Kapitel 1.3.

Das Differenzierungspotential von Stammzellen

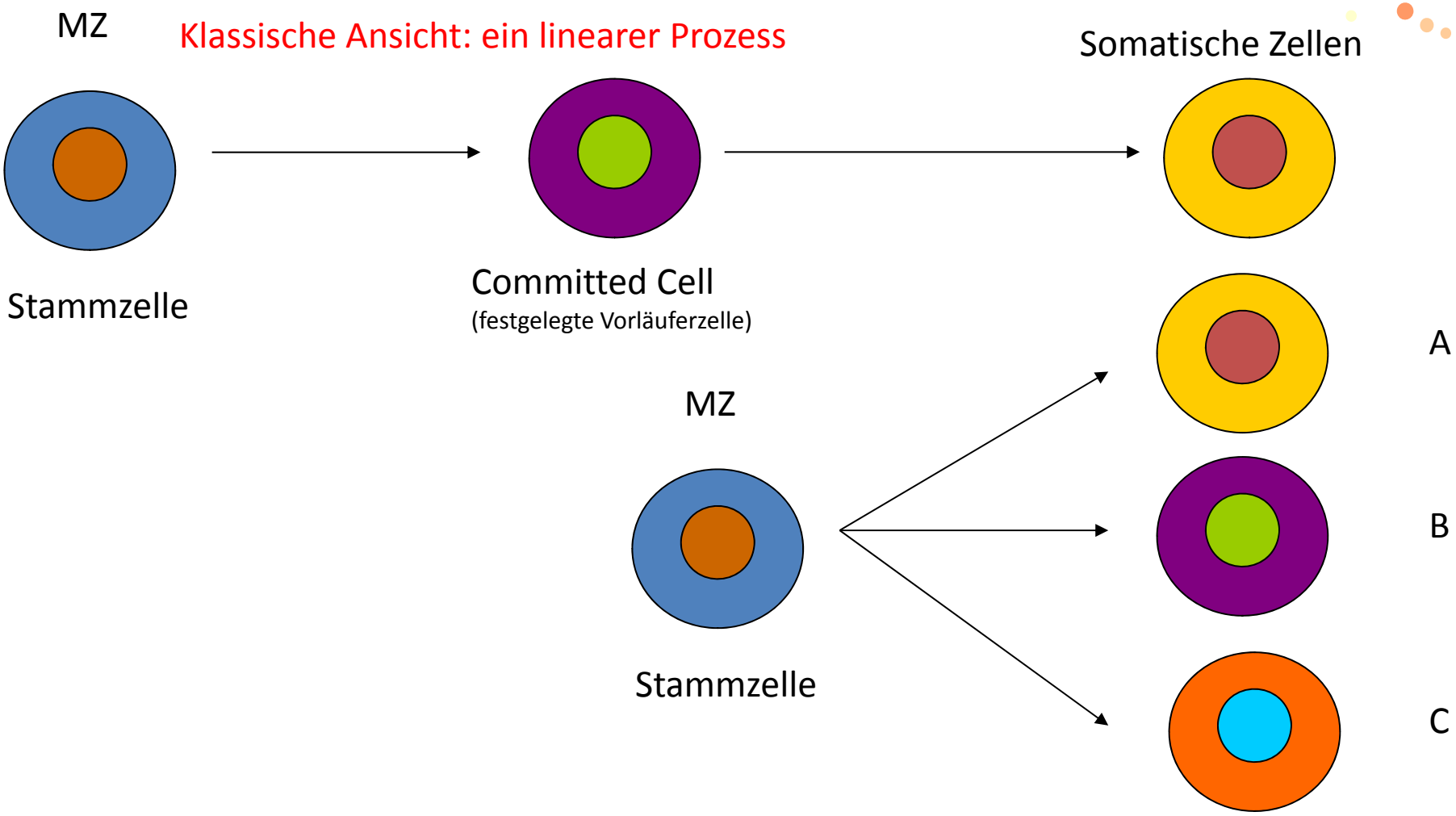
Potentialität von Stammzellen

Potency

Differentiation potential

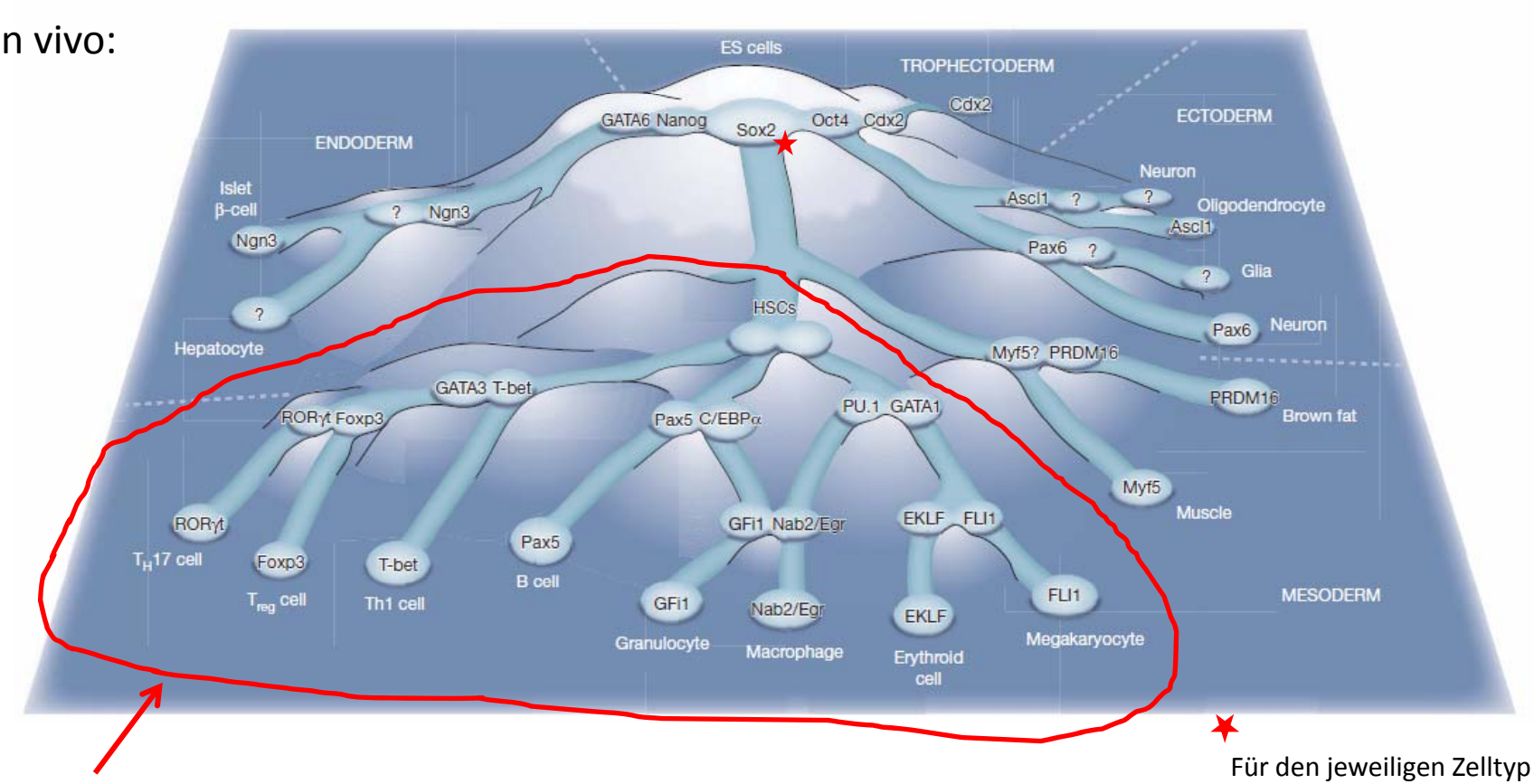
Georg Weitzer

Potenzialität von Stammzellen



Pluripotente embryonale Stammzellen (ESCs) können sich zu über 200 verschiedene somatische Zelltypen entwickeln.

In vivo:



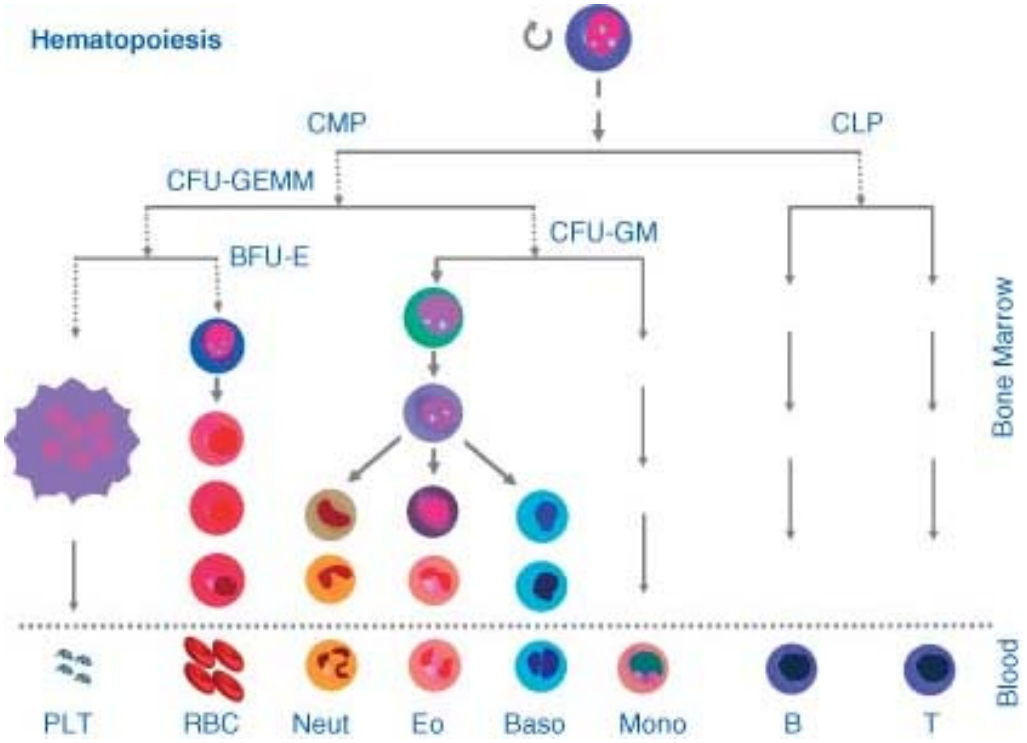
Hämatopoetische Stammzellen und ihre Derivate
(siehe auch nächste Folei)

Für den jeweiligen Zelltyp typische Proteine

Figure 5 | Transcription factor cross-antagonisms in a cascading landscape of unstable and stable cell states. The territory, represented as a mountain range, depicts all possible solutions of a single regulatory network that specifies cell identity. Robust network states correspond to stably differentiated cell types (deep basins in the low-lying plains) whereas unstable solutions correspond to ridges and slopes in the landscape. The latter are only fleetingly occupied during development and thus unlikely to correspond to observable cell types. ES cells, embryonic stem cells; HSCs, haematopoietic stem cells.

Beispiel dafür, dass die Unterscheidung von Stammzelle und Vorläuferzell nicht eindeutig möglich ist.

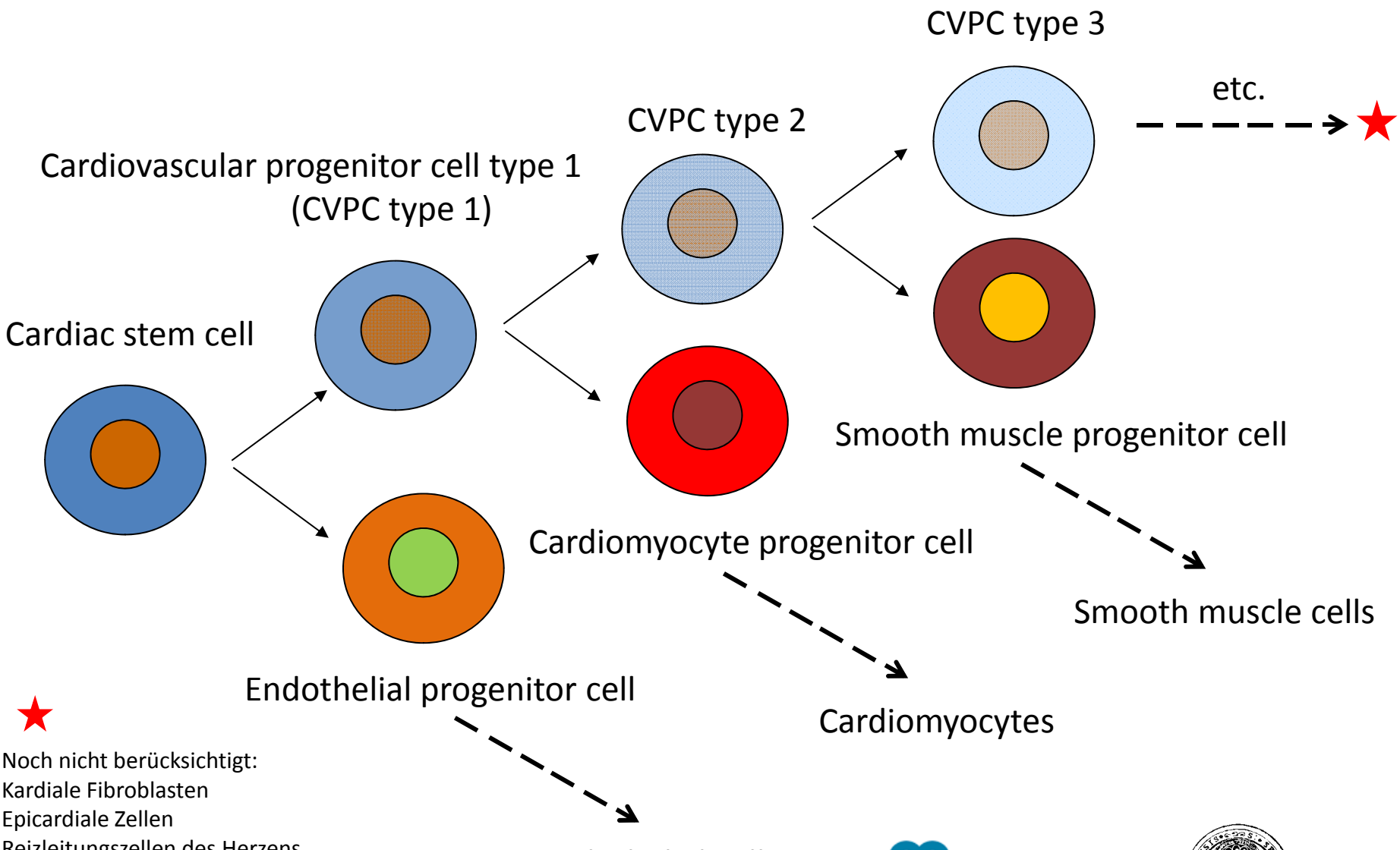
Blutbildende Stammzelle



„Vorläuferzellen“

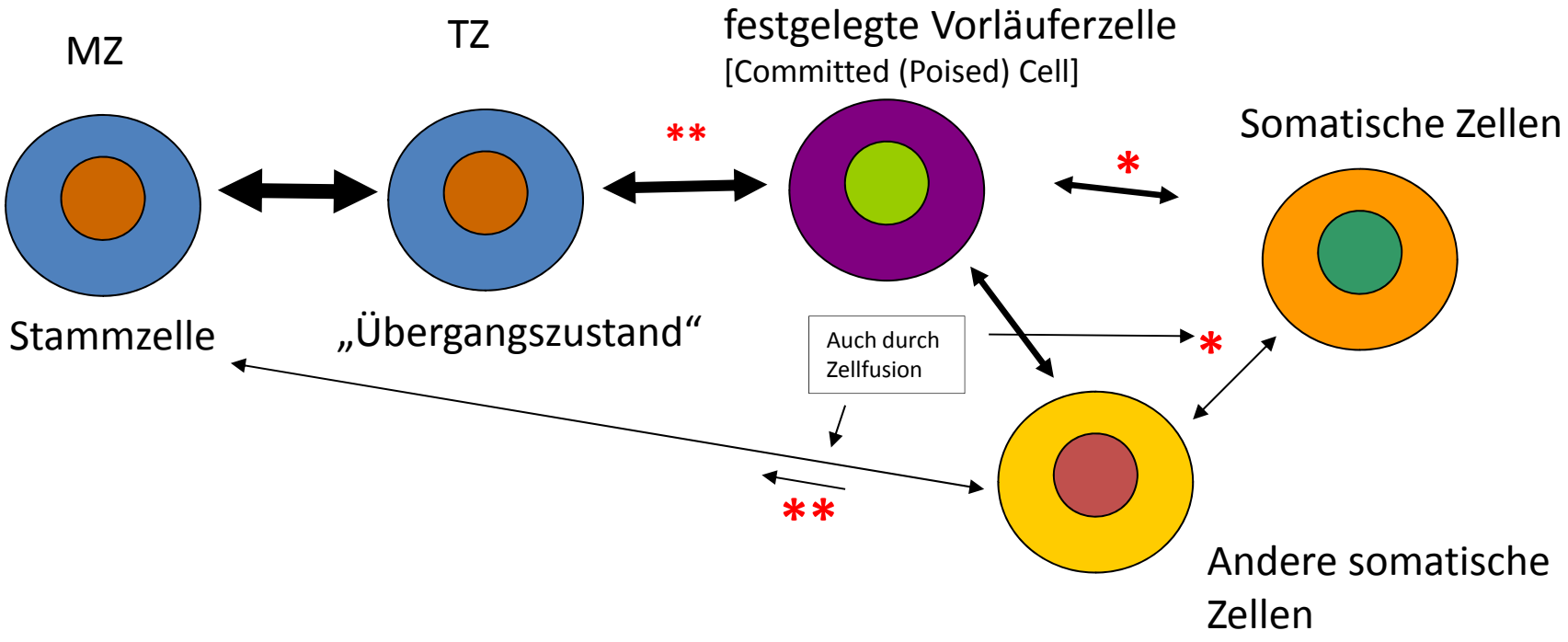
Dingli David, Pacheco JorgeM.. Modeling the architecture and dynamics of hematopoiesis. *WIREs Syst Biol Med* 2010, 2: 235-244. doi: 10.1002/wsbm.56

Einfaches Modell für die Differenzierung von somatischen Herzstammzellen:



Noch nicht berücksichtigt:
Kardiale Fibroblasten
Epicardiale Zellen
Reizleitungszellen des Herzens
Verschiedenen Typen von Herzmuskelzellen etc.

Potenzialität von Stammzellen und Vorläuferzellen (in Nischen ?)

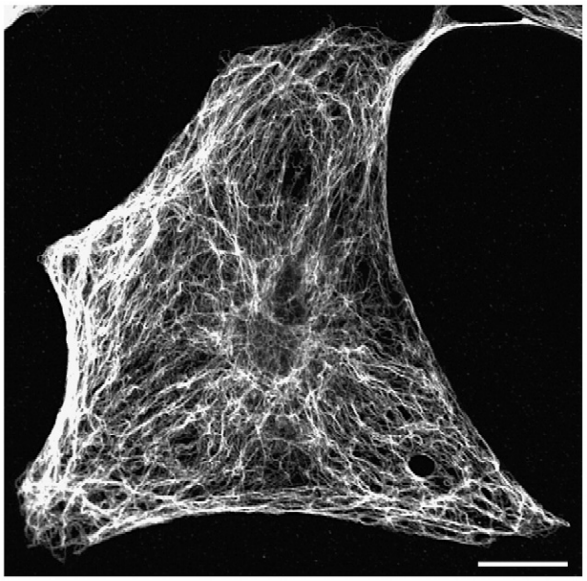


* Plastizität, Transdifferenzierung
z.B.: Wundheilung: Myofibroblasten

** Reprogrammierung

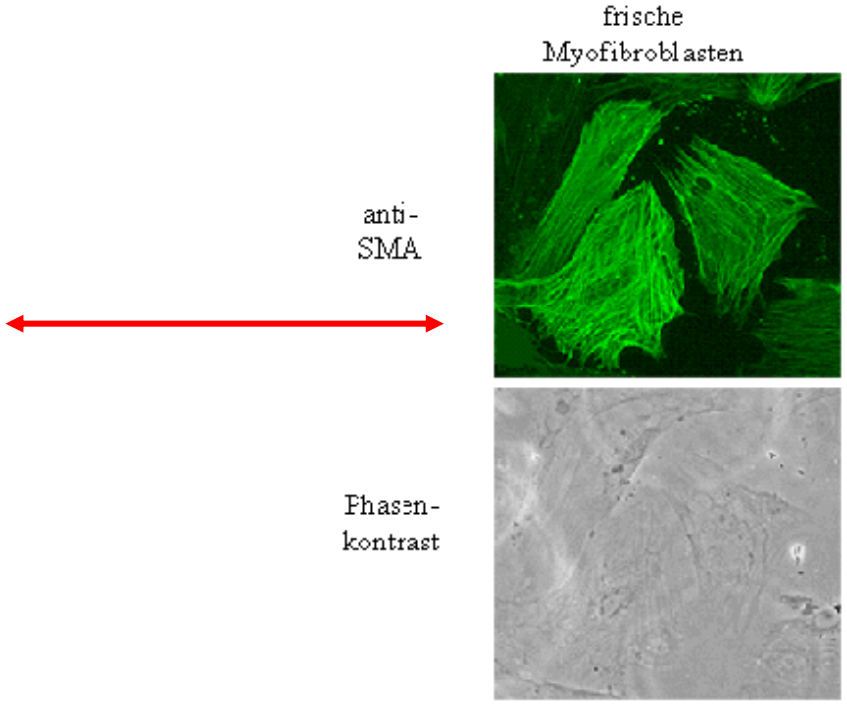
Wundheilung: Plastizität / Transdifferentiation

Vimentin (IFs)



Chou et al. Exp. Cell Res. 2007

Smooth muscle actin (SMA)



http://edoc.hu-berlin.de/dissertationen/kraemer-liv-2005-04-15/HTML/Kraemer_html_664dc9ac.gif

Fibroblast (fb) ⟷ Myofibroblast (mfb)

Beispiele für induzierte Transdiffernzierungen

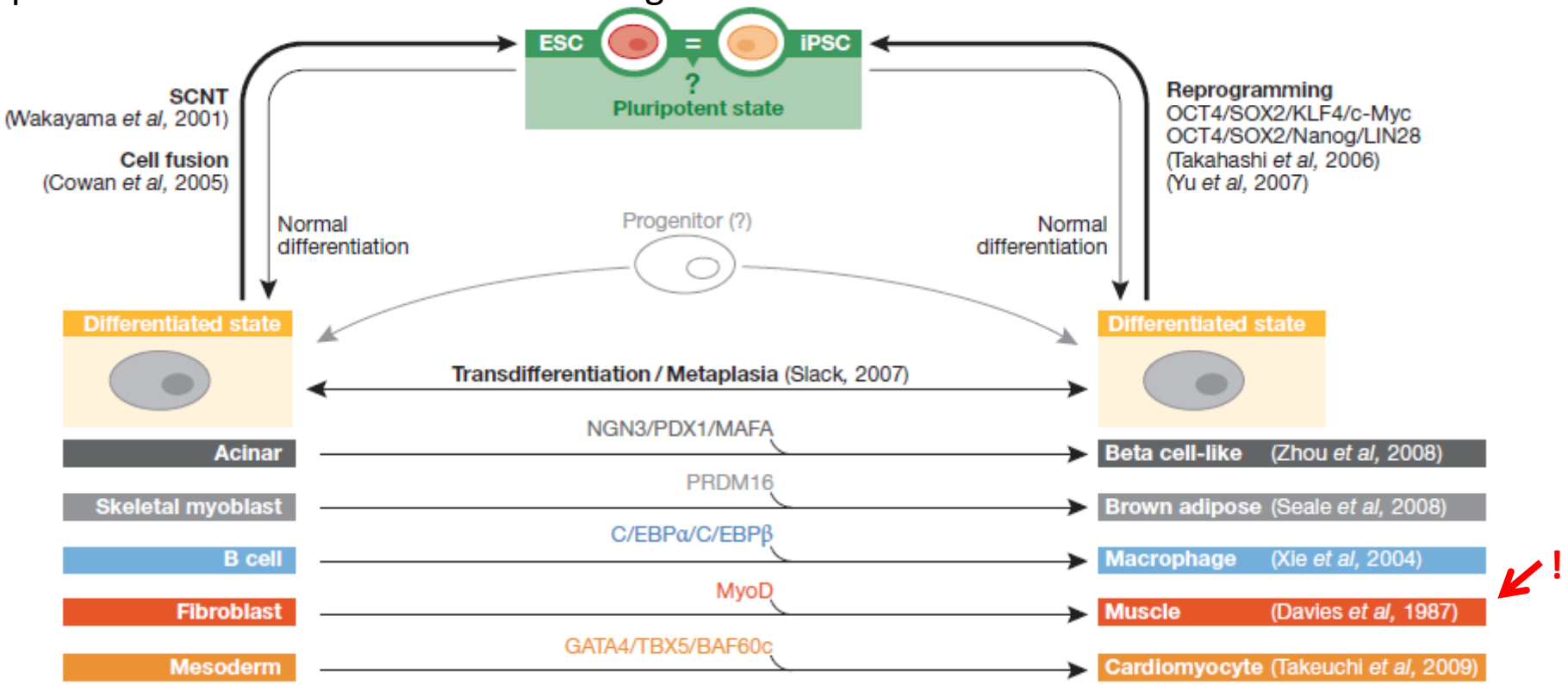


Fig 2 | Interconvertible cellular states. The reprogramming of differentiated cells towards pluripotency by SCNT, cell fusion and reprogramming with the combination of either OSKM or OSNL. Transdifferentiation between somatic cell fates is seen in pathological situations (metaplasia) and can be experimentally induced by overexpression of factors such as MyoD, PRDM16, PDX1, MAFA, NGN3, C/EBPα and C/EBPβ. A progenitor intermediate might be involved in these transitions. BAF60c, cardiac specific subunit of BAF chromatin-remodelling complexes; C/EBP, ccaat enhancer binding protein; ESC, embryonic stem cell; GATA4, GATA-binding protein 4; iPSC, induced pluripotent stem cell; KLF4, kruppel-like factor 4; MyoD, myogenic differentiation 1; NGN3, neurogenin 3; OCT4, octamer 4; OSKM, OCT4, SOX2, KLF4, c-Myc; OSNL, OCT4, SOX2, Nanog, LIN28; PDX1, pancreatic and duodenal homeobox 1; PRDM16, PR domain-containing protein 16; SCNT, somatic cell nuclear transfer; SOX2, SRY-box 2; TBX5, T-box 5.

Aus:

Induced pluripotent stem cells and the stability of the differentiated state

Alan Colman⁺ & Oliver Dreesen

Institute of Medical Biology, Immunos, Singapore

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2727431/pdf/embor2009142.pdf

In need of answers (as of 2009)

(i) What is the molecular mechanism of reprogramming and what role does each factor have?

(ii) How similar are embryonic stem cells and induced pluripotent stem cells? Do they have equal differentiation capabilities? YES

(iii) Can reprogramming be achieved solely with chemical compounds? Hopefully not

(iv) Is epigenetic memory completely erased during reprogramming? NO

(v) Could chromatin modifiers such as valproic acid enhance transdifferentiation? YES

(vi) Does cell division enhance the ability of a cell to change fate?

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Abstufungen der Potenzialität:

Totipotenz (Omnipotenz): Zygote, 2 -16 Blastomere (siehe Embryoentwicklung)
(Oocyten und Spermien ???)

Pluripotenz: ESCs, PGCs, EGCs

(Im Gegensatz zu den Maus ESCs, machen Menschen ESCs auch trophektodermale Zellen obwohl sie eher schon dem Primitiven Ectoderm als der Inneren Zellmasse ähnlich sind.)

(Oligo-)Multipotenz: MSCs, HSCs (in vitro und in vivo widersprechende Resultate.)

(Mono-) Unipotenz: Somatische Zellen (→ Impotenz: Seneszenz und Zelltod)

Änderung dews Phänotypes

- natürlich:
  Plastizität, Transdifferentiation,
  Redifferenzierung in Vorläuferzellen,
  Fusionierung von Zellen
- künstlich:
  Reprogrammierung (Takahashi and Yamanaka, 2006; Wernig et al., 2007)
  Klonen (Tachibana et al., 2013)