

homeodomain is sufficient for the binding to *cad* mRNA; other regions of the protein, or other homeodomain proteins such as *cad*, orthodenticle and the homeodomain of antennapedia, did not bind. That the *bcd* homeodomain interacts with *cad* mRNA *in vitro* is consistent with the *in vivo* observation, suggesting that the homeodomain of *bcd* is necessary for the formation of the *cad* gradient (Fig. 1f, g). The failure of other homeodomain proteins to bind *cad* mRNA does not rule out the possibility that they possess RNA-binding properties as preceded by zinc-finger-type transcription factors¹⁰.

To assess the functional significance of the *in vitro* interaction between *bcd* and *cad* mRNA, we performed co-transfection experiments with *Drosophila* Schneider cells¹¹. We used chloramphenicol acetyl transferase (CAT) reporter gene constructs¹¹ containing different 3' UTR sequences (Fig. 3). The reporter gene constructs were set under the control of the *bcd*-responsive, *cis*-acting element of the zygotic *hunchback* promoter¹². After co-transfection with *bcd*, we determined the stimulated transcription of CAT mRNA by reverse transcription-polymerase chain reaction (RT-PCR)¹³, and the translation of the CAT mRNAs with the different 3' UTRs by assaying CAT activity¹¹.

CAT mRNAs containing the *Drosophila cad* 3' UTR sequences or the regions including the BBR produced about sevenfold less CAT activity than CAT mRNA containing the *cad* 3' UTR sequences of *Clogmia* or the 3' half of the 3' UTR of *Drosophila cad* (Fig. 3a–c). CAT mRNA containing the BBR within the simian virus 40 (SV40) 3' UTR¹¹ were also translated less efficiently than those containing only the SV40 3' UTR. These results suggest that *bcd* may not only act as a transcriptional activator in the assay system, but also reduce the translation efficiency of the BBR-containing mRNAs.

To show that *bcd* does indeed suppress the translation of BBR-containing mRNA, we examined reporter gene constructs containing the SV40 3' UTR with or without the BBR that were transcriptionally activated by the yeast GAL4 transcriptional activator¹⁴. In the absence of *bcd*, the GAL4-stimulated CAT mRNAs were translated with similar efficiency (Fig. 4). In the presence of *bcd*, however, the translation of the BBR-containing CAT mRNA was significantly reduced, but the translation of CAT mRNA without the BBR was not significantly affected. This shows that *bcd* suppresses the translation of BBR-containing mRNA.

Our results are consistent with the argument that the anterior determinant *bcd* acts not only as a transcriptional activator but also functions in a manner analogous to the key components of the posterior maternal pattern-organizer system^{15–20}, which acts by translational repression through the activities of *nanos* and *pumilio*^{15–20}. After binding the *pumilio* protein and a 55K protein to the *nanos*-response element within the 3' UTR of *hunchback* mRNA^{17,20}, the *nanos* protein is thought to interact with this 'landing pad' to provide region-specific translational repression of the evenly distributed maternal *hunchback* mRNA^{15–19}. This allows for the activation of the posterior gap genes *knirps* and *giant* in response to *cad*⁵. Thus, while in the posterior region of the embryo translational and transcriptional control are conducted through separate components, the anterior determinant *bcd* can exert both regulatory functions. Our findings also imply that the asymmetric distribution of the key components of the anterior and posterior maternal pattern-forming systems, which was thought to be set up independently^{1,2}, is linked through the dual function of *bcd*. □

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ADDENDUM

Identification of the breast cancer susceptibility gene *BRCA2*

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THE sequence for the *BRCA2* gene is now available at the web page of the Institute of Cancer Research, address <http://www.icr.ac.uk/molcarc/brca2.htm>, as well as from Genbank. □

ERRATUM

Mechanosensory signalling in *C. elegans* mediated by the GLR-1 glutamate receptor

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FIGURES 3 and 4 of this Letter were inadvertently transposed during the production process; the legend to Fig. 3 therefore describes the figure published as Fig. 4 and vice versa. □