

Birth of Parthenogenetic Mice that Can Develop to Adulthood

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To explore and compare features of the parthenotes, we carried out global gene expression analysis by oligonucleotide mouse 11K microarray at day 12.5 of gestation. The phenotypes were similar to those of the control fetuses, although the fetal and placental weights of parthenotes were significantly lower than those of the controls. Interestingly, the umbilical cord was of normal thickness in the $ng^{H19[DELTA]13}/fg^{wt}$ parthenotes, but was very poor in the ng^{wt}/fg^{wt} parthenotes. The proportion of embryos developing to day 12.5 of gestation was not significantly different between $ng^{H19[DELTA]13}/fg^{wt}$ (35%, 16/46) and ng^{wt}/fg^{wt} (25%, 14/56) embryos. Clustering of the expression data and imaging were done using the Cluster and TreeView programs, respectively. The gene expression profiles of the $ng^{H19[DELTA]13}/fg^{wt}$ parthenotes differed from that of the ng^{wt}/fg^{wt} parthenotes, over a wide range of genes. For 1,038 genes, statistical significance was shown at the nominal significance level ($p < 0.001$) of each univariate test. By ontology comparison, these genes can be classified into three categories: cell communication (15.1%), cell growth/maintenance (19.1%) and metabolism (21.9%). These results suggest that the extended development in the $ng^{H19[DELTA]13}/fg^{wt}$ parthenotes is the product of a wide-ranging alteration of gene expression.

The oligonucleotide microarray analysis also showed that in the $ng^{H19[DELTA]13}/fg^{wt}$ parthenotes, normalization occurred in all of the imprinted genes analysed. Out of 34 imprinted genes, only two genes, *Grb10* and *Nnat*, were respectively up- and downregulated at more than double and less than half the level in controls. However, 11 of the genes were downregulated and one gene, *Grb10*, was upregulated in the ng^{wt}/fg^{wt} parthenotes. Furthermore, the number of genes that were expressed differentially at a level greater than twofold (\log_2 (Cy5/Cy3) ratio $> +1$ and < -1) compared with controls for each fetus, ranged from only 11 to 42 (average 30) in the $ng^{H19[DELTA]13}/fg^{wt}$ parthenotes. In contrast, in the ng^{wt}/fg^{wt} parthenotes, a remarkably large number of genes, ranging from 431 to 1,324 (average 842), showed differential expression. Of these, *Dlk1* is the only gene that displayed changes in expression in all four $ng^{H19[DELTA]13}/fg^{wt}$ parthenotes, whereas a common set of 329 genes with varied expression was found in the ng^{wt}/fg^{wt} parthenotes. When $ng^{H19[DELTA]13}/fg^{wt}$ and ng^{wt}/fg^{wt} parthenotes were compared with each other, from 131 to 295 (average 208) genes displayed greater than twofold changes. Thus, the data clearly show that a marked normalization of expression of a wide-range of genes occurred in the $ng^{H19[DELTA]13}/fg^{wt}$ parthenotes, and the more physiological pattern of gene expression provided sufficient developmental competence for these parthenotes.