

## 5. Doppelstunde am 4.11.2015

## 1.1.4. Molekulare Regulation der Selbsterneuerung

## 1.1.4.1. Intrinsische Faktoren (zellautonom)

- Transkriptionsfaktor Netzwerke, DNA-RNA Polymerase II und Telomerase

## 1.1.4.2. Extrinsische Faktoren (parakrin)

- Signalübertragungsmechanismen

1.1.4.3. Stammzell-Nischen (bereits besprochen)

- Zell-Zell Wechselwirkungen; humorale und metabolische Einflüsse und topologische Aspekte

## 1.1.4. Molekulare Regulation der Selbsterneuerung

## 1.1.4.1. Intrinsische Faktoren (zellautonom)

- **Transkriptionsfaktor Netzwerke**, DNA-RNA Polymerase II und Telomerase

## 1.1.4.1.1. Trinity factors

Oct 3/4 → Oct 4 (Gen: *pou5f1*) POU Domain – homeodomain TF

13 splice-Varianten, 10 Pseudogene

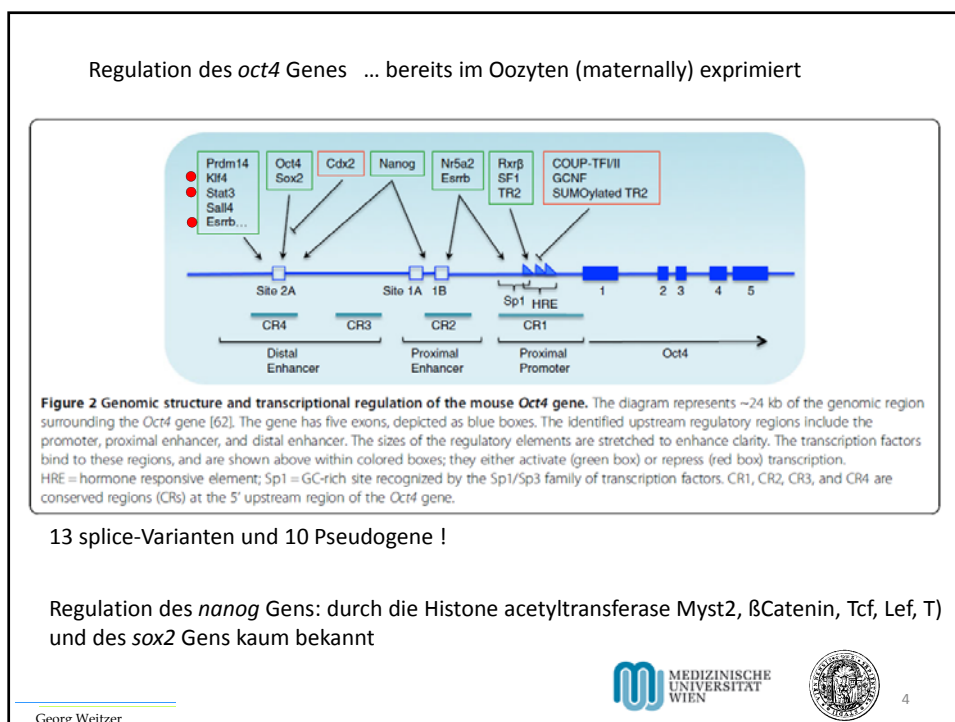
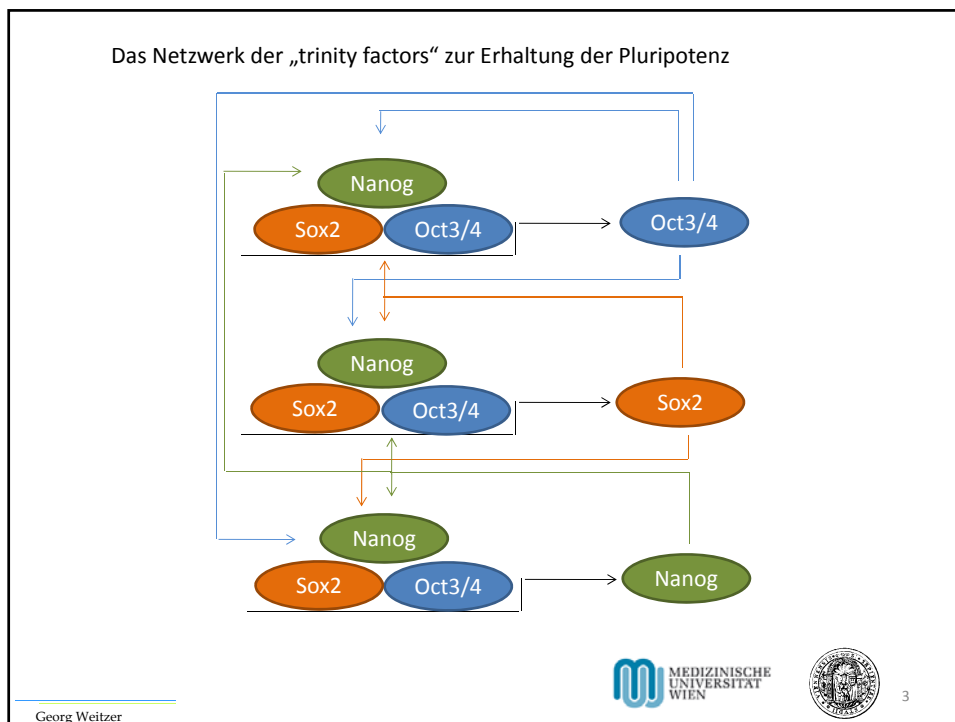
Nanog a homeodomain TF

11 Pseudogene in Hominiden

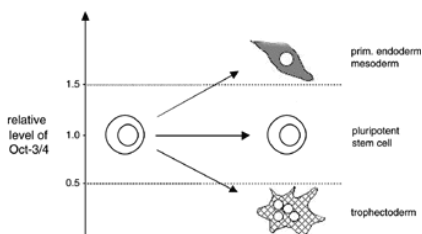
Sox2 = SRY-like box 2 (SRY = Sex determining Region Y) a HMG-box TF

20 sehr ähnliche Gene





### Der Einfluss der Oct4 Proteinkonzentration auf die Selbsterneuerung „Oct4-dosage effects“ oder „nuclear dwelling kinetics“

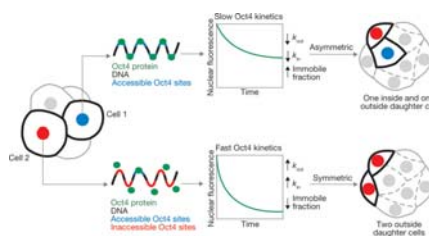


**Figure 6. Functions of Oct-3/4 in pluripotent stem cells.** Relationship between Oct-3/4 expression level and stem-cell fate. To maintain the undifferentiated stem-cell phenotype, Oct-3/4 expression must remain within plus or minus 50% of normal diploid expression. If Oct-3/4 expression is increased beyond the upper threshold level, differentiation is triggered into primitive endoderm or mesoderm. If Oct-3/4 expression is decreased, stem cells are redirected into the trophectoderm lineage.

doi:10.1038/74199  
Quantitative expression of Oct-3/4 defines differentiation, dedifferentiation or self-renewal of ES cells.  
Hitoshi Niwa Jun-ichi Miyazaki & Austin G. Smith  
*Nature Genetics* **24**, 372 - 376 (2000) doi:10.1038/74199



Georg Weitzer



**Figure 5: Schematic illustration of Oct4-paGFP kinetics and cell lineage allocation in the early mouse embryo.** From [Oct4 kinetics predict cell lineage patterning in the early mammalian embryo](#)

**Figure 5.** Schematic illustration of Oct4-paGFP kinetics and cell lineage allocation in the early mouse embryo. Different accessibility of Oct4 DNA binding sites among cells, possibly due to a differential chromatin structure, the presence of an excess of another factor that blocks access or the absence of a cofactor required for high-affinity binding, results in segregation of Oct4-paGFP kinetic properties before lineage allocation. Cells with slower kinetics and a large immobile fraction divide more frequently in an asymmetric manner during the 8- to 16-cell transition, contributing more cells to the pluripotent cell lineage, whereas cells with faster kinetics and a small immobile fraction contribute more cells to the extra-embryonic lineage through symmetric divisions.

doi: 10.1038/ncb2154  
Nicolas Plachta, Tobias Bollenbach, Shirley Pease, Scott E. Fraser and Periklis Pantazis  
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5

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Esrrb Klf4, STAT3, Sall4, Paf1 ..... → Oct 4

STAT3, Brachyury (T)..... → Nanog

Klf4 (?), miR21..... → Sox2

Esrrb ... oestrogen-related receptor beta,  
Paf 1 ... DNA-RNA-Polymerase complex



