academicJournals

Vol. 8(6), pp. 110-113, June 2014
DOI: 10.5897/JCAB2014.0416
Article Number: 19BFC1D46148
ISSN 1996-0867

http://www.academicjournals.org/JCAB

Journal of Cell and Animal Biology

Short Communication

A note on interaction and pre-implantation development stages

Justin R. Chimka* and Leiying Jiang

Department of Industrial Engineering, University of Arkansas, Fayetteville, AR 72701, USA.

Received 10 June, 2014; Accepted 25 June, 2014

Having obtained observations of gene expression profiles from the literature, we estimated autoregressive models of mouse preimplantation development and observed interaction among stages. Gene expression profile at the earliest stage is not generally significant, but for observations where profiles at 8-cell embryo and morula stages are relatively great, the effect of unfertilized egg is significantly positive.

Key words: Cellular biology, embryology, gene expression, interaction, linear regression, multivariate analysis, preimplantation development, temporal changes.

INTRODUCTION

Preimplantation development is important to reproductive biology applications including livestock breeding and treatments that repair defective tissues (Hamatani et al., 2004; Wang and Dey, 2006; Chakrabarty et al., 2007), and developmental biology may be studied with genomics (Ko, 2001), Canestro et al. (2007).More specifically we can learn from changes in gene expression during preimplantation development in the mouse (Tanaka et al., 2000; Zeng and Schultz, 2003; Wobus and Boheler 2005).

This research note describes statistical analysis and results of global gene expression profiles at preimplantation development stages. Regression models of stage profiles were estimated as linear functions of earlier stage profiles, and investigation of insignificant variables led us to discover significant interaction between preimplantation development stages. This interaction is important to understanding temporal changes during preimplantation development.

METHODOLOGY

We obtained 21,940 observations of gene expression profiles across the following stages of preimplantation development and assigned to them variables names (in parentheses): unfertilized egg (a), fertilized egg (b), 2-cell embryo (c), 4-cell embryo (d), 8-cell embryo (e), morula (f), and blastocyst (g). The raw data are Supplemental Data for Hamatani et al. (2004): “Embryos were collected from super-ovulated C57BL/6J mice by the standard method. MRNAs were extracted using a Quickprep micro

*Corresponding author. E-mail: jchimka@uark.edu.

Table 1. Independent variable coefficient values versus models of preimplantation stages.

Response	b	c	d	e	f	g
Constant	0.184	0.219	0.0497	0.314	-0.054	0.027
Coefficient a	0.941	-0.199	0.134	0.931	-0.140	0.009
Coefficient b		1.130	-0.0214	-0.887	0.121	0.129
Coefficient c			0.874	0.287	0.080	-0.151
Coefficient d				0.568	0.384	-0.069
Coefficient e					0.574	0.460
Coefficient f						0.630

poly-A RNA Extraction Kit and linear acrylamide as a carrier. Intensity was extracted from scanned microarray images using Feature Extraction 5.1.1 software (p. 130)." For our research, main effects models of each stage were estimated as functions of the previous stages. Where insignificant variables were found, we fit the full second-order model to investigate interaction between main effects.

RESULTS

Preimplantation development stages up to and including the morula enjoyed consistently significant relationships with previous stages in the main effects models of global gene expression profiles. Table 1 shows coefficient values of the first five linear regression models that did not require investigation into interaction (see Responses b through f), and the final model of blastocyst which is not a significant function of the gene expression profile at the unfertilized egg stage (see Coefficient a).

Based on the fact that we cannot reject the hypothesis that co-efficient a = zero in a model of the blastocyst stage, we feel obliged to consider interaction with the full second-order model. While the unfertilized egg stage may not be generally significant to the blastocyst stage, significance may be found for relatively great and/or small gene expression profiles at other stages. In the full second-order model of blastocyst stage the unfertilized eggs stage interacts significantly with 8-cell embryo (e), and morula (f). To further investigate interaction, we used k-means clustering, separated observations according to gene expression profiles at the 8-cell embryo and morula stages, and refit models of the blastocyst stage separately for each cluster.

For observations, where gene expression profiles at 8-cell embryo and morula stages are relatively great the effect of unfertilized egg was positively significantly. For observations where gene expression profiles at 8-cell embryo and morula stages are relatively small, the effect of unfertilized egg was negatively significant. In order to make the distinction between relatively great and small gene expression profiles at 8-cell embryo (e) and morula (f) stages, we fit a linear probability model of the binary cluster variable as a function of e and f:

$$E(\text{cluster}) = -1.547 + 0.378e + 0.274f \quad (1)$$

Figure 1 of fitted values versus observations of the cluster confirms that a cut-point of 0.5 is reasonable. In other words, whenever the fitted value associated with a new observation and Equation 1 is greater than 0.5 one should assume the effect of unfertilized egg on blastocyst is positively significant, and an appropriate model for prediction of temporal changes. When the fitted value associated with a new observation and Equation 1 is less than 0.5 it is assumed that the effect of unfertilized egg on blastocyst is negatively significant, and an appropriate model.

We refit separate models of blastocyst according to the 0.5 rule described above and verified the interaction. Table 2 shows significant independent variable coefficient values for the separate models. They are consistent but for the opposite signs associated with unfertilized egg.

DISCUSSION

Articles which have used statistical analysis to study preimplantation development include studies on the early stages of the mouse embryo (Fleming and Pickering, 1985). Jurisicova et al. (1996) investigated the association between expression in human embryos and factors known to influence *in vitro* fertilization pregnancy outcomes. Takai et al. (2000) explained how prenatal exposure to an estrogenic compound alters postnatal development. Cervero et al. (2004) studied body weight and reproductive function during human embryonic preimplantation development.

We found a textbook case of interaction among preimplantation development phases. Gene expression profile at the earliest stage is not generally significant in a main effects model of the final stage. However, for observations where gene expression profiles at 8-cell embryo and morula stages are relatively great (small), the effect of unfertilized egg is positive (negative)

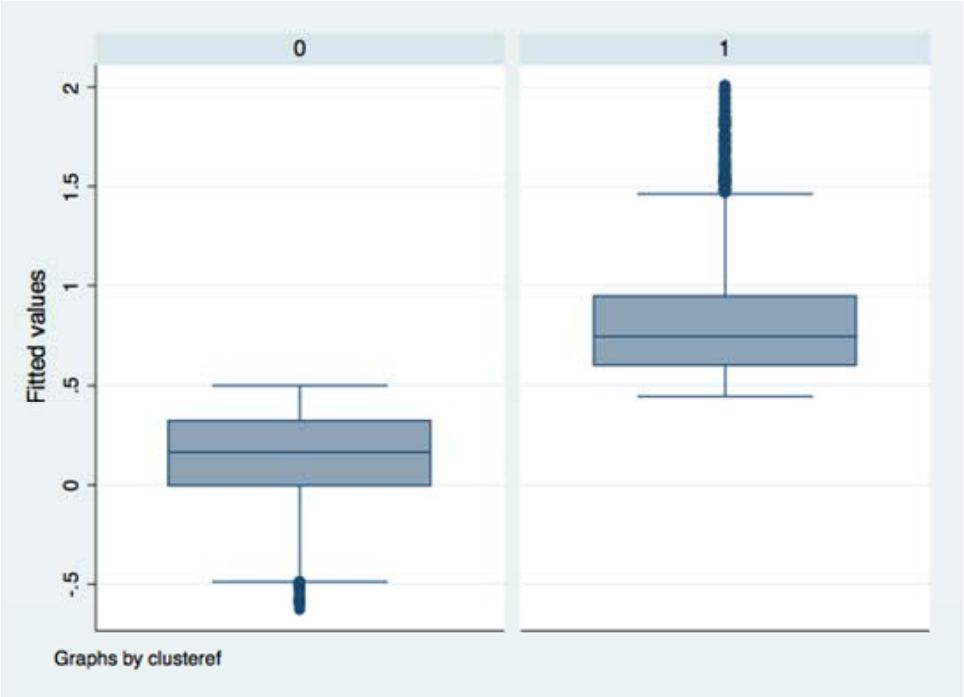

Figure 1. Fitted values versus observations of cluster.

Table 2. Independent variable coefficient values versus models of the blastocyst stage.

Response	g (relatively small e and f)	g (relatively great e and f)
Constant	0.107	-0.078
Coefficient a	-0.019	0.050
Coefficient b	0.127	0.024
Coefficient c	-0.127	-1.645
Coefficient d	-0.027	-0.115
Coefficient e	0.385	0.493
Coefficient f	0.622	0.674

significant. Future work should justify assumptions of the statistical models or search for more theoretically appropriate ones. Also, we hope other authors like Hamatani et al. (2004) will publish their data making it possible to verify these results and discover new ones.

Conflict of Interest

The author(s) have not declared any conflict of interests.

REFERENCES

Canestro, C.; Yokoi, H.; Postlewait, J.H. Evolutionary developmental biology and genomics. Nature Reviews Genetics 2007, 8, 932-942.

Cervero A, Horcajadas JA, Martin J, Pellicer A, Simon C (2004). The leptin system during human endometrial receptivity and preimplantation development. J. Clin. Endocrinol. Metab. 89:2442-2451.

Chakrabarty A, Tranguch S, Daikoku T, Jensen K, Furneaux H, Dey SK (2007). MicroRNA regulation of cyclooxygenase-2 during embryo implantation. Proc. Natl. Acad. Sci. USA 104:15144-15149.

Fleming TP, Pickering SJ (1985). Maturation and polarization of the endocytotic system in outside blastomeres during mouse preimplantation development. J. Emroyol. Exp. Morphol. 89:175-208.

Hamatani T, Carter MG, Sharov AA, Ko MSH (2004). Dynamics of global gene expression changes during mouse preimplantation development. Dev. Cell 6:117-131.

Jurisicova A, Casper RF, MacLusky NJ, Librach CL (1996). Embryonic human leukocyte antigen-G expression: Possible implications for human preimplantation development. Fertil. Steril. 65:997-1002.

Ko MSW (2001). Emryogenomics: developmental biology meets genomics. Trends Biotechnol. 12:511-518.

Takai Y, Tsutsumi O, Ikezuki Y, Kamei Y, Osuga Y, Yano T, Taketan Y (2000). Preimplantation exposure to bisphenol A advances postnatal development. Reprod. Toxicol. 15:71-74.

Tanaka TS, Jaradat SA, Lim MK, Kargul GL, Wang X, Grahavoc MJ, Pantano S, Sano Y, Nagaraja R, Doi H, Wood III WH, Becker KG, Ko

MSH (2000). Genome-wide expression profiling of mid-gestation placenta and embryo using a 15,000 mouse developmental cDNA microarray. Proc. Natl. Acad. Sci. USA. 97:9127-9132.
Wang H, Dey SK (2006). Roadmap to embryo implantation: Clues from mouse models. Nat. Rev. Genet. 7:185-199.
Wobus AM, Boheler KR (2005). Embryonic stem cells: Prospects for developmental biology and cell therapy. Physiol. Rev. 85:635-678.
Zeng F, Schultz RM (2003). Gene expression in mouse oocytes and preimplantation embryos: Use of suppression subtractive hybridization to identify oocyte- and embryo-specific genes. Biol. Reprod. 68:31-39.