

Epigenetic evaluation of fetal/placental unit in normal and growth restricted (IUGR) pregnancies

M Miozzo¹, S Tabano¹, P Colapietro¹, F Grati^{1,2}, F Rossella¹, S De Toffol^{1,2}, S Zanutto¹, C Mandò³, S Sirchia¹, I Cetin³

1)Medical Genetics, Department of Medicine, Surgery and Dentistry, University of Milan, Italy. 2)Units of Research and Development, Cytogenetics and Molecular Biology, TOMA Laboratory, Busto Arsizio, Italy. 3) Unit of Obstetrics and Gynecology, Department of Clinical Sciences L.Sacco, University of Milan, Italy

Genomic imprinting (GI) is an epigenetic process resulting in the different gene expression, based on the parental origin of the allele. Imprinted genes are mainly expressed in placenta where they have a role in controlling nutrient supply. The major mechanisms altering GI status are methylation defects and UPD (Uniparental Disomy). The latter occurs when the two copies of a chromosome pair derive from one parent only. Insulin growth factor II (*IGF2*) and *H19* are imprinted genes (11p15.5), regulated by allelic specific methylation of the Control Region 1 (ICR1) and *H19* promoter, resulting in paternal *IGF2* and maternal *H19* allele expression. Genetic and epigenetic alterations in the *IGF2/H19* locus occur in Beckwith-Wiedemann and in Silver-Russel syndromes, both presenting pre- and post-natal growth defects.

We evaluated the epigenetic signatures of fetal/placental tissues in both normal and IUGR pregnancies to assess: 1) the imprinting status of *IGF2/H19*, possibly correlated to IUGR; 2) global methylation of the genome before and after birth; 3) the occurrence of UPD in IUGR fetuses.

We found that: 1) *IGF2/H19* methylation pattern is similar in normal and IUGR placentas.

Surprisingly, we found hypomethylation of *H19* locus in all samples, suggesting that *H19* is not imprinted in human placenta. 2) A global hypomethylation was present in extraembryonic tissues, respect to fetal blood in all samples; 3) UPD was found in 1(UPD7) out of 24 IUGR cases, therefore it is an infrequent event in IUGR.

In conclusion, our data contribute to improve the knowledge of epigenetic status of fetal/placental unit for the comprehension of the mechanisms regulating fetal growth and development.