methylation pattern of RARRES1 was quantified by pyrosequencing. Changes of cell-cell contact were determined by Electric cell-substrate impedance sensing.

Results: Choriocarcinoma cell-lines showed a hypermethylation of the RARRES1 promotor, accompanied by significant reduced gene-expression. In analogy, DNA derived from choriocarcinoma tissue showed a higher RARRES1 methylation as compared to healthy first trimester DNA. In contrast, a significant higher RARRES1 expression was observed in primary trophoblasts from PE cases compared to controls. Additionally, we found a significant induction of RARRES1 expression relative to increasing cell-density. In concordance, RARRES1 overexpression in Jeg-3 cells enhanced the measured impedance, indicating stronger cell-cell connectivity.

Conclusions: Our findings strengthened the hypothesis that RARRES1 functions in a tumor-suppressive manner and is dysregulated in placental diseases. We showed that RARRES1 expression is tightly regulated by DNA-methylation. Based on our findings, we hypothesize high RARRES1 expression, as observed in PE, might increase cell-cell adhesion and thus negatively influences trophoblast invasion or proliferation. On the other hand, epigenetic silencing of RARRES1 in choriocarcinomas might reduce cell adhesion and promote the tumorigenic potential of trophoblastic cells by enhancing epithelial-to-mesenchymal transition.

NI1.02

IMPAIRED GENE-EXPRESSION AND EPIGENETIC REGULATION OF RETINOIC ACID RECEPTOR RESPONDER 1 IN PREECLAMPSIA AND CHORIOCARCINOMA

Hanna Huebner [1], Fabian B. Fahlbusch [2], Pamela L. Strissel [1], Reiner Strick [1], David Wachter [3], Matthias W. Beckmann [1], Matthias Ruebner [1]. [1] *Department of Gynaecology and Obstetrics, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nuremberg, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany;* [2] *Department of Pediatrics and Adolescent Medicine, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nuremberg, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany;* [3] *Department of Pathology, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nuremberg, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany*

Objectives: Human placental development resembles tumorigenesis in its invasive and proliferative capacity. In contrast to cancer, these features are tightly regulated. Disturbances within this regulation are thought to contribute to gestational diseases, like choriocarcinoma, preeclampsia (PE) and intrauterine growth restriction (IUGR). Retinoic acid receptor responder 1 (RARRES1) is a tumor-suppressor known to be epigenetically silenced in many cancers. The aim of our study was to investigate the expression and epigenetic regulation of RARRES1 in PE, IUGR and choriocarcinoma.

Methods: Immunhistochemical staining of RARRES1 on healthy and pathological (choriocarcinoma, PE, IUGR) placental sections was performed. Gene-expression was analyzed by qRT-PCR of RNA derived from total placental tissue, isolated primary trophoblasts, the first-trimester cell-line Swan71 and choriocarcinoma cell-lines (Jeg-3, JAR, BeWo). The