1.4. Das Ruhen von Stammzellen

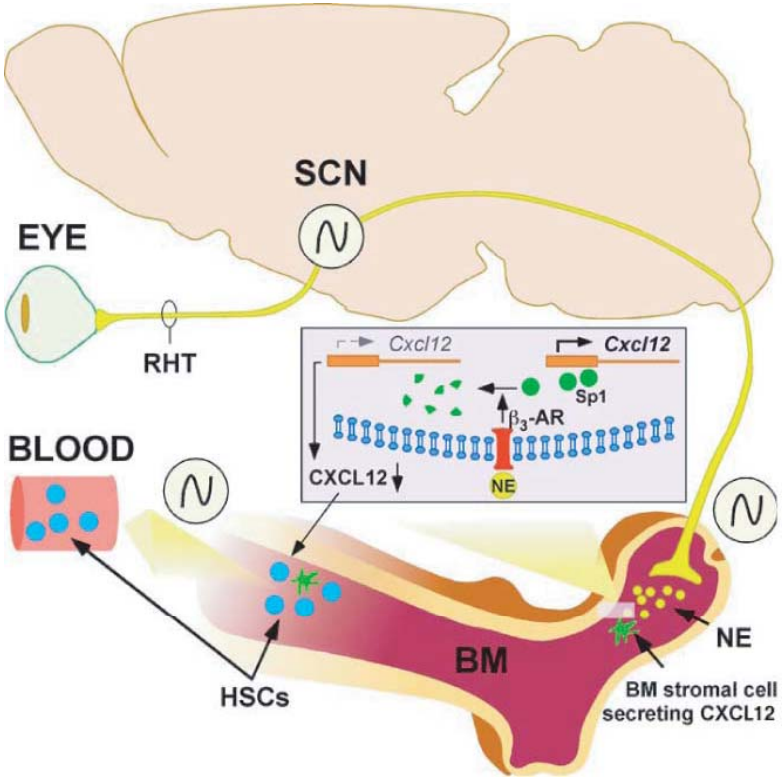
(Dormancy, hibernation, ….)

Wie können Zellen mit hohen Selbsterneuerungspotential
zeitweilig die Zellteilung (fast) ganz einstellen,
um sie später wieder zu aktivieren?

1.

Krebsstammzellen können offensichtlich jahrelang ruhen, einer Chemotherapie entkommen, und bei neuerlichen (unbekannten) Reizen, wieder zu proliferieren beginnen → Metastasierung.

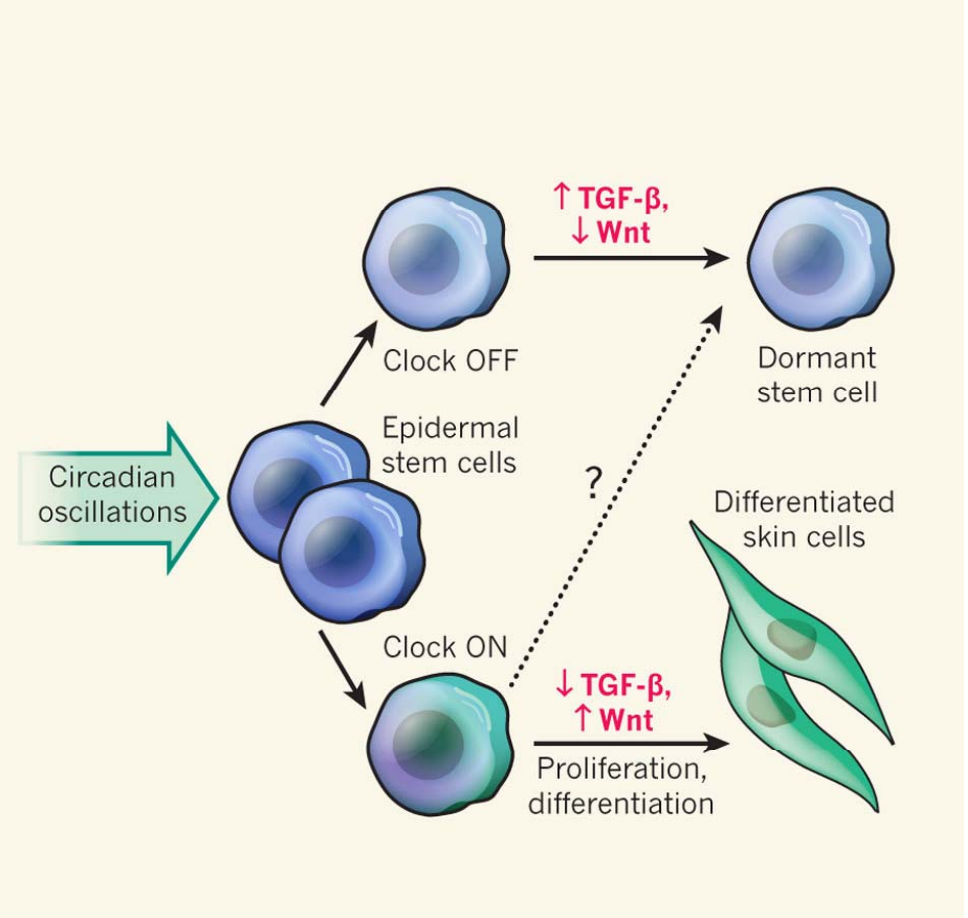
2. Ausschüttung von Hämatopoetischen Stammzellen aus dem Knochenmark



Model for circadian regulation of trafficking of HSCs and their progenitors. b3-AR, b3-adrenergic receptor; BM, bone marrow; NA, noradrenaline; RHT, retinal–hypothalamic tract; SCN, suprachiasmatic nucleus.

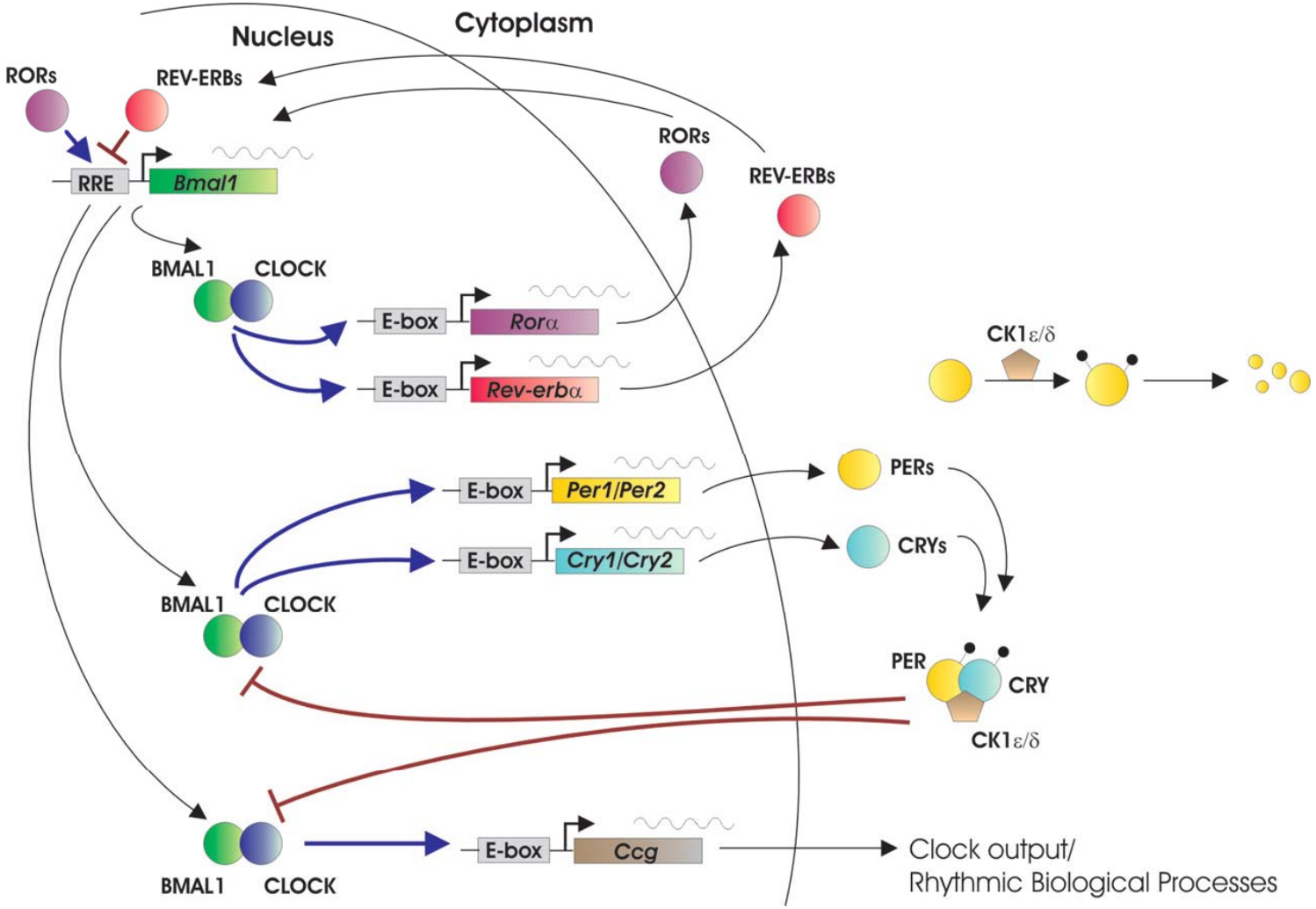
From: Haematopoietic stem cell release isregulated by circadian oscillations
Simo´n Me´ndez-Ferrer, Daniel Lucas, Michela Battista & Paul S. Frenette
Nature Vol 452|27 March **2008**| doi:10.1038/nature06685

3. Somatische Stammzellen der **Epidermis** werden durch die molekulare circadiane Uhr beeinflusst.



From: Stem cells: The **clock** within.
Aguilar-Arnal L, Sassone-Corsi P.
Nature. **2011** Dec 7;480(7376):185-7. doi: 10.1038/480185a.

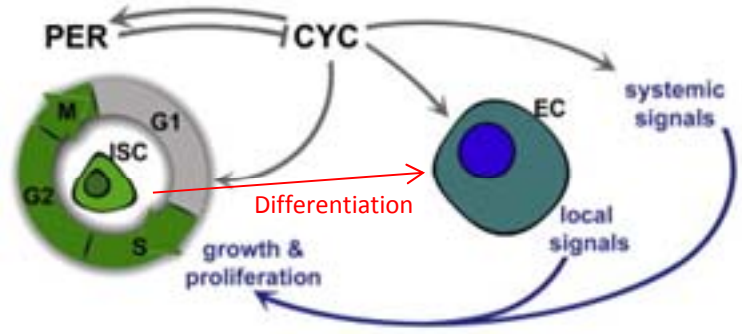
A network of transcriptional–translational feedback loops constitutes the mammalian circadian clock.



Ko C H , and Takahashi J S Hum. Mol. Genet. 2006;15:R271-R277

Human Molecular Genetics

4. Regulation des Zellzyklus in Stammzellen in den Grübchen der Darmwand



The Drosophila circadian pacemaker comprises the transcription factor partners clock (clk) and cycle (cyc), which are negatively regulated by per and timeless (tim; Hardin, 2011). One transcriptional target of CLK/CYC is per itself, which represses its own production and causes the cyclical transcriptional rhythms that underlie circadian rhythms. The existence of independent clocks throughout Drosophila tissues is known (Plautzet al., 1997).

A model of how the clock synchronizes ISC division: CYC is important for the transition through G1, and the clock also initiates systemic signals and local niche signals originating from ECs. Together, these signals activate ISC divisions, most likely through nonautonomous mechanisms.

ISC, **intestinal stem cells**; EC, enterocytes (somatic cell product of ISC;
PER, period 1/2/3; CYC, cycle.

The Circadian Clock Gates the Intestinal Stem Cell Regenerative State
Phillip Karpowicz, Yong Zhang, John B. Hogenesch, Patrick Emery, Norbert Perrimon
Stem Cell Reports Volume 3, Issue 4, 25 April **2013**, Pages 996–1004

Cycle (cyc) = Bmal
Timeless (tim) = cryptochrome

Wer oder was zählt die Anzahl der Zellzyklen oder misst die Zeit der Ruhe von Stammzellen?

Hayflick limit (1961) :

Humane embryonale zellpopulationen teilen sich 40 bis 60 mal,
dann werden sie seneszent und sterben.
Ein Grund: Das Kürzer werden der Telomere.