Muhammed Kashif
Dr. sc. hum.

Cross-coupling of the transcription factors NF-E2 and AP-1 regulates cell-autonomously trophoblast syncytium formation and placental vascularisation

Geboren am 01.04.1976 in Lahore, Pakistan.
Diplom der Fachrichtung Biologie, am Feb. 2002, an der Universität Heidelberg.

Promotionsfach: Innere Medizin
Doktorvater: Priv.-Doz. Dr. med. Berend Isermann.

Absence of the transcription factor p45 NF-E2, which is thought to be restricted to hematopoietic cells, results in thrombocytopenia, impaired placental vascularisation and intrauterine growth restriction (IUGR) in mice. The mechanism underlying the placental defect and IUGR remains unknown. Here we show that the mechanism resulting in the placental defect and IUGR of p45 NF-E2-/- embryos is caused by a novel function of p45 NF-E2 during syncytiotrophoblast differentiation unrelated to thrombocytopenia. In trophoblast cells p45 NF -E2 acts cell autonomously as a transcriptional repressor reducing (a) JunD binding activity, (b) expression of Gcm-1 and Gcm-1 dependent genes, (c) acetylation of nuclear proteins, and (d) syncytiotrophoblast formation. Crosscoupling of p45 NF-E2 with JunD – in part via acetylation – is a novel mechanism regulating syncytiotrophoblast differentiation. These studies imply a crucial role of acetylation during syncytiotrophoblast formation and they identify a new function of p45 NF-E2 and JunD in trophoblast cells, which underlies a novel mechanism regulating placental development and embryonic growth.