A **predoctoral (Master) position** on **cell cycle dynamics in trophoblast cells** is available in the lab of **Prof. Dr. rer. nat. Dipl. Ing. Felix B. Engel** at the **Universitätsklinikum Erlangen**

The position is part of a collaboration project of the Emerging Fields Initiative (EFI) *"Cell Cycle in Disease and Regeneration"*. The EFI Cyder (http://www.efi.fau.de/projekte/cyder/) is an interdisciplinary research consortium that provides a stimulating work environment and ideal conditions to get in touch with current research subjects such as advanced imaging, genome editing and stem cell biology. We are seeking for a highly motivated master student that is interested in characterizing the cell cycle dynamics of the mammalian transcriptional activators E2F1-3.

Background: Endocycles are a non-canonical cell cycle variant in which cells replicate their DNA without undergoing mitosis and thereby lead to the formation of polyploid cells (for a detailed review see *Zielke et al. CSH Persp Biol, 2013; Edgar et al. Nat Rev MCB, 2014)*. Cell size increases proportional to the degree of ploidy, and hence endocycling represents an effective strategy for post-mitotic growth that is often employed during tissue regeneration. Endocycles are best understood in the vinegar fly *Drosophila melanogaster*, but also occur in certain mammalian cell types such as the hepatocyctes of the liver or the throphoblast giant cells (TGCs) of the placenta. Our previous work defined the regulatory network of the endocycle in the *Drosophila* salivary gland *(Zielke et al. Gen&Dev, 2008; Zielke et al. Nature, 2011)*. The rate-limiting factor of this network is the transcriptional activator E2F1, which is periodically targeted by the S phase-specific ubiquitin ligases $CRL4^{Cdt2}$. The best-studied mammalian cell type undergoing endocycles are the trophoblast giant cells, which can be differentiated *in vitro* from trophoblast stem cells (TSCs). The molecular mechanisms of the TGC endocycle are ill defined, but it has been suggested that endoreplication in TGCs relies on a bi-phasic oscillator involving negative feedback provided by the cyclin-dependent kinase inhibitor (CKI) $p57^{Kip2}$. In addition, the proposed network contains two S phase-promoting CDKs (CycE/Cdk2, CycA/Cdk2), the licensing inhibitor Geminin and at least three ubiquitin ligases (APC/C^{Cdh1}, $CRL1^{Fbw7}$, $CRL1^{Skp2}$). Earlier work on cancer cell lines revealed that human E2F1 is a substrate of the $CRL1^{Skp2}$ ubiquitin ligase *(Marti et al. Nat Cell Biol, 1998)*, suggesting that the remaining family members (E2F2-3) could be regulated by an analogous mechanism.

Objectives: The main objective of the project is to explore the role of the mammalian E2Fs in endocycling TGCs. The project aims to compare the dynamics of GFP-E2F1-3 fusion proteins 3 in cultured TGCs to the cell cycle oscillations in mitotic Hek293 cells.

Involved methods:	Stem cell culture, immunohistochemistry, quantitative imaging and live-microscopy
Desired qualifications:	Bachelor degree in Biological Sciences
Date of Commencement:	The project may begin as soon as 01.04.2015
Application deadline:	31.03.2015

For further information, please contact Prof. Dr. Felix Engel or Dr. Norman Zielke.

To apply, please send a letter of motivation, CV, transcripts, and contact information for at least two referees as a single pdf to:

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