GENOMICS

Snapshots of mouse development

Using staged embryos, researchers report a genomic analysis of mouse gastrulation and organogenesis.

The post-implantation period is a dramatic one for the mouse embryo. Over the course of about 3 days, the body is patterned: the three germ layers emerge, morphogenetic movements occur, and rudimentary organ systems are formed. What is happening to global gene expression during this period?

Julie Baker and Nesanet Mitiku at Stanford University now answer this question for the first time. In an effort involving dissection of hundreds of embryos at each time point, the researchers report a microarray analysis of gene expression in the mouse embryo, sampling every 6 hours over the course of gastrulation and organogenesis, and providing developmental biologists with a high-resolution dataset for use in their own studies.

"What was critical was that we were very strict in our criteria as to the stage of the embryos," says Baker. "You need enough embryos, you need to have them rigorously staged, and you need enough RNA to do the analysis. And it's not as easy as in, say, the frog, because the mouse embryo is so small and so inaccessible."

The data reveal several interesting patterns. There is little change in transcription during gastrulation even though the embryo does undergo substantial morphological transitions at this time. However, a burst of transcriptional activity accompanies somitogenesis (**Fig. 1**). "Clearly," says Baker, "there's something major going on at this point. It's about the time when the cell cycle starts to slow down in the mouse. So what I think we're seeing is differentiation starting to play a role as the embryo goes into organogenesis."

When Baker and Mitiku looked for temporal patterns in the data, seven sets of genes emerged, each with distinct expression patterns. What is more, genes in one set did not overlap much with genes in any other set in regard to their functional (gene ontology) annotations. For instance, pluripotency genes and genes involved in ion transport were expressed early, and genes implicated in organogenesis were expressed late. A particularly interesting set were those enriched in RNA processing and cell-cycle functions, which were strongly downregulated during early somitogenesis.

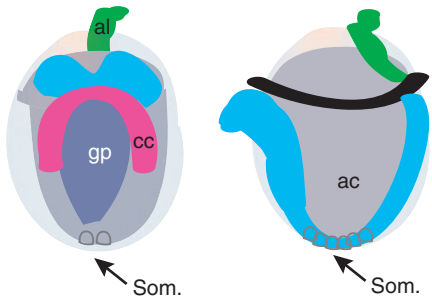

Figure 1 | Early somitogenic stages in mouse. Depiction of the mouse embryo (left, anterior view with 0–4 somite pairs (som.); right, lateral view with 5–8 somite pairs) at embryonic day 8. Gp, gut pocket; cc, cardiac crescent; al, allantois; ac, amniotic cavity. Reprinted with permission from Elsevier.

Some genes were physically clustered as well. This was particularly apparent for genes activated around somitogenesis, which are enriched and clustered on chromosome 7. Coexpression of genes during development may thus involve higher-order chromosomal effects. Or, as Baker succinctly put it, "there seems to be a bigger plan."

Establishing the importance of these observed patterns for mouse development will need more experiments. Especially in light of potential chromatin effects, it is possible that not all genes upregulated during development are indeed functionally involved in the process. Moreover, as Baker emphasizes, the data in this study report on RNA levels, but not on translation of the RNA into protein. "It's going to be important which set of transcripts actually gets chosen for translation," she says. "That's what is interesting about our RNA binding cluster. Some of those genes may be involved in deciding which transcripts get processed and which don't."

Another aspect of the dataset is that it reports gene expression in the entire mouse embryo and not in specific lineages, cell types or tissues. "It's really important to know what the spatial profile is," says Baker. "That's the sort of thing you can do by sorting and microarrays in *C. elegans*." But both the difficulty of obtaining large amounts of material and the lack of good markers still hinder a lineage-specific genomic analysis in mouse.

Speaking of recent work profiling gene expression in haematopoetic stem cells (HSCs), Baker says, "if we could have an equivalent in the embryo of the HSC—where we could say, this is early mesoderm, and this is mesoderm committed to cardiac, and this is mesoderm committed to muscle, and sort the cells and see what's expressed—that's where we'd all like to be. But in the early mouse embryo, that's something we can only dream of." However, several labs, including Baker's, have turned recently to the study of differentiation in embryonic stem cells. Although it comes with all the substantial caveats to working *in vitro*, this may get around some of the difficulties inherent to working in the mouse embryo.

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Mitiku, N. & Baker. J. C. Genomic analysis of gastrulation and organogenesis in the mouse. *Dev. Cell* **13**, 897–907 (2007).