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COMMENTARY

Reply: Cell fate in the early mouse embryo: Sorting out the influence of developmental history on lineage choice

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In his response, Yamanaka (2011) acknowledges the similarity in our datasets when a high proportion of cells are internalised in the 8- to 16-cell-stage transition. In these instances it is not surprising that there is no correlation between EPI/PE fate, since there is only one major pool of cells from which to segregate these lineages. From our work, and in previous studies, it is more common for a closer parity to exist between cells dividing asymmetrically in the first and second waves — in these embryos the relationship between developmental history and cell fate is revealed. Embryos with such a high proportion of cells dividing asymmetrically in the 8- to 16-cell-stage transition are rare, and I agree with Yamanaka's proposal to test the underlying cause leading to an increase in this subset. Strain dependence is a recurrent issue in the field and the potential for microinjection to disrupt polarity clearly warrants further investigation. As noted by Yamanaka, the experimental conditions are very specific; it is important to note here that in our study we injected blastomeres prior to compaction and polarisation and do not observe polarity disruption in these earlier stages.

The flexibility and robust nature of development is unequivocal and remarkable. This does not mean we should disregard clear evidence that developmental history guides cell fate decisions. Rather, gaining an understanding of the biases related to a cell's journey through development could well provide a foothold to guide our understanding of the molecular mechanisms involved. I wholeheartedly agree with Dr. Yamanaka that this is an exciting time for the field and thank him for participating and engaging in this productive discussion.

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