

The human Brn-3b POU transcription factor shows only limited homology to the Brn-3a/RDC-1 factor outside the conserved POU domain

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The Brn-3 transcription factor was originally identified and characterized as a member of the POU family on the basis of the isolation of cDNA clones encoding its POU domain from rat brain (1). Subsequently we isolated identical rat POU domain cDNA clones as well as others for a closely related factor which differs by seven amino acids in the POU domain (2). We refer to this novel factor as Brn-3b to distinguish it from the original factor which we refer to as Brn-3a (2). Recently Collum *et al.*, (3) have reported the first isolation of a full length cDNA clone for a member of the Brn-3 family. This RDC-1 factor, isolated from human neuroepithelioma cells has a POU domain identical to the rat Brn-3a factor at all the amino acids where Brn-3a and b diverge (2, 3) and appears to represent the human homologue of Brn-3a.

In order to probe further the relationship of the Brn-3a and b factors, we screened a human testis cDNA library with a Brn-3a POU domain probe. DNA sequence analysis of the clones isolated in this way indicated that they contained a long open reading frame capable of encoding a protein of 264 amino acids (Figure 1). As in RDC-1/Brn 3a, the POU domain is located near the C-terminus of the protein but in this case the clone resembles Brn-3b rather than Brn-3a at all the amino acids where Brn-3a and b differ indicating that is likely to be the human homologue of Brn-3b.

Outside the closely related POU domain (91.8% homology of the amino acid level) the two factors are much less closely related (28.9% homology) with the strongest homology in the very short region C-terminal to the POU domain where four out of seven amino acids are identical with the stop codon being located at the same position in both proteins. Similarly, in Brn-3b, an N-terminal region of homology between the two factors, contains a methionine residue in the equivalent position to the suggested initiator methionine of Brn-3a/RDC-1 (3) and both factors contain a run of histidine residues in this N-terminal region. Further downstream however, the two proteins show only limited homology until the POU domain is reached and regions of Brn-3a containing predominantly glycine residues are absent in Brn-3b resulting in the predicted Brn-3b protein being sixty seven amino acids smaller than Brn-3a. This together with the limited differences between the two factors even in the POU domain suggests that Brn-3a and b are encoded by different genes, although these may be derived from a single ancestral gene with subsequent duplication and divergence of the encoded proteins to serve distinct but possibly related functions.

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REFERENCES

1. He,X., Treacy,M.N., Simmons,D.M., Ingraham,H.A., Swanson,L.S. and Rosenfeld, M.G. (1989) *Nature* **340** 35–42.
2. Lillycrop,K.A., Budhram,V.S., Lakin,N.D., Terrenghi,C., Wood,J.N., Polak,J.M. and Latchman,D.S. (1992) *Nucleic Acids Res.* **20** 5093–5096.
3. Collum,R.G., Fisher,P.E., Datta,M., Mellis,S., Thiele,C., Huebner,K., Croce,C.M., Israel,M.A., Theil,T., Moroy,T., De Pinho,R. Alt,F.W. (1992) *Nucleic Acids Res.* **20** 4919–4925.
4. Lai,J-S., Cleary,M.A. and Herr,W. (1992) *Genes and Development* **6** 2058–2065.

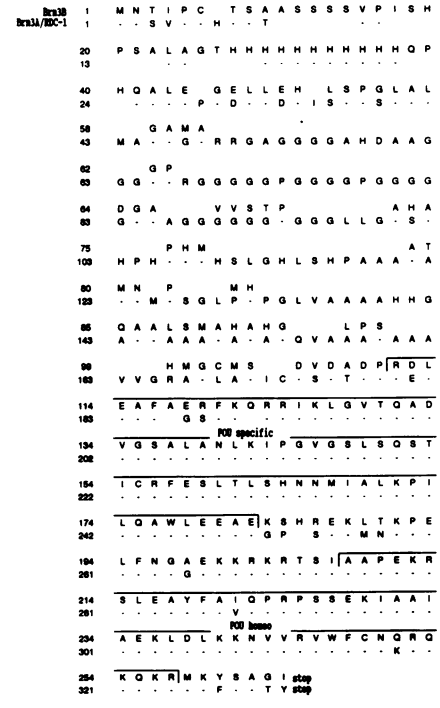

Figure 1. Comparison of the predicted amino acid sequence of Brn-3b with that of RDC-1/Brn-3a (3). Identity is shown by a dash, a blank indicates a gap included to maximize alignment. The POU-specific and POU homeodomains are indicated.

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