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INSEL SPITAL
HOPITAL DE L'ILE

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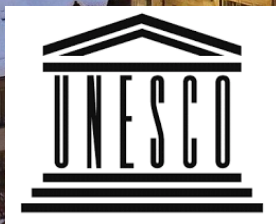
**UNIVERSITÄT
BERN**



Willkommen
an der

Klinik und Poliklinik
für
Medizinische Onkologie

Prof. Martin Fey



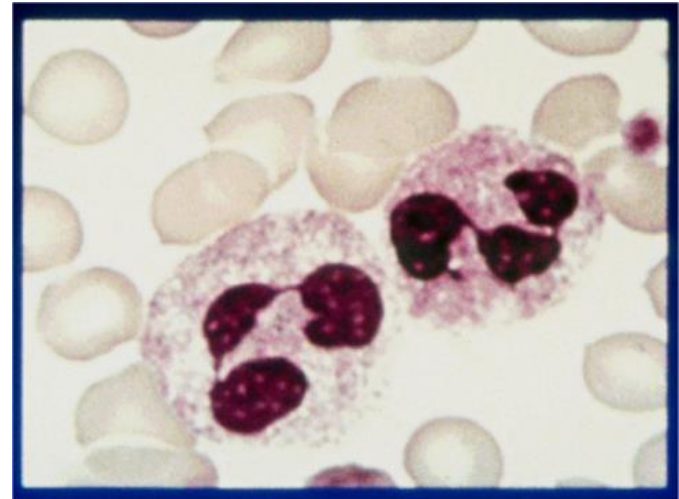
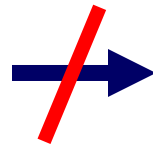
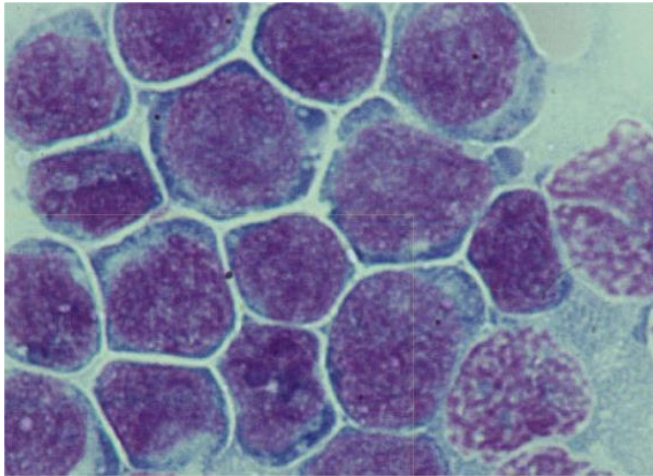
Haematology Centre @ Tallinn



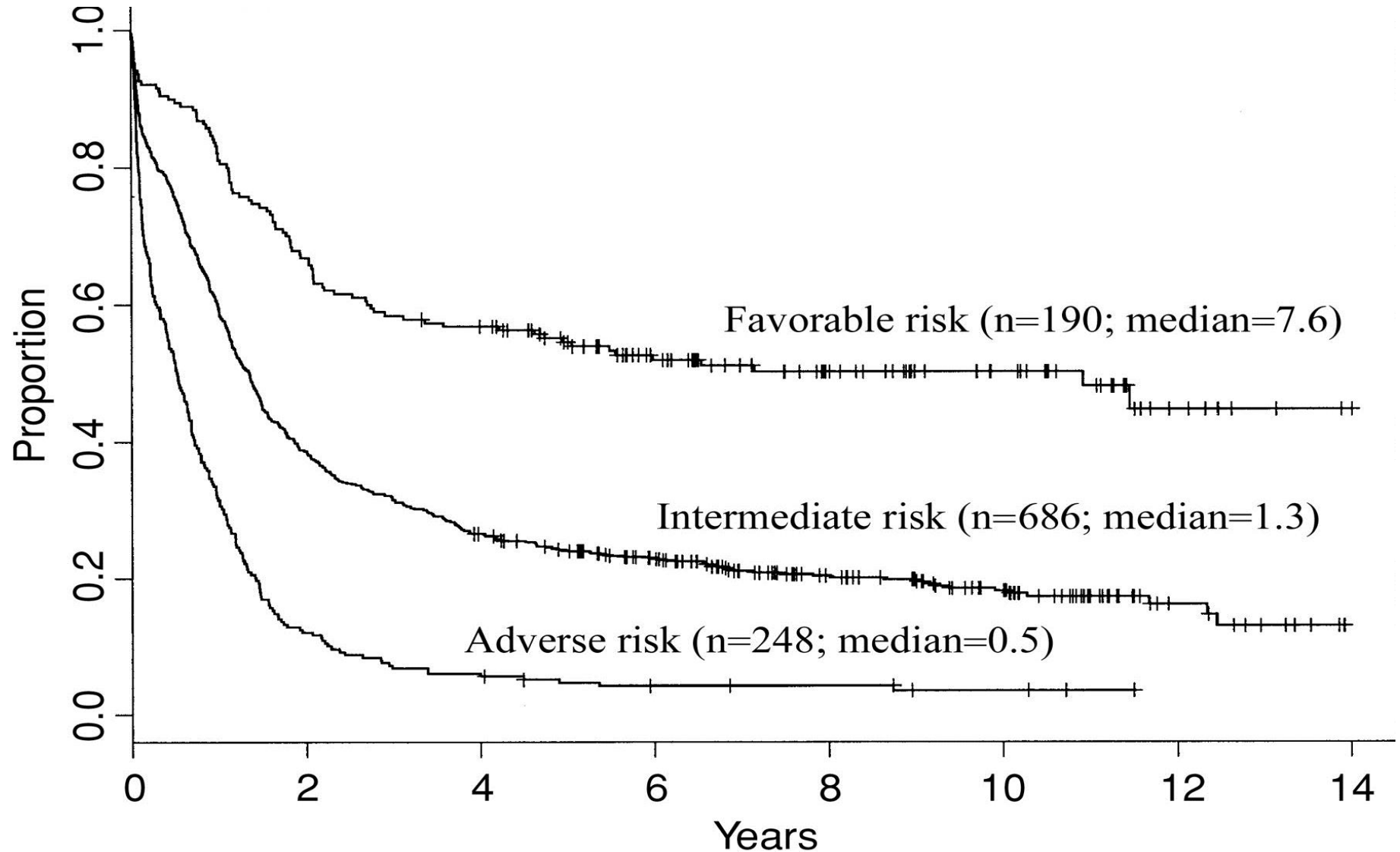
Acute Myeloid Leukaemia

Blasts

- fail to die
- fail to differentiate
- fail to function properly



AML overall survival



Leukaemia Ward

„R Nord“

125

126a

126b

127a

127b

128

3+7
AML

3+7
AML

3+7
AML

3+7
AML

3+7
AML

130

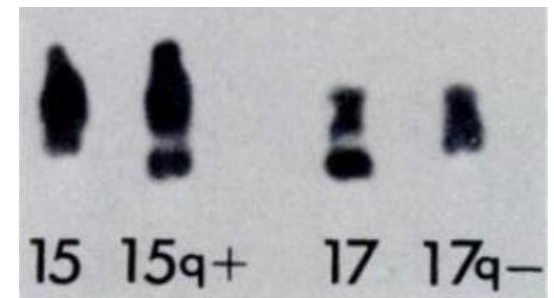
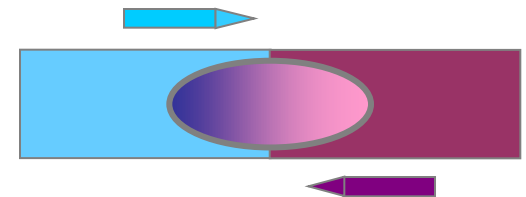
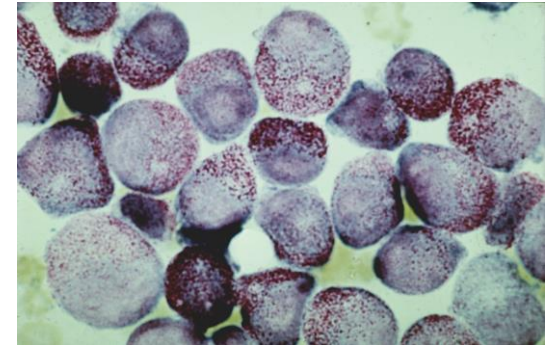
131

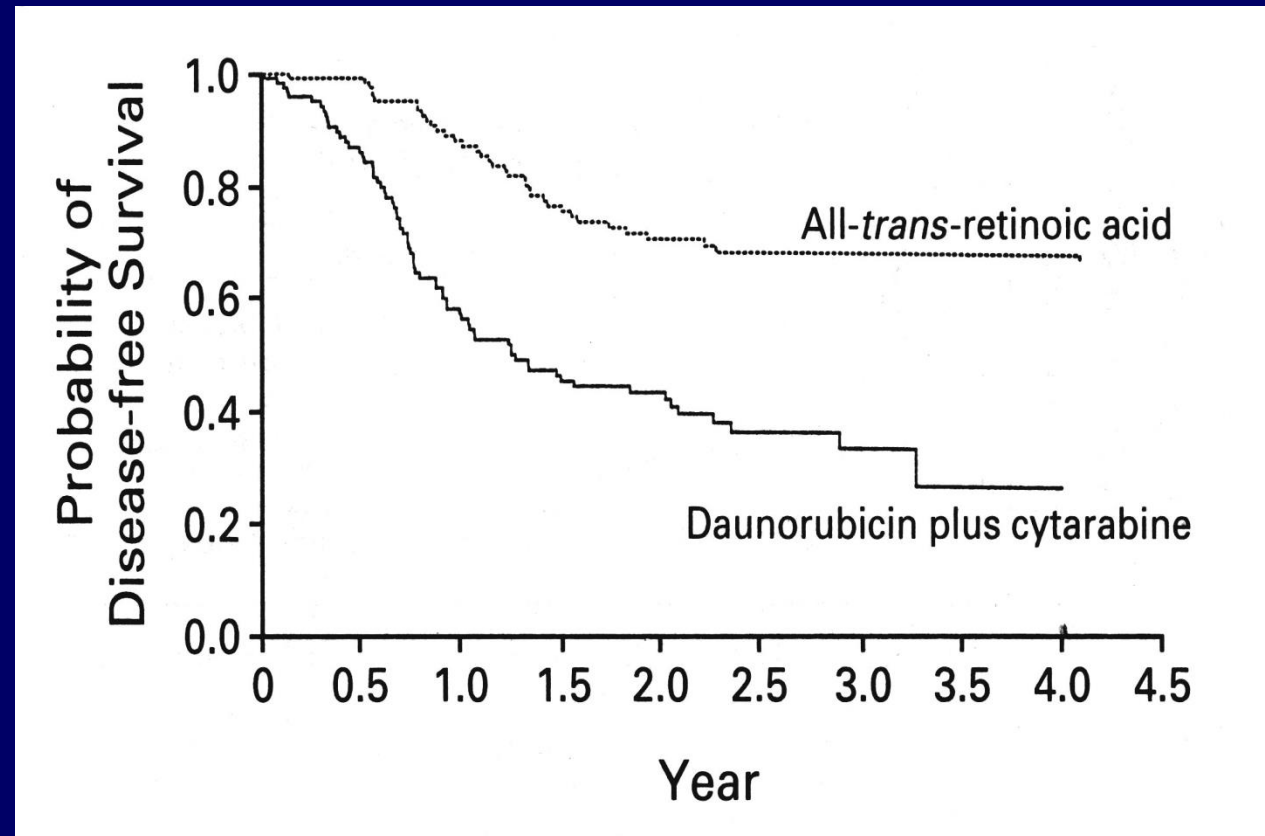
3+7
AML

Acute promyelocytic leukaemia

APL (FAB M3)

- Distinct AML subtype
- Good prognosis
- Translocation **t(15;17)**
- PML-RAR α fusion protein blocking RAR α -mediated gene transcription:
= **myeloid maturation block**





ATRA as a treatment for APL NEJM 1997; 337: 1021

Leukaemia Ward

„R Nord“

125

126a

126b

127a

127b

128

3+7
AML

3+7
AML

3+7
AML

3+7
AML

3+7 ATRA
AML

130

131

3+7
AML

AML

50 %

t(15;17)

t(8;21)

abn(11q23)

inv(16)

monosomies

complex

karyotype

etc.

50 %

**Normal
karyotype**

125

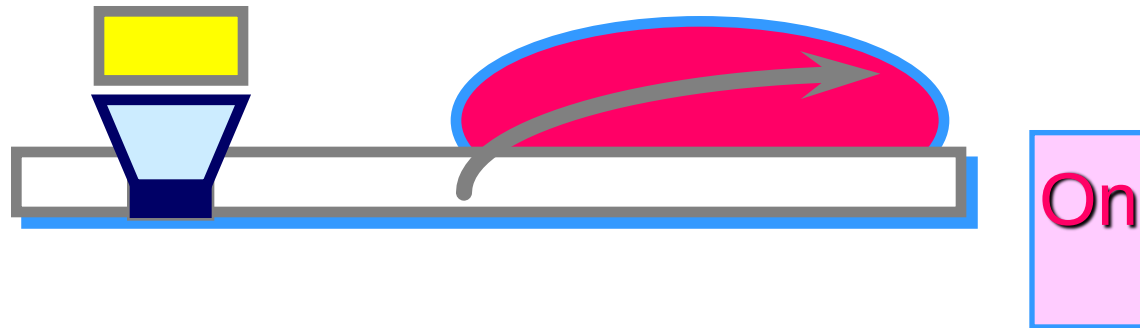
AML

Leukaemia ward „R Nord“

125	126a	126b	127a	127b	128
3+7 AML	3+7 AML	3+7 AML	3+7 AML		3+7 ATRA APL
AML with a normal karyotype and with a mutation in the C CAAT / E nhancer B inding P rotein α gene CEBP α POS AML				130	131
					3+7 AML

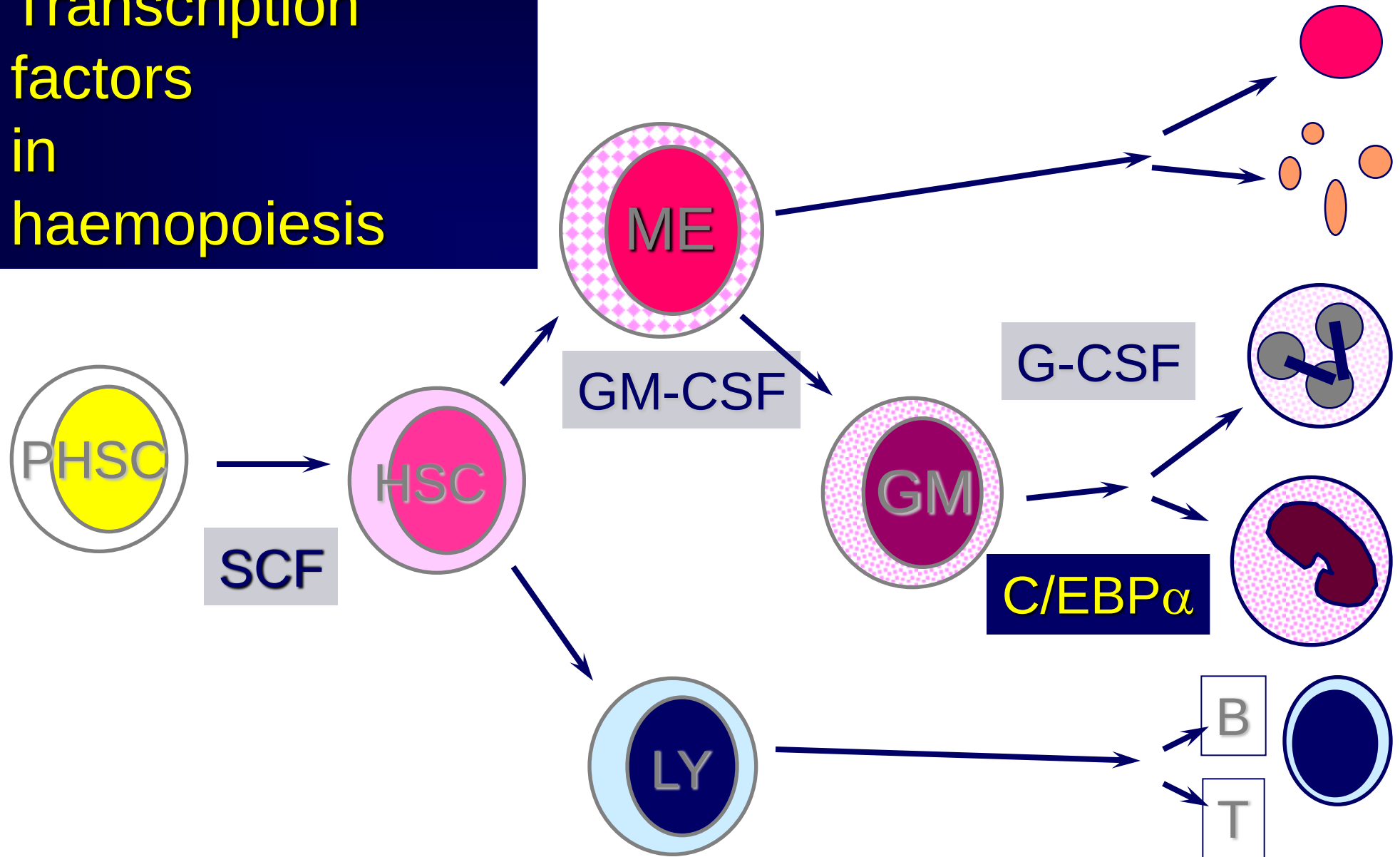
Transcription factors

Gene

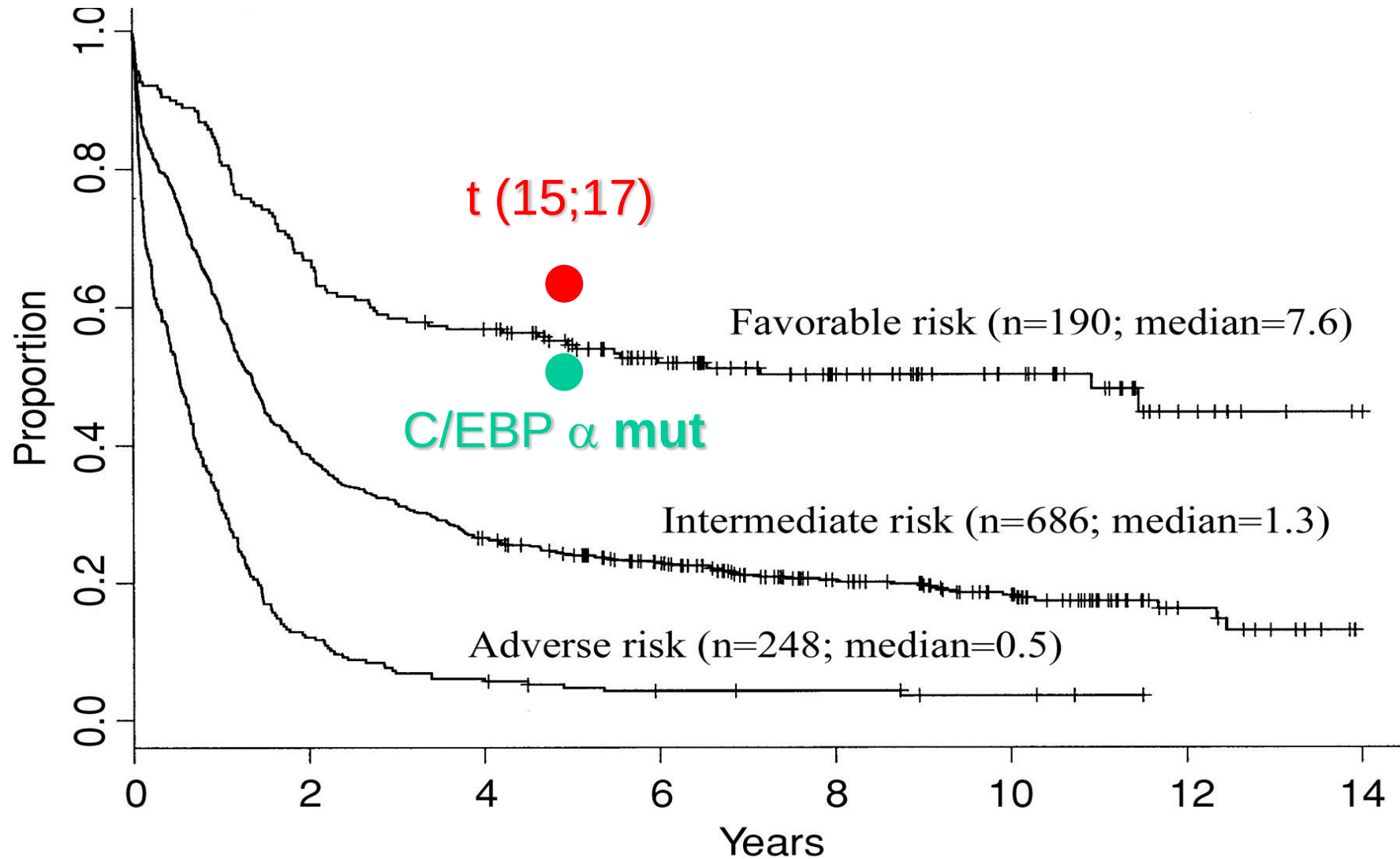


Regulation of gene transcription

Transcription factors in haemopoiesis



Prognosis of AML with C/EBP α mutations



AML

50 %

t(15;17)
t(8;21)
abn(11q23)
inv(16)
monosomies
complex
karyotype
etc.

50 %

**Normal
karyotype**

C/EBP α mut

NPM_c+

FLT3 ITD

Leukaemia ward

„R Nord“

125

126a

126b

127a

127b

128

3+7
No allo

3+7

3+7

3+7

3+7 ATRA
APL

AML

Normal karyotype

C/EBP α - POS

130

131

3+7

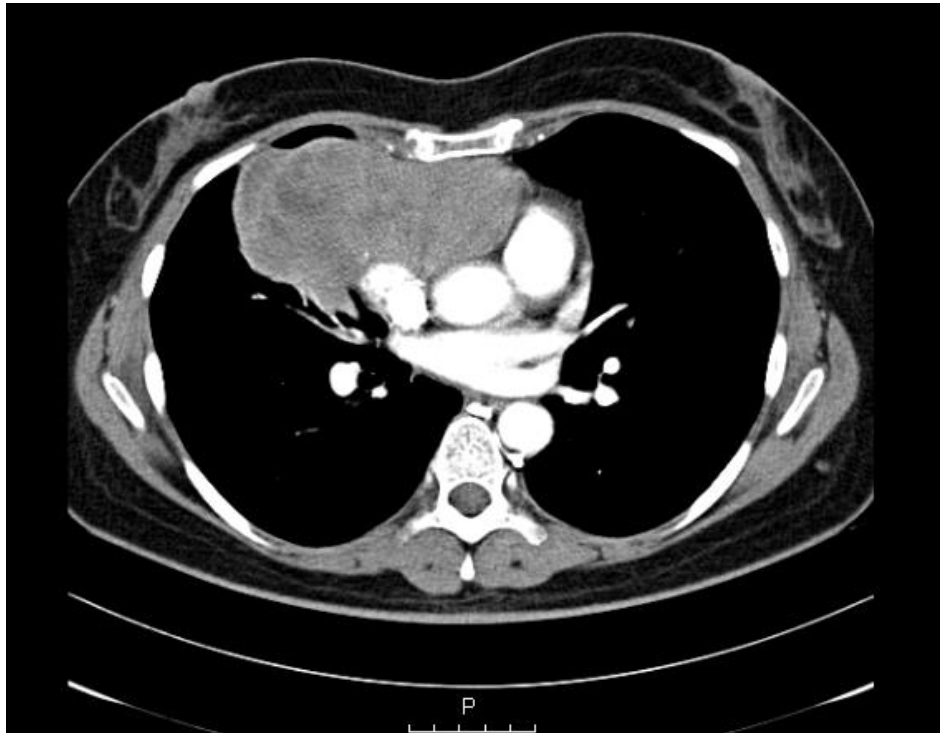
Leukaemia molecular biology

- Molecular AML entities with distinct diagnostic features, clinical characteristics and predictive markers to select the best treatment options
- 3+7 is **no** longer a glove that fits all !



Pat. D. J. *1968 - 46 years old

2012 cough and dyspnoea
CT scan of thorax



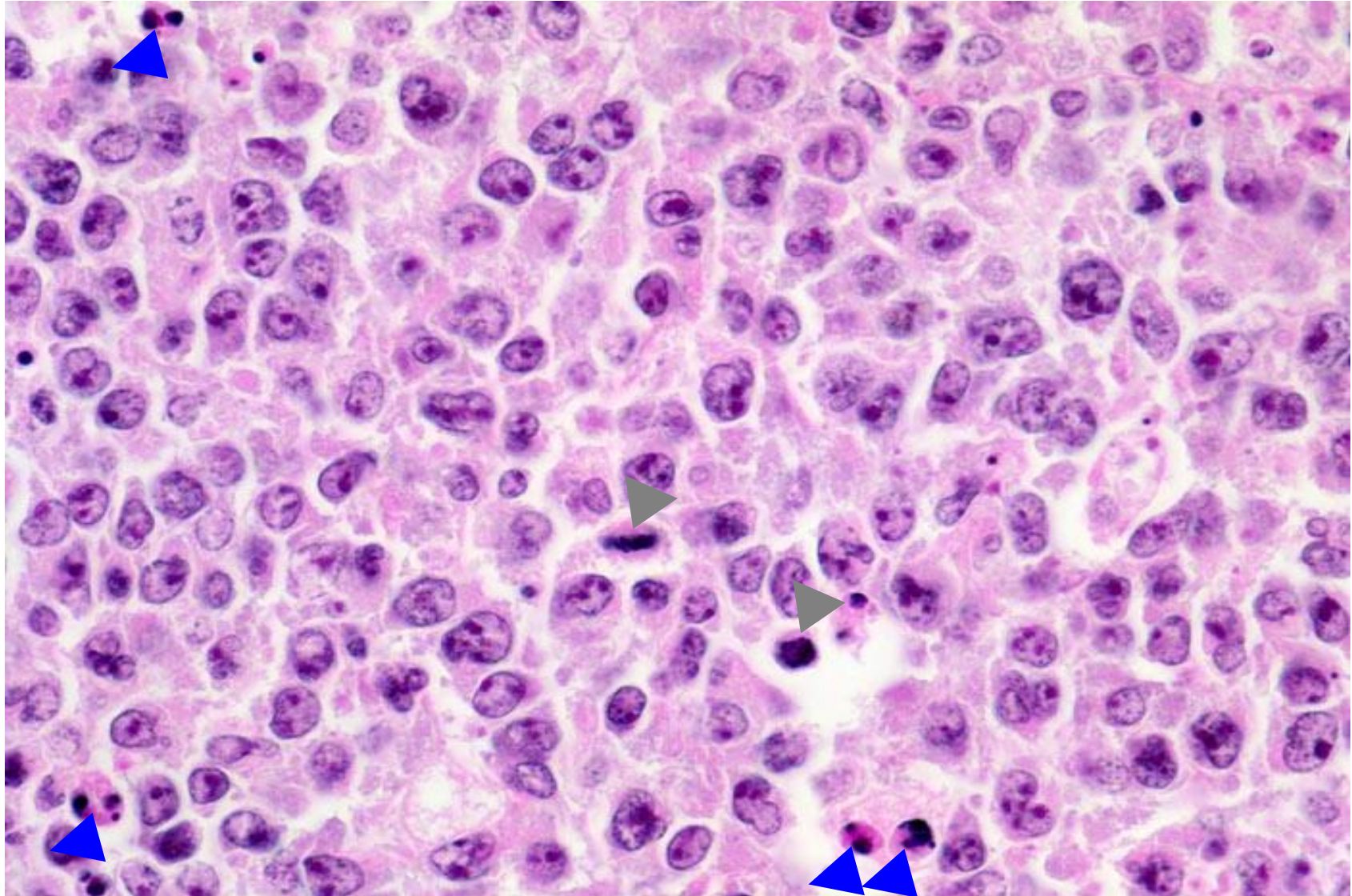
She could have ...

- Hodgkin's lymphoma
- Diffuse large B-cell Non Hodgkin's lymphoma
- Primary mediastinal large B-cell lymphoma (sclerosing)
- ... another cancer ...

Diffuse large B-cell Non Hodgkin's lymphoma

Apoptotic debris

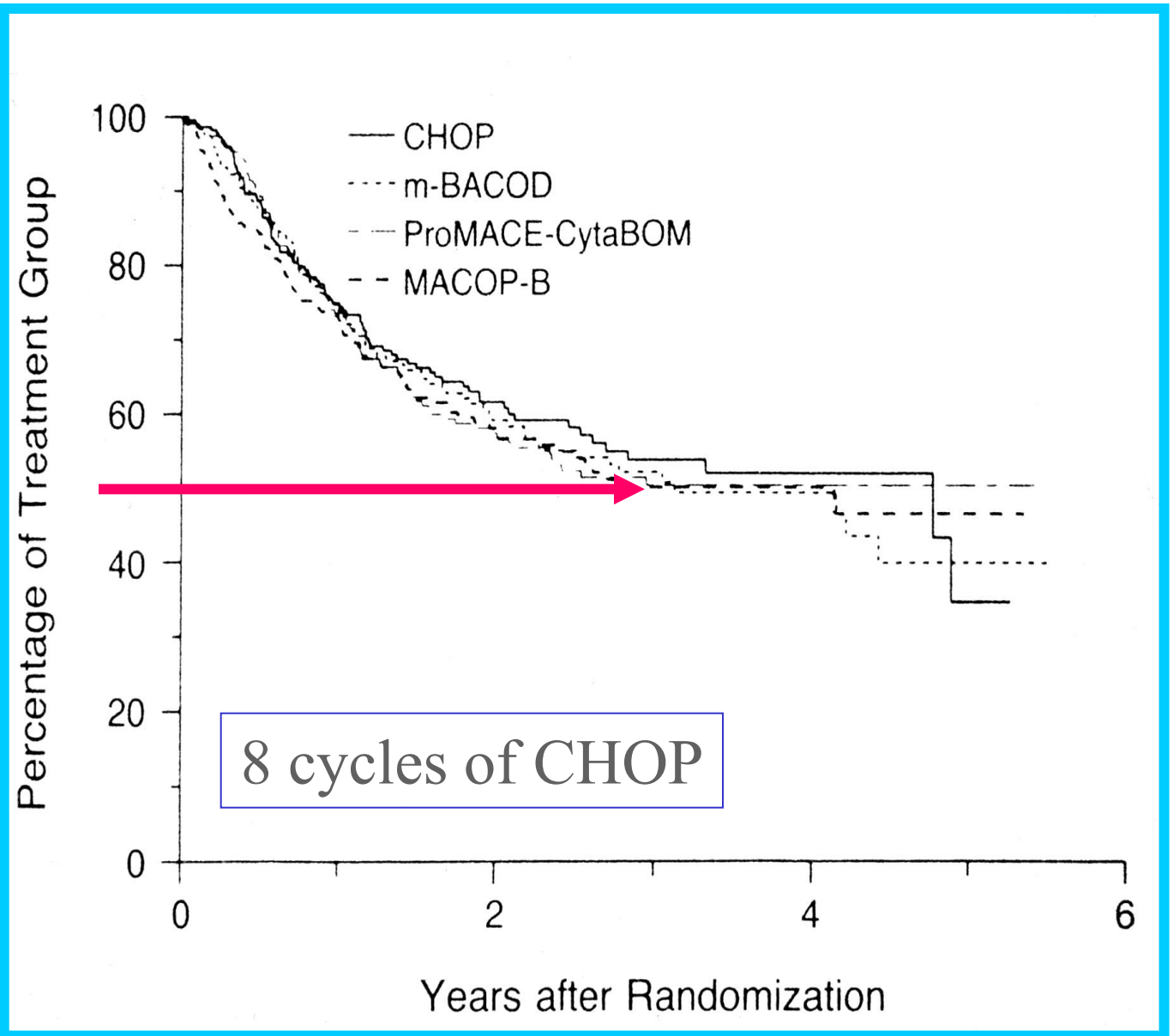
Mitotic figures



Intergroup

NEJM 1993

„Diffuse
large B-cell“
Non Hodgkin
Lymphom



Tumour therapy with new drugs



-mabs

Monoclonal antibodies

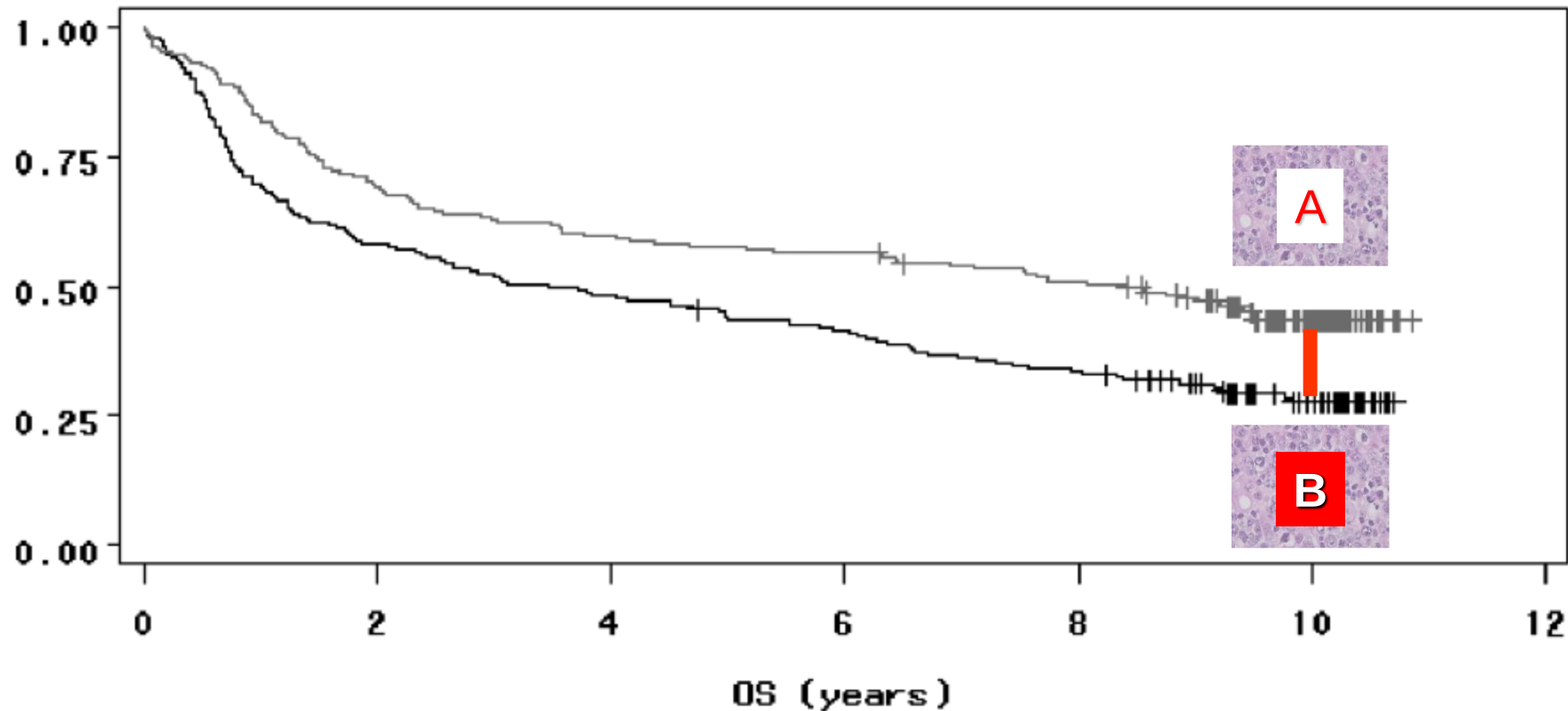
-nibs

„small molecules“
mostly
tyrosine kinase inhibitors

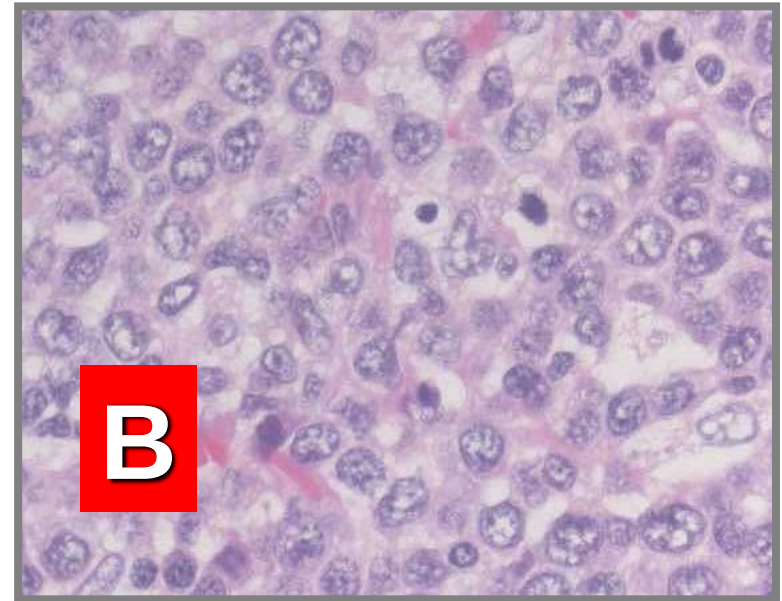
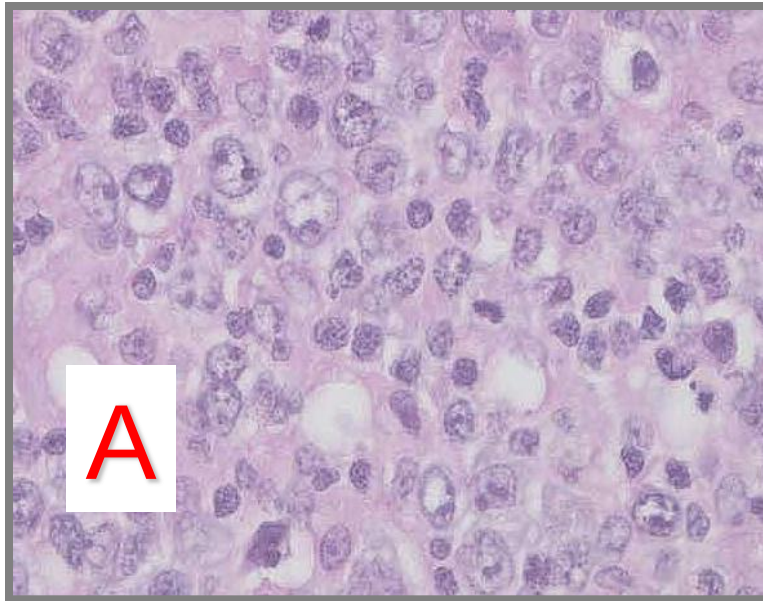


Rituximab – an anti-CD20 mab - in diffuse large B-cell NHL

Patients aged 60 – 80 years. Blood 2010; 116: 2040



DLBCL? like is not like!



Single gene



off



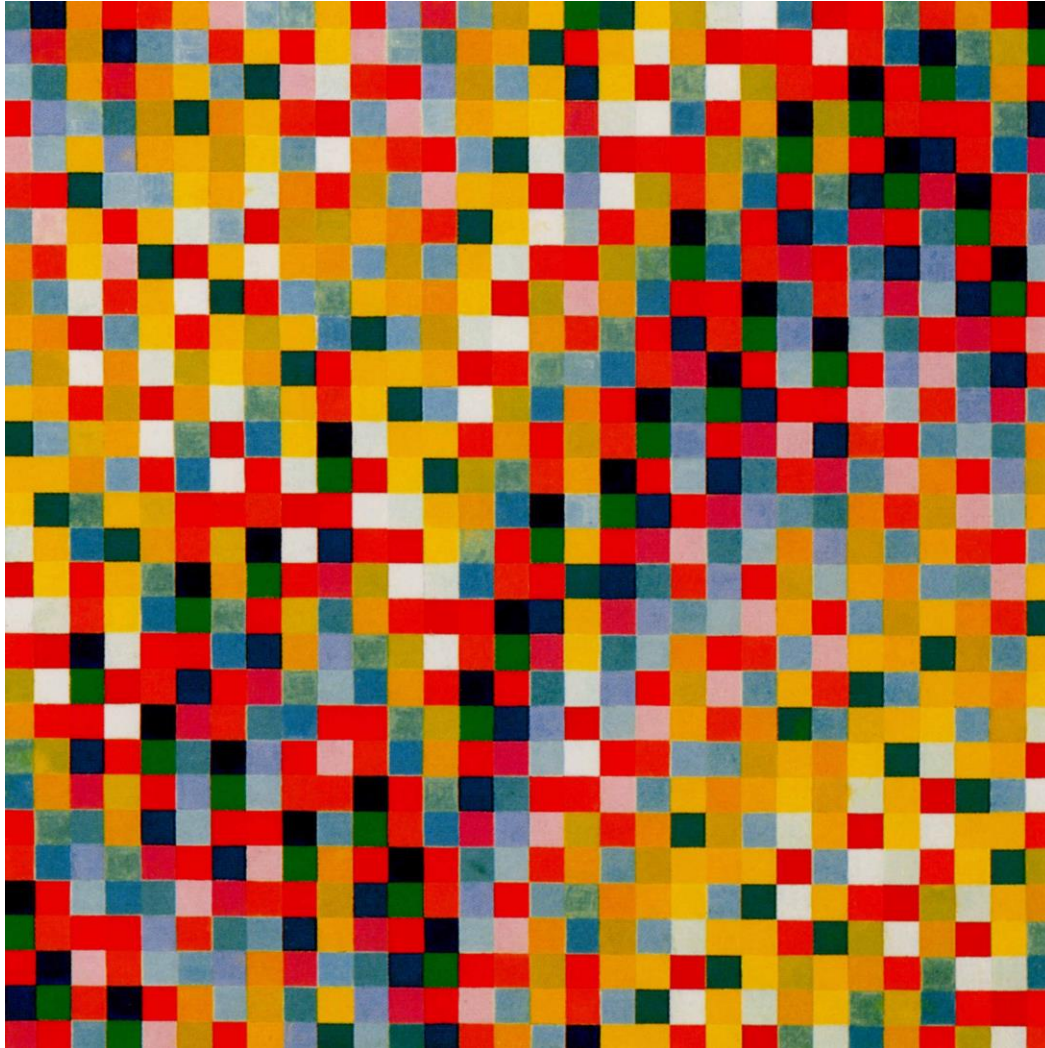
Gene expression profiling GEP

Comprehensive survey on
gene expression in a
cancer



A global view of the planet





each field = one expressed gene

Richard Lohse

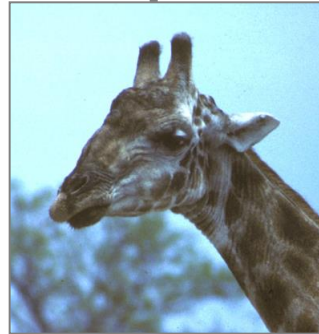
1902 - 1988

Swiss painter and graphic artist



Carnivora

Even-toed
ungulates

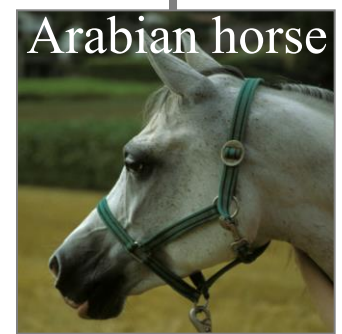


Ungulates

Odd-toed
ungulates



Zebra



Arabian horse



Grévy



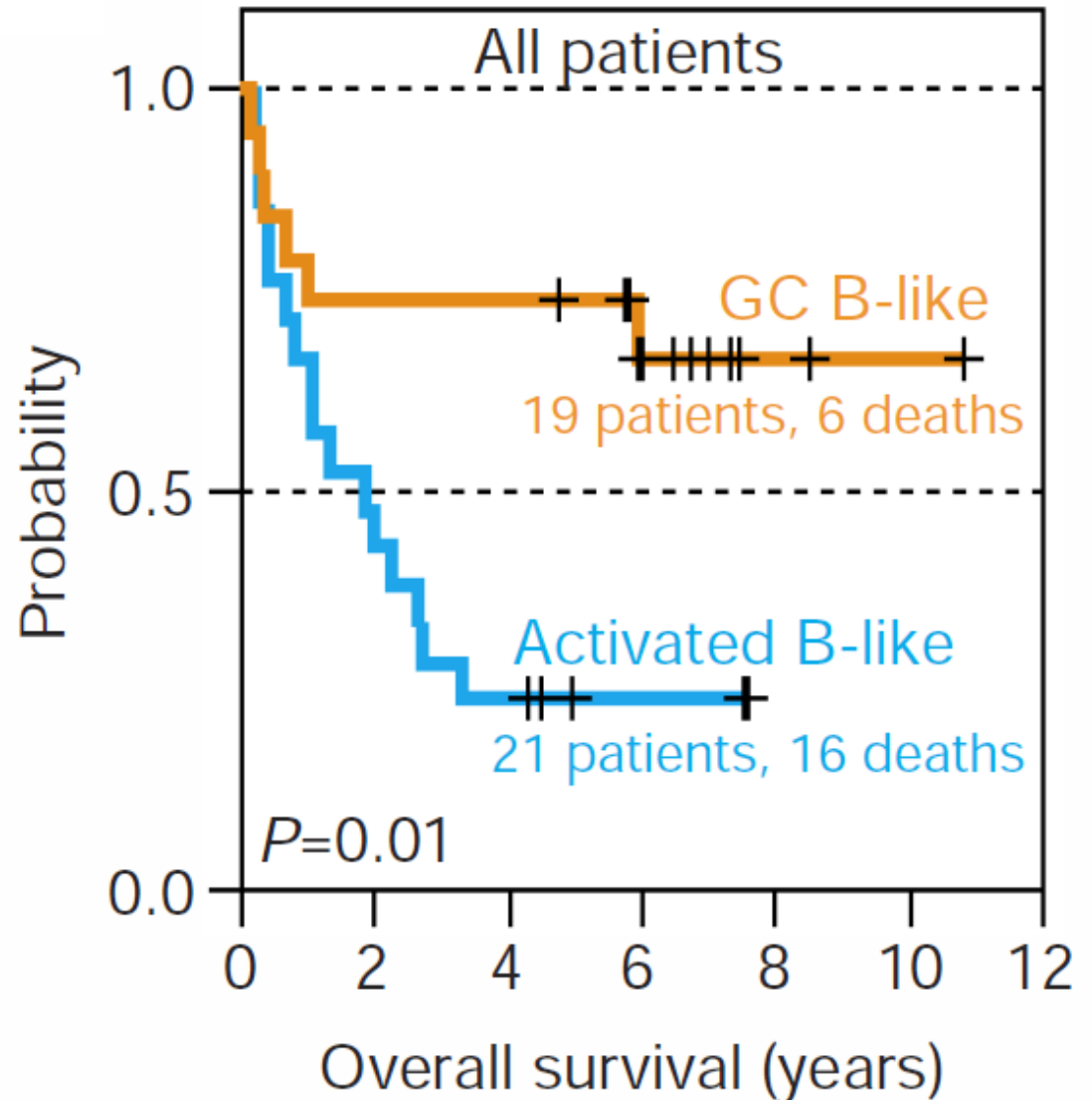
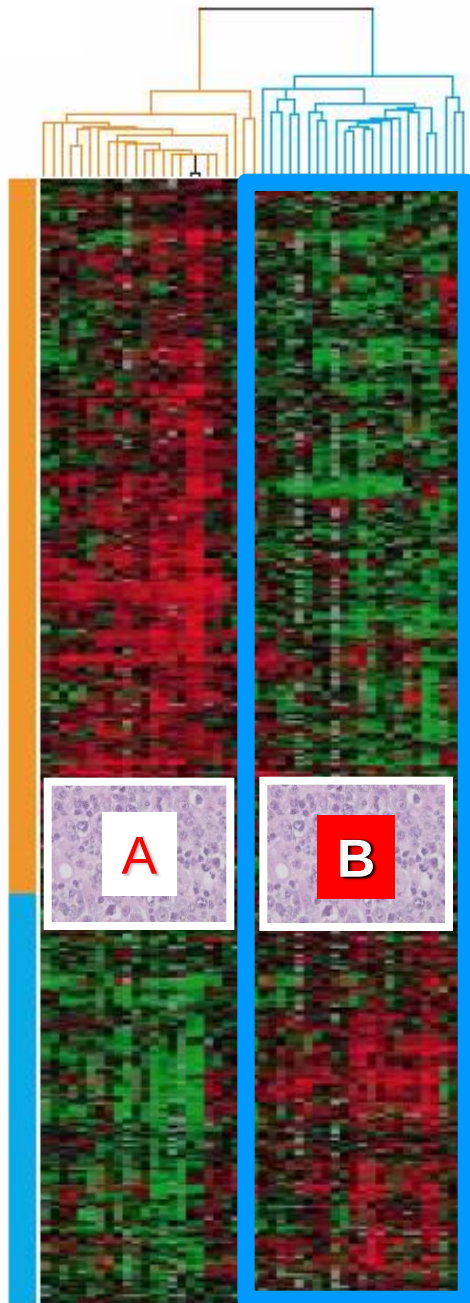
Burchell

Mammals

**Order ?
Species ?
Subspecies ?**

Two types of DLBCL

NATURE 2000; 403: 503



Summary

Molecular biology and «molecular» haem onc

- Defines molecular disease entities
- Improves diagnostic precision
- Identifies targets/target pathways for therapy
- Permits selection of good candidates for a particular therapy
- Helps to improve outcome

