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CHARACTERISATION OF THE TUMOR-SUPPRESSOR GENE GASTROKINE 2 IN THE HUMAN PLACENTA

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Objectives: Gastrokine-1 and -2 (GKNs) act as stomach-specific tumor suppressor genes. Beyond its role in the gastric mucosa, we have recently identified GKN1 in human placenta. Its expression was specific for extravillous trophoblasts (EVT) and treatment of the extravillous cell line JEG3 with GKN1 inhibited cell migration. Similarly, GKN2 is known to inhibit the proliferation, migration and invasion of gastric cancer cells. This study was designed to analyse expression and localisation of GKN2 in the human placenta.

Methods: Placental localisation of GKN2 was determined by immunohistochemistry in first and third trimester placentas. We analysed the expression levels of GKN2 via sqPCR in healthy placental tissue, in placental pathologies (IUGR, PE and HELLP) and in various trophoblast-like cell lines (JEG-3, Jar, BeWo, Swan-71).
Results: In the first trimester, GKN2 was located in all trophoblast compartments. In the third trimester, EVTs stained strongly for GKN2. While in healthy placental tissue the syncytiotrophoblast only showed minor positive staining for GKN2, we found a more pronounced GKN2 positivity in the syncytiotrophoblast of IUGR. Additionally, GKN2 was detected in the stroma of fibrotic villi of IUGR and in smooth muscle cells of the villous vessels. SqPCR indicated a significant induction of GKN2 expression in all placental pathologies investigated. No expression of GKN2 was found in trophoblast-like cell lines.
Conclusion: Our study is the first to characterise GKN2 in placenta. Its expression was absent in invasive trophoblast-like cell lines, supporting its role as a tumor suppressor. The fact that GKN2 is expressed in all first trimester trophoblast compartments, while more distinctly distributed in the third trimester, points to a role of GKN2 in placental development. Whether the increase of GKN2 in placental pathologies is of trophoblast origin or secondary to the accompanying villous fibrosis remains to be elucidated.