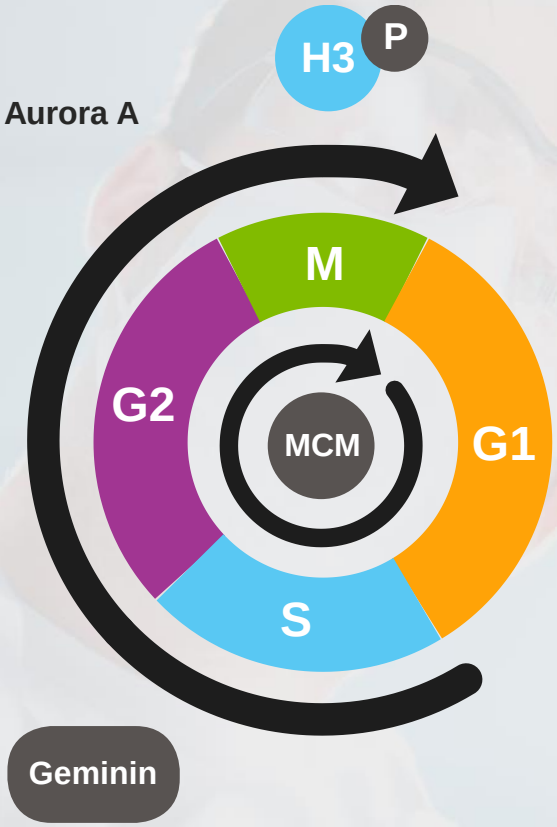


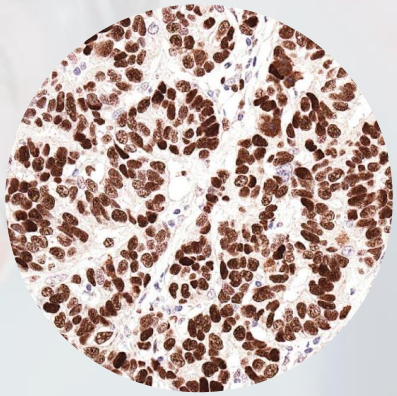
Requirement for Prognostic and Predictive Markers in Breast cancer

1/3 of node-positive patients not receiving adjuvant therapy will be disease-free after 10 years

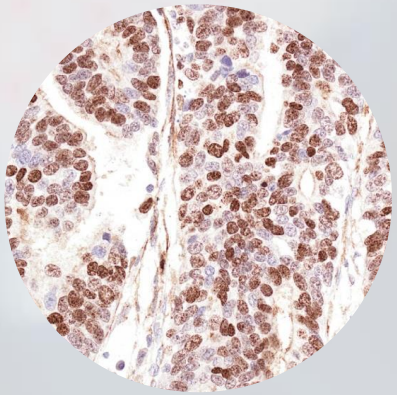


Cell Cycle Phase Progression in Breast Cancer

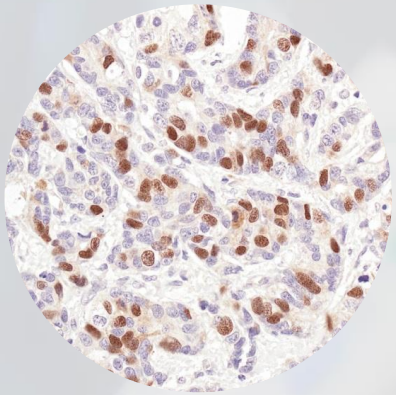




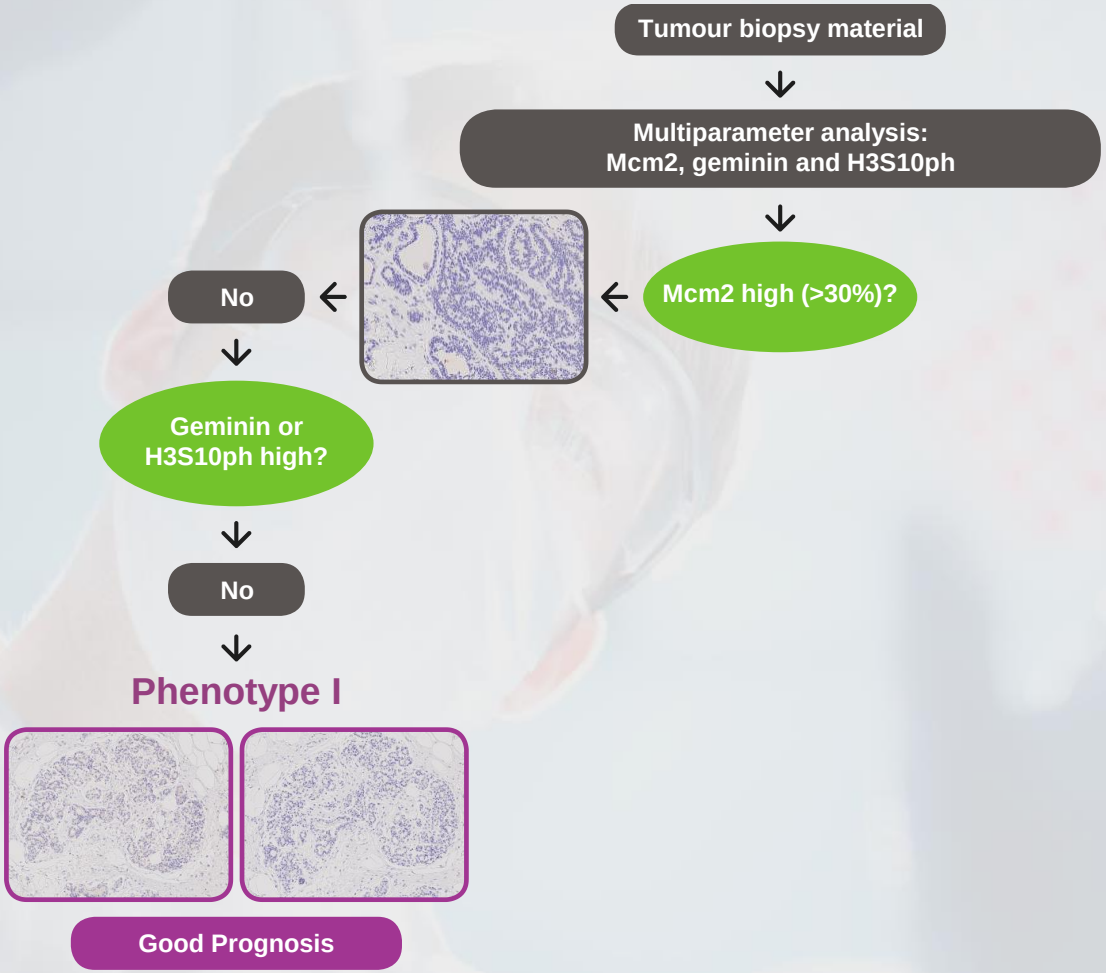
MCM2

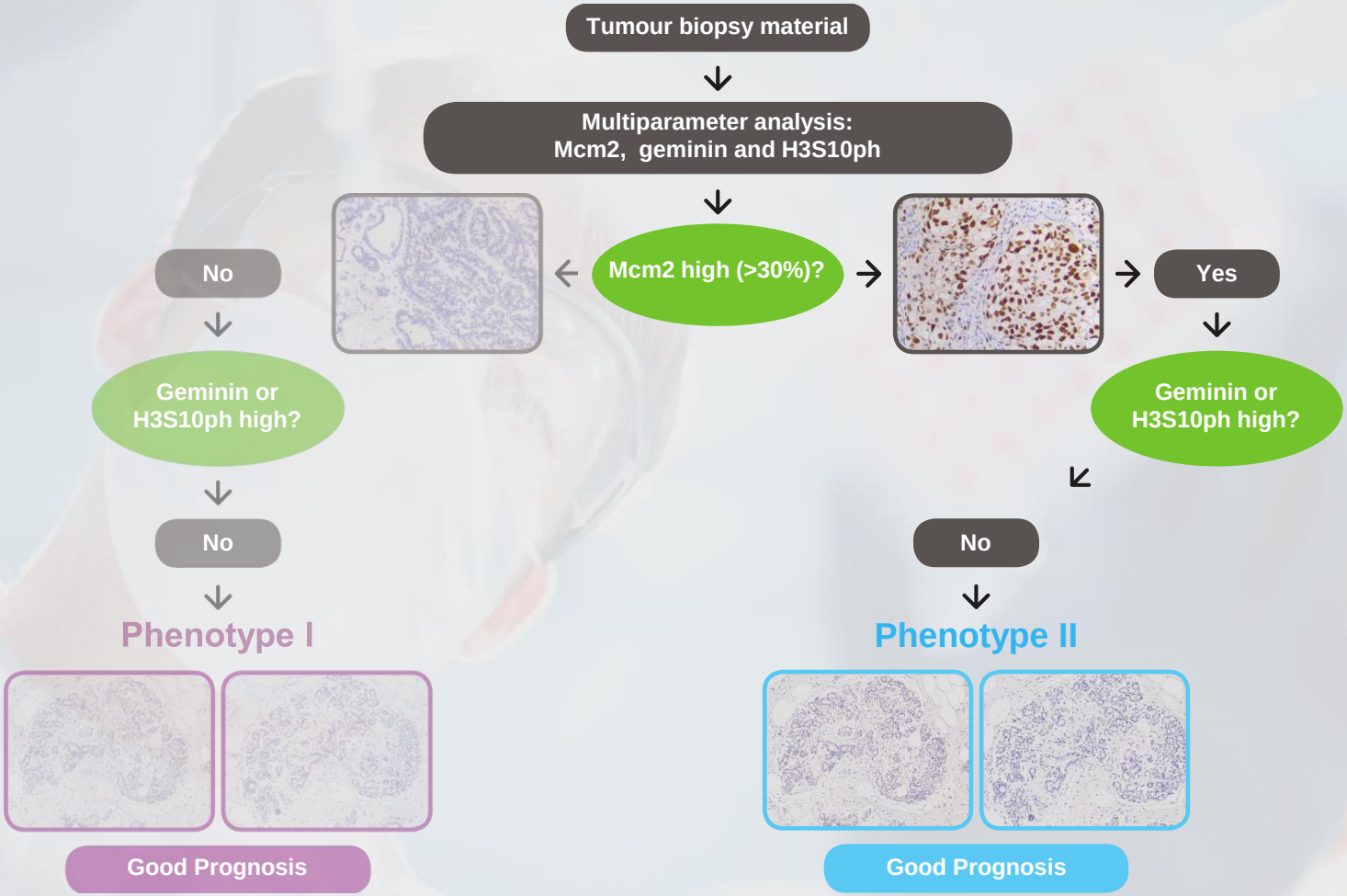


Ki67



Geminin


Tumour biopsy material
Multiparameter analysis:
Mcm2, geminin and H3S10ph
Mcm2 high (>30%)?
No
Geminin or
H3S10ph high?
No
Phenotype I
Good Prognosis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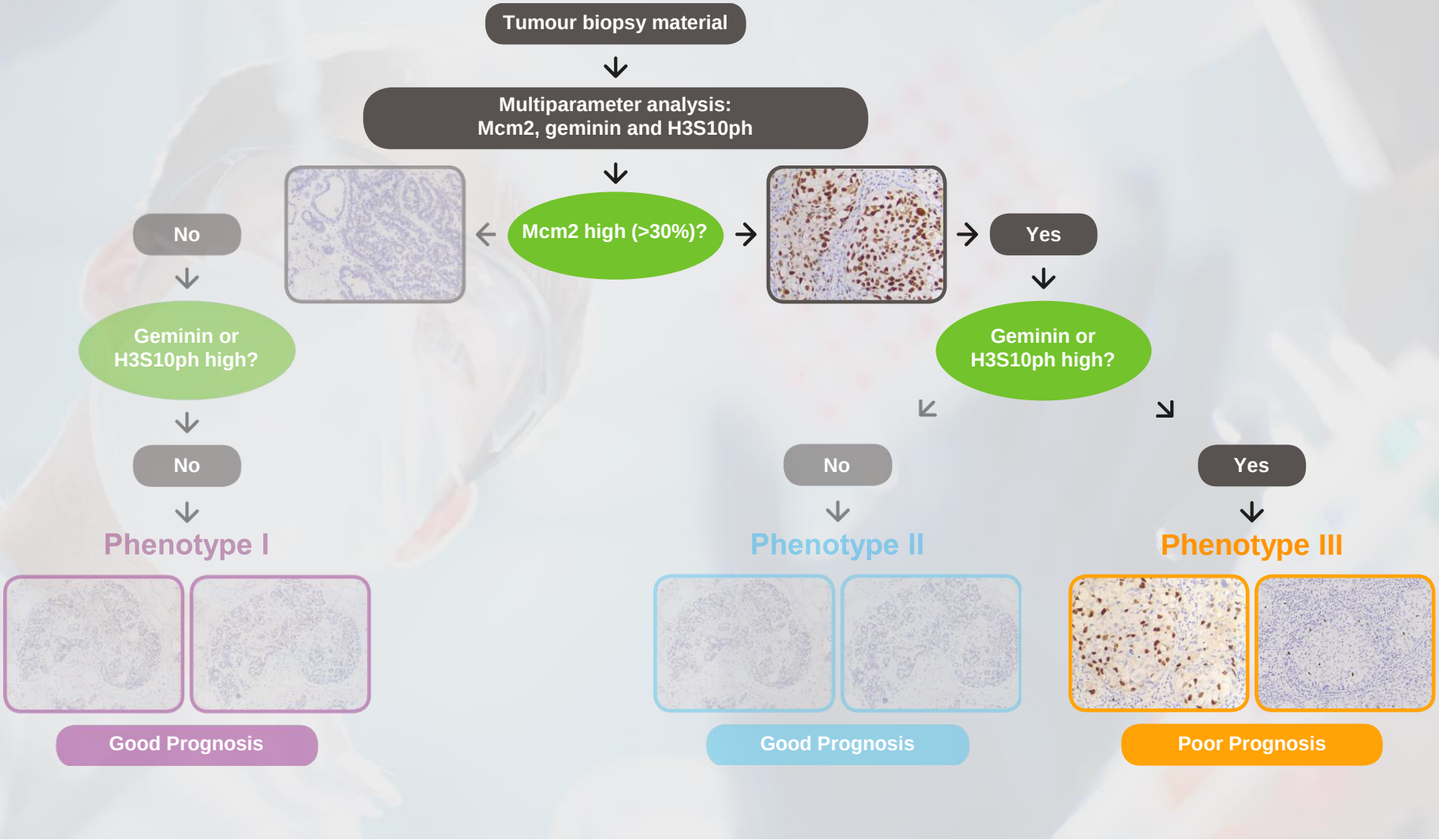
Mcm2 high (>30%)?
No
Yes
Geminin or
H3S10ph high?
Geminin or
H3S10ph high?
No
No
Phenotype I
Phenotype II
Good Prognosis
Good Prognosis


Tumour biopsy material
Multiparameter analysis:
Mcm2, geminin and H3S10ph
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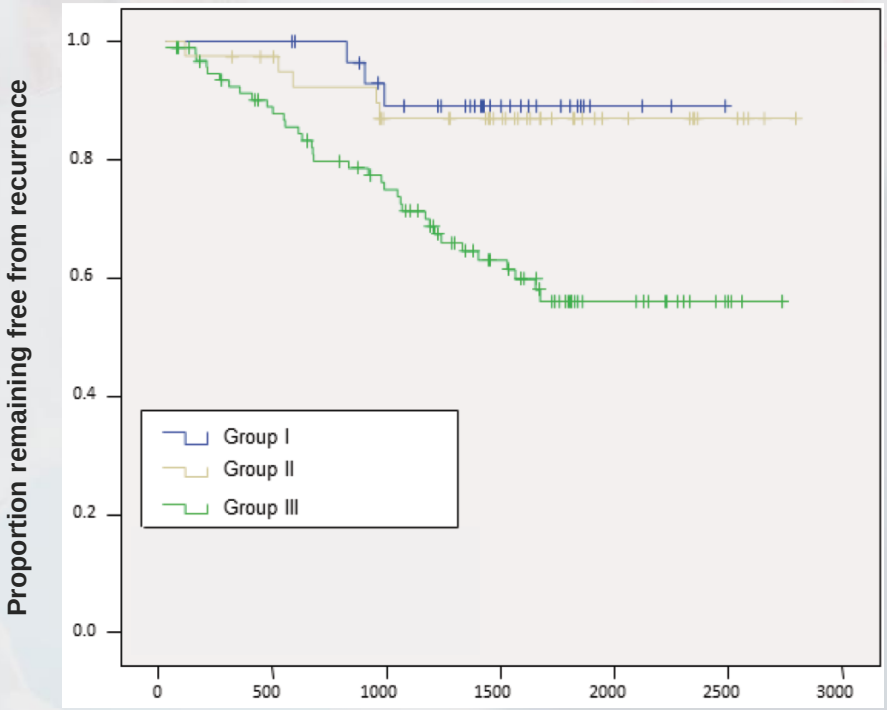
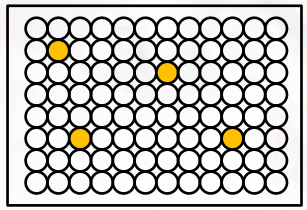
No
Yes
Geminin or
H3S10ph high?
Geminin or
H3S10ph high?
No
No
Yes
Phenotype I
Phenotype II
Phenotype III
Good Prognosis
Good Prognosis
Poor Prognosis

Cell Cycle State Predicts the Outcome of Breast Cancer after Surgery





Immunisation

↓

Clone generation

many clones

Clone pre-selection (ELISA)

12

Clonal stability and Isotype homogeneity

11

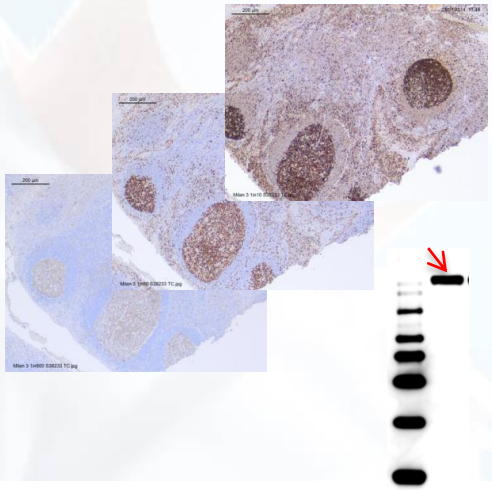
IHC titration and reproducibility

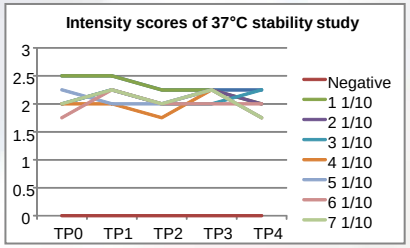
7

Accelerated antibody stability study

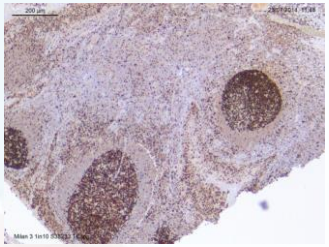
3

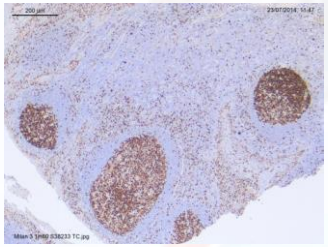
Development

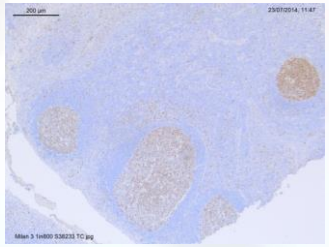


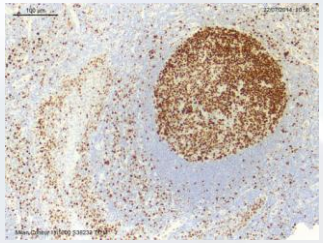


IHC titration curve Mcm2 antibodies





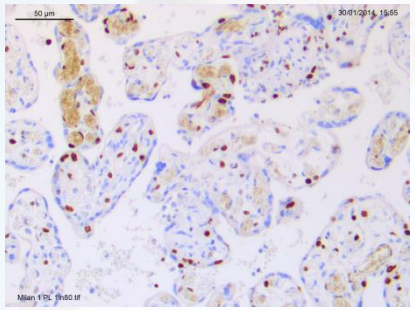




Mcm2 BD Ab

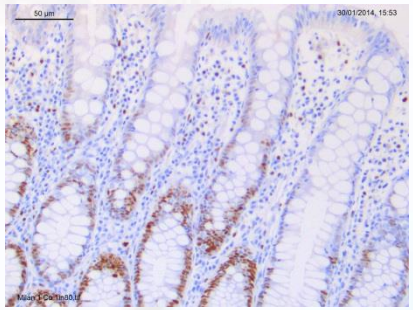
Validation in tissues with **varying expression** levels

High



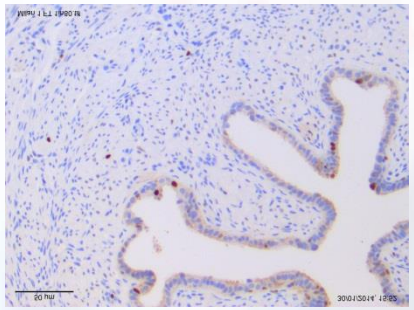
Placenta

Medium



Colon

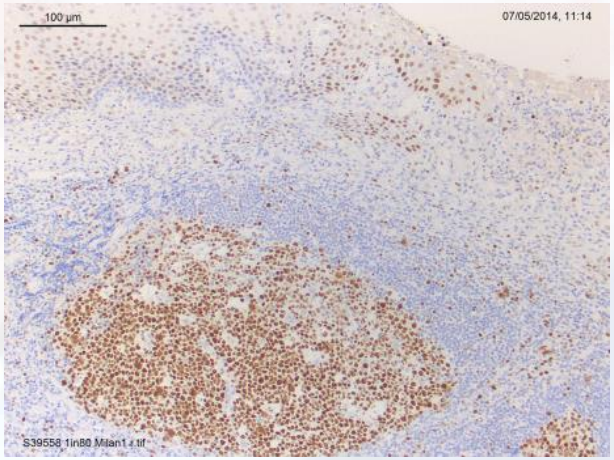
Low



Fallopian tube

Stability testing of Ab clones

37°C Stability
Study day 80



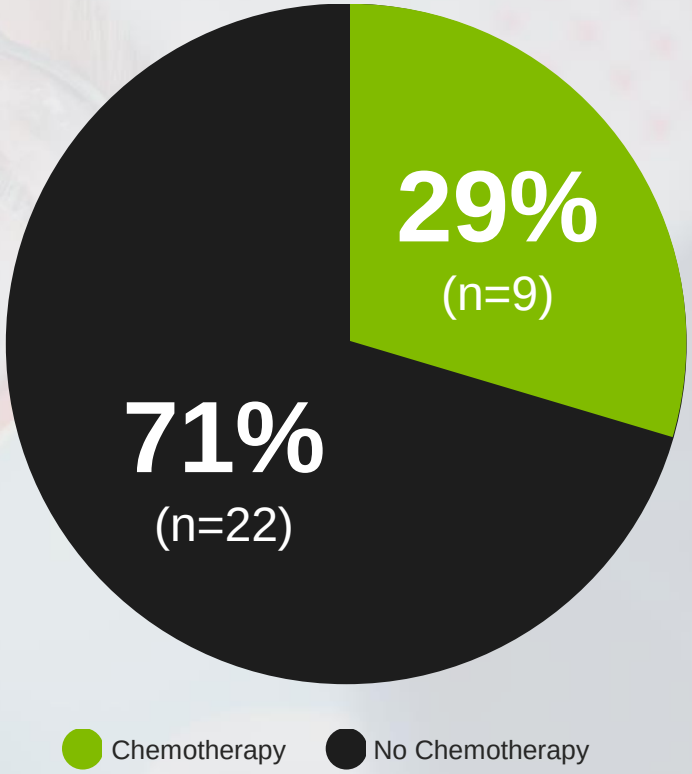
Select stable clones at a minimum of 18 months equivalent real time

Over and **under treatment** for patients with breast cancer?

Over and undertreatment for patients with breast cancer?

Phenotype I

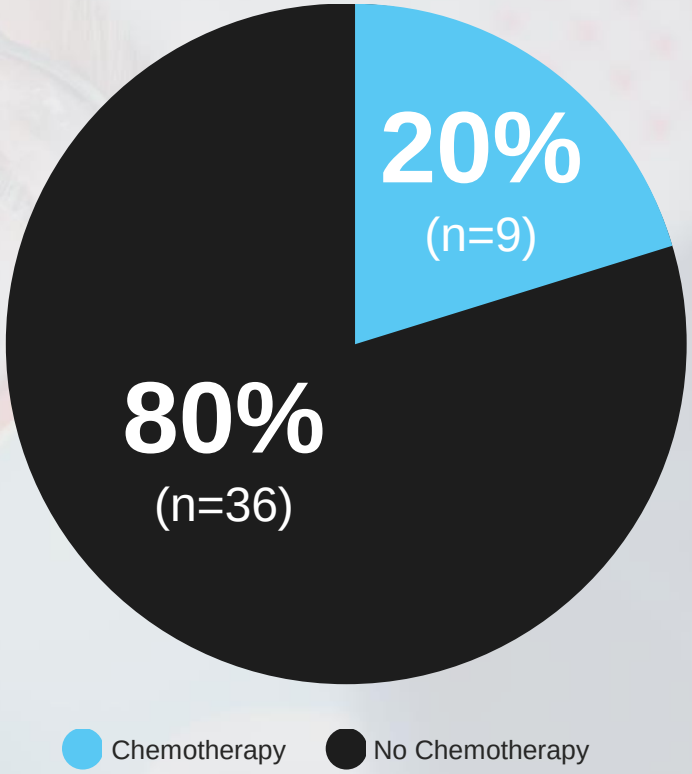
24% (18/76) of patients received adjuvant chemotherapy with minimal benefit



Over and undertreatment for patients with breast cancer?

Phenotype II

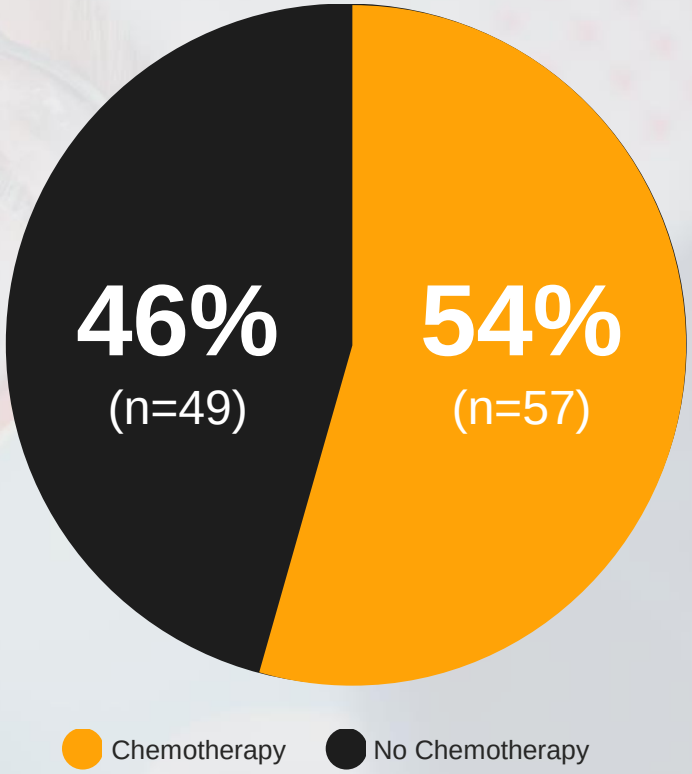
24% (18/76) of patients received adjuvant chemotherapy with minimal benefit



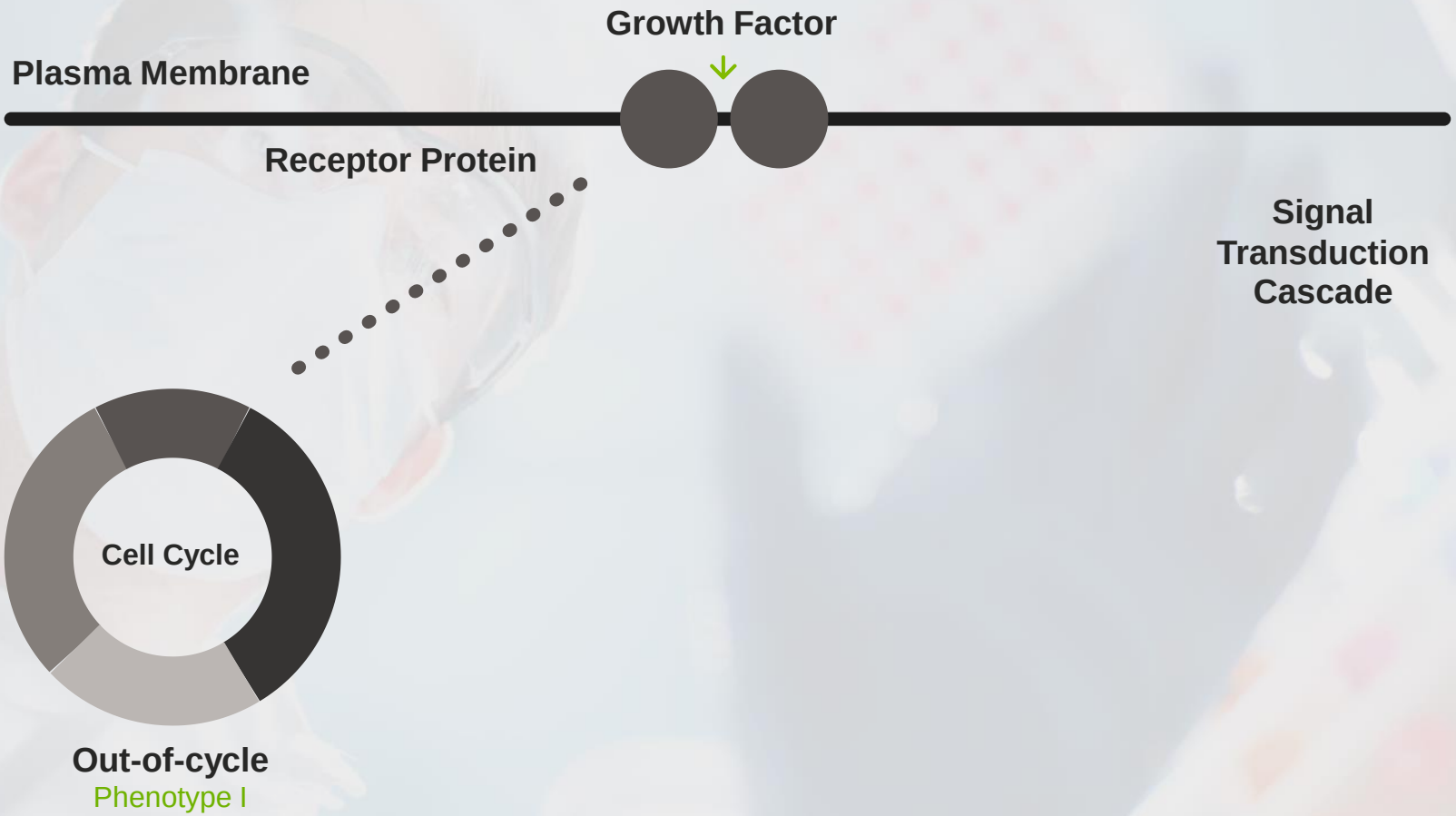
Over and **under treatment** for patients with breast cancer?

Phenotype III

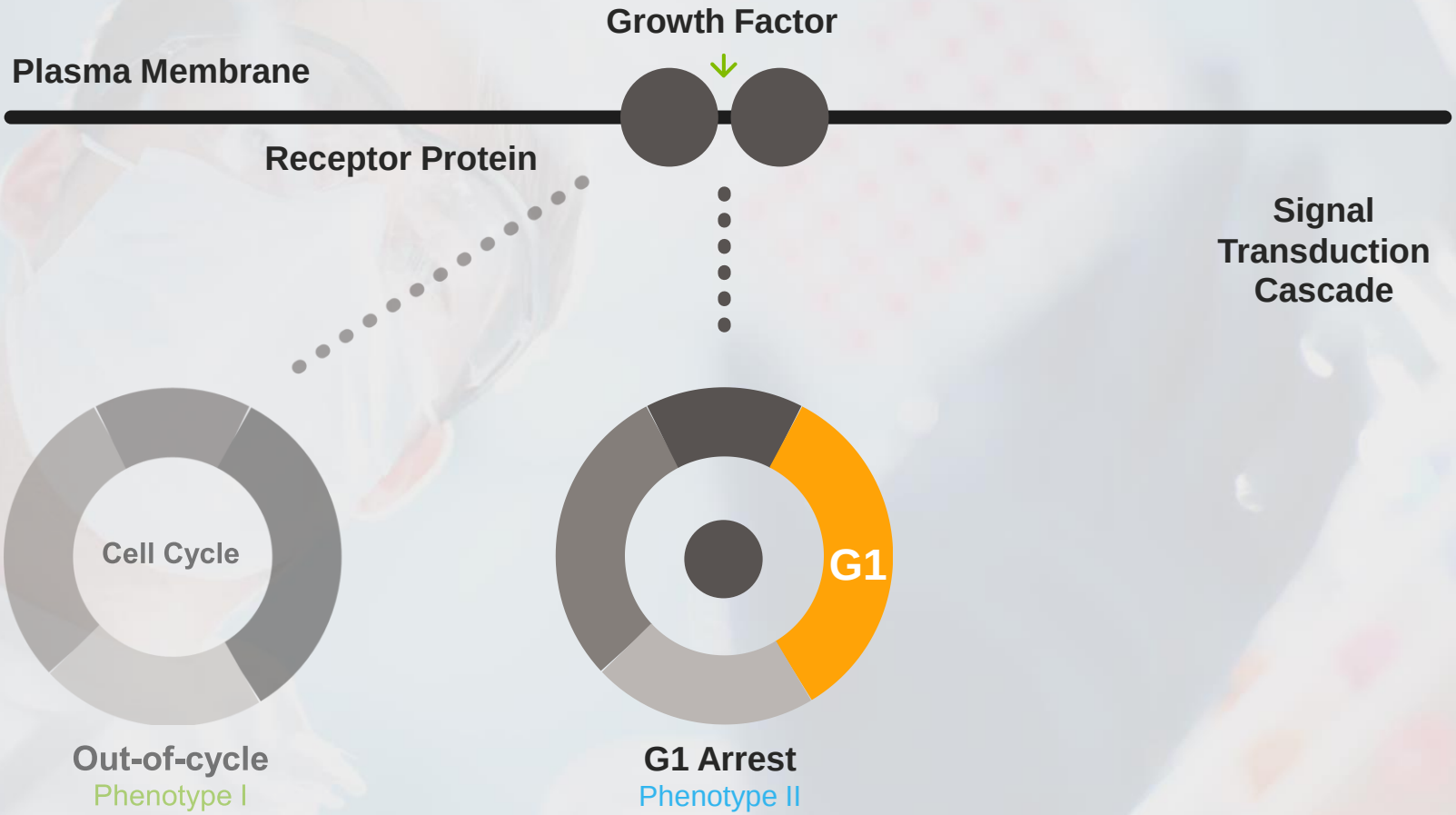
46% (49/106) of patients did not receive treatment with adjuvant chemotherapy



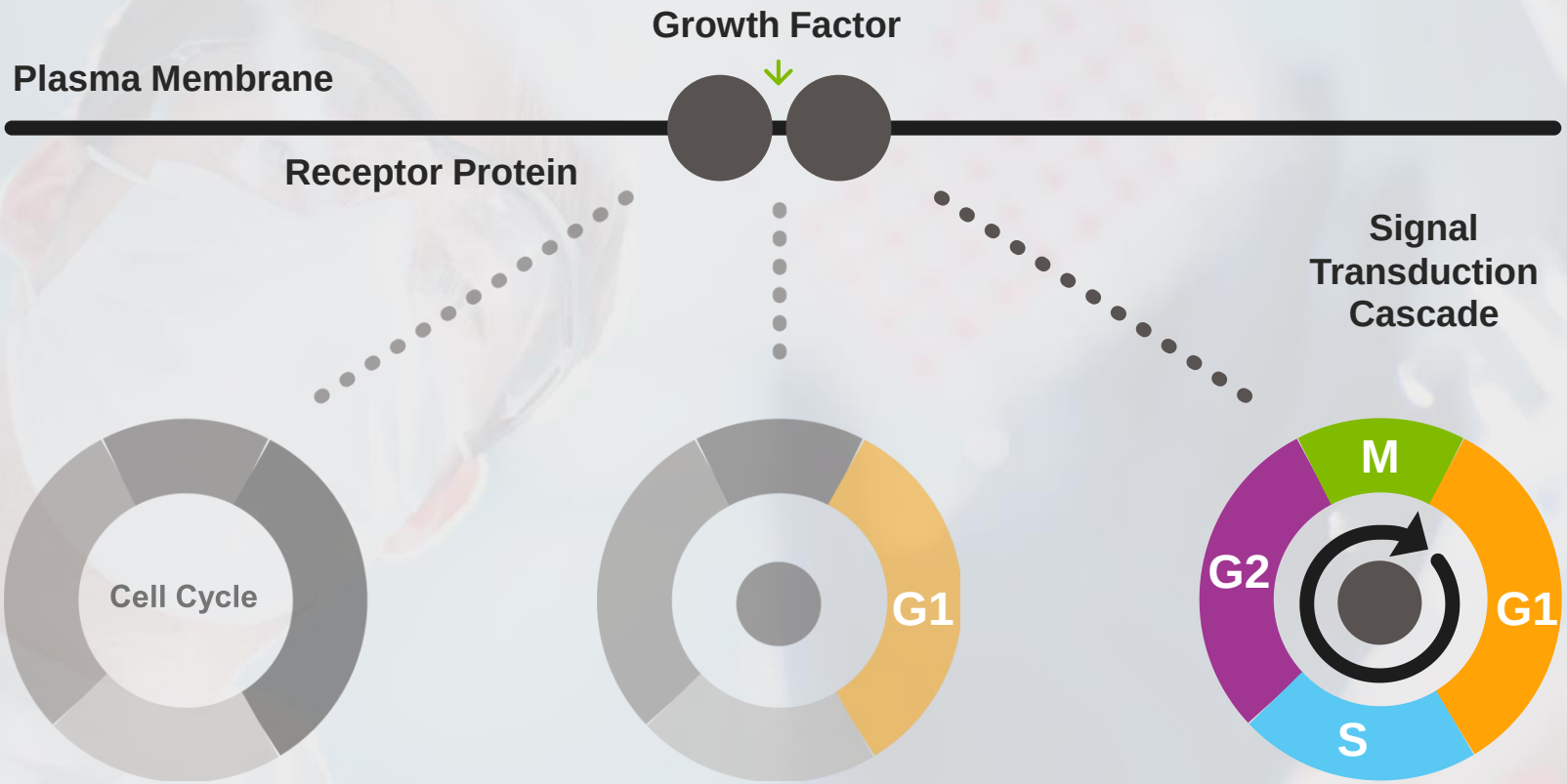
Failed trials? Let FGL find out why…



Failed trials? Let FGL find out why…



Failed Clinical trials? Let FGL find out why…



Advantages

- Can be used for all forms of breast cancer
- Simple, inexpensive IHC based test
- Identification of CT sensitive and insensitive tumours for breast cancers
- Enables patient stratification for clinical oncology trials
- Applicable to FFPE samples

Thank You
www.fglabs.com