Characterization of NLRP7 Expression and Regulation in Normal and Tumor Human Placentation during the First Trimester of Pregnancy

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Choriocarcinoma is a veritable placental cancer that develop upon abnormal pregnancies, such as Hydatidiform moles (HMs). Choriocarcinoma can metastasis in multiple maternal organs, such as the lung, the vagina, the pelvic, the brain, and the liver. Recent studies established an association between recurrent HMs and mutations in a protein called NLRP7. NLRP7 is member of a new family of proteins involved in inflammatory processes. Nevertheless, the role and the biological functions of NLRP7 remain to be elucidated in normal and tumor human placentation. Using normal trophoblast cells (HTR), placental explants and choriocarcinoma cells (JEG3), we investigated NLRP7 expression, regulation and role in human placenta. Also, we compared its protein and mRNA levels in a cohort of HM patients’ and gestational age matched controls.

We demonstrated that NLRP7 was more expressed during the hypoxic period of placental development compared to its oxygenated period. In HTR cells “normal trophoblast cells”, hypoxia increased NLRP7 expression and its invalidation decreased their proliferation and increased their invasion. These results were confirmed in placental explant cultures. In JEG3 cells, NLRP7 expression was much higher compared to HTR cells and NLRP7 invalidation in JEG3 cells decreased their degree of invasion. More importantly, analyses of the normal and HM cohorts showed differential localization of NLRP7 within the placentas, along with a significant increase in its mRNA levels in HM patients.

Altogether our results demonstrate that NLRP7 is involved in normal placental development during the first trimester of pregnancy and that its deregulation might be associated to choriocarcinoma development. Its direct and differential control of trophoblast invasion in normal vs tumor trophoblast cells strongly suggest its potential involvement in choriocarcinoma progression. Further studies are ongoing to elucidate the role of this new protein in placental tumorogenesis.