

## Placental melatonin system is present throughout pregnancy and regulates villous trophoblast differentiation

**Abstract:** Melatonin is highly produced in the placenta where it protects against molecular damage and cellular dysfunction arising from hypoxia/re-oxygenation-induced oxidative stress as observed in primary cultures of syncytiotrophoblast. However, little is known about melatonin and its receptors in the human placenta throughout pregnancy and their role in villous trophoblast development. The purpose of this study was to determine melatonin-synthesizing enzymes, arylalkylamine N-acetyltransferase (AANAT) and hydroxyindole O-methyltransferase (HIOMT), and melatonin receptors (MT1 and MT2) expression throughout pregnancy as well as the role of melatonin and its receptors in villous trophoblast syncytialization. Our data show that the melatonin generating system is expressed throughout pregnancy (from week 7 to term) in placental tissues. AANAT and HIOMT show maximal expression at the 3rd trimester of pregnancy. MT1 receptor expression is maximal at the 1st trimester compared to the 2nd and 3rd trimesters, while MT2 receptor expression does not change significantly during pregnancy. Moreover, during primary villous cytotrophoblast syncytialization, MT1 receptor expression increases, while MT2 receptor expression decreases. Treatment of primary villous cytotrophoblast with an increasing concentration of melatonin (10 pM–1 mM) increases the fusion index (syncytium formation; 21% augmentation at 1 mM melatonin vs. vehicle) and  $\beta$ -hCG secretion (121% augmentation at 1 mM melatonin vs. vehicle). This effect of melatonin appears to be mediated via its MT1 and MT2 receptors. In sum, melatonin machinery (synthesizing enzymes and receptors) is expressed in human placenta throughout pregnancy and promotes syncytium formation, suggesting an essential role of this indolamine in placental function and pregnancy well-being.

**Ahmed Soliman, Andrée-Anne Lacasse, Dave Lanoix, Lucas Sagrillo-Fagundes, Véronique Boulard and Cathy Vaillancourt**

INRS-Institut Armand-Frapplier and BioMed research Center, Université du Québec, Laval, QC, Canada

**Key words:** arylalkylamine N-acetyltransferase, HIOMT (ASMT), human chorionic gonadotropin, MT1 melatonin receptor, MT2 melatonin receptor, syncytiotrophoblast, villous cytotrophoblast

Address reprint requests to Cathy Vaillancourt, INRS-Institut Armand-Frapplier, 531, boul. des Prairies, Building 18, Laval (Québec) H7V 1B7, Canada.

E-mail: cathy.vaillancourt@iaf.inrs.ca

Received March 20, 2015;  
Accepted March 27, 2015.