

Hyperglycosylated HCG expression in pregnancy: cellular origin and clinical applications. G. Kovalevskaya¹, J.F.O'Connor¹, T. Kakuma², S. Birken³,
¹-Irving Center for Clinical Research, ³-Department of Obstetric and Gynecology, Columbia University, New York, USA; ²-Biostatistical Center, Kurume University, Kurume, Fukuoka, Japan

Introduction: Antibody B152 was produced in R. Canfield's laboratory (Columbia University) as a fortuitous development of a carbohydrate-sensitive antibody during an effort to produce an antibody to nicked hCG using a choriocarcinoma form of nicked hCG purified in the laboratory of L. Cole.

Methods: To monitor the expression of different isoforms of hCG throughout pregnancy two IRMA's were applied: B152-B207 (choriocarcinoma hCG-specific assay) and B109-B108 (measures standard hCG isoforms found in the WHO reference preparation of hCG). The same WHO hCG standard was used in both assays. The results were presented as a ratio of hCG as measured by each assay (B152/B109 ratio). The cellular origin of two different glycoforms of hCG was identified by analysis of cell media from cytotrophoblasts (CTBs) and syncytiotrophoblasts (STBs). Cell conditioned media was prepared in S. Fisher's laboratory (University of California, San Francisco) and described in (G. Kovalevskaya, O. Genbacev, et al. Mol Cell Endocrinol, 2002,194:147-155).

Results: In early pregnancy urine samples the concentration of B152 hCG was significantly higher in normal pregnancy (NP) compared with early pregnancy loss (EPL) (O'Connor et al., Prenatal Diagn, 1998, 18:1232-1240). Analysis of both naturally conceived and assisted pregnancies from a fertility center demonstrated that the choriocarcinoma-like B152-recognized forms of hCG that appeared early during pregnancy and were replaced by the standard, less glycosylated hCG isoforms recognized by B109 antibody by the end of the first trimester. Analysis of matched serum-urine samples from the first and third trimesters revealed that B152 hCG form is predominant both in serum and in urine in the first trimester of pregnancy as compared with the third trimester, but the proportion of B152 hCG form is higher in urine than in serum. There was also a significant difference in the B152/B109 ratio between days 5-20 from embryo transfer (or between days 5-15 from the 1st day of hCG detection) in normally developing pregnancy vs. EPL in urine of IVF patients. In the case of spontaneous abortion (SA) the level of B109 hCG remained higher in NP compared with SA. But the B152/B109 ratio declined with gestational age faster in SA than in NP.

Conclusions: Analysis of the forms of hCG during early pregnancy by the B152 assay system can provide important clinical information on the normal progress of the pregnancy. Analysis of placental cell conditioned media demonstrated that isolated CTBs expressed predominantly hyperglycosylated B152 hCG. The level of expression was the highest in the first trimester. STBs produced predominantly the less glycosylated B109 hCG. This work was supported by grants ES0789 (NIEHS, NIH), RR00645 (NCRR, NIH).