To the Editor:

Bora et al.1 describe the cloning of a cDNA for a protein designated human nup36. They suggest that the 96.8% identity of the deduced protein to the yeast nucleopore protein nup100 is "predictable," given the high conservation of nucleoporins. In fact, this degree of identity between human and yeast proteins would be highly unusual. It instead suggests that the putative cDNA is actually a yeast sequence.

Because the complete nup36 sequence is not yet publicly available, two stretches of 150 bp of sequence from the 5' end and close to the 3' end were input by hand for comparison with GenBank using BLAST (National Library of Medicine) (Fig. 1). The 5' sequence shows 97% identity with the yeast nup100 sequence and seems to correspond to the coding sequence, the 3' sequence shows 98% identity with a yeast transposon sequence. Although the whole sequence has not been compared yet, the extremely close match of widely separated regions of nup36 suggests that the whole sequence is of yeast origin. The few differences may represent polymorphisms or sequence errors. Furthermore, the lack of a polyA tail suggests that this clone is a yeast genomic fragment, not a cDNA. Unfortunately, the presence of yeast sequences in human cDNA libraries from Clontech is not unprecedented.

A surprising feature of the nup36 clone is the local divergence in sequence corresponding to the N-terminal peptide sequence against which the probe was directed (Fig. 1). This is puzzling and might warrant a reexamination of the sequencing gels.

The other data supporting the identification of nup36 as a human sequence are not strongly compelling.

![Sequence Comparison](Image)

**FIGURE 1.** (top) Comparison of 150 bp from the 5’ end of nup36 with nup100. (middle) Comparison of 15 bp close to the 3’ end of nup36 with nup100. (bottom) Comparison of sequences around the putative translation start site of nup36, indicated by ***.

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The southern blot easily could represent cross-hybridization, and the western blot is also weak. Although the presence of a yeast protein in the serum of patients suffering from a form of uveitis might be of interest, it seems likely that the nup36 sequence presented is an experimental artifact unrelated to the pathology in question.

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**References**


**Note added in proof**: The sequence of nup36 has now been released in GenBank (U23479) and has been examined. The 97% identity with yeast genomic DNA is found throughout in both coding and noncoding sequence. Even though some protein sequences are well conserved between yeast and human, such a match at the nucleotide level would be completely unprecedented. This sequence must be of yeast origin.

**The authors reply:**

We thank Dr. Wistow for his interest in our article and appreciate the opportunity to respond to his concerns.

nup-36 clone was isolated from a cDNA library and has many of the characteristics of a cDNA. There is a possibility that the cDNA library obtained from Clontech might be contaminated with yeast; however, based on the following observations and those reported in the article (i.e., transfection–expression studies and southern blot analysis), we think that it is unlikely.

We have taken and additional look at our sequencing gels, and the sequences are correctly reported in the article. Like Dr. Wistow, we were surprised initially by the high identity (96.8%) of the deduced protein to yeast nup-100. However, approximately 75% to 86% identity exists between some human and yeast proteins, as reported in the literature. Trip 1 (thyroid hormone-receptor interacting protein) shares striking similarity to the yeast transcriptional mediator Sug 1, with 86% amino acid identity in the conserved ATPase (CAD) domain at the C-terminus and 76% over the full length of both proteins. Spi 1, a newly identified yeast gene, shares 81.4% amino acid identity with a human protein TC4 throughout the length of the proteins.

High-sequence identity (97% to 98%) in the 5' region, the open reading frame, and in the 3' region with nup-100 and yeast transposon may suggest that yeast genes have been incorporated in the human genome. This interesting possibility is supported by the southern blot analysis reported in our article. Furthermore, at present, three genomic clones hybridizing (under stringent conditions) with nup-36 cDNA are being characterized. These clones were isolated from a human lymphocyte genomic library obtained from Stratagene—a different company than the one that supplied the original cDNA library we explored.

Recent results from our laboratory suggest that nup-36 is a part of, or is associated with, a high molecular weight chimeric–fusion protein of approximately 98 kDa. Experiments are under way to identify these unknown proteins. Precedent exists for the creation of chimeric–fusion proteins in the literature. For example, CAN protein, which is a human nucleopore complex protein, has been reported to be associated with myeloid leukemogenesis. CAN has been shown to form a fusion gene with DEK, a novel gene present on chromosome 6. The fusion mRNA encodes a chimeric DEK–CAN protein of 165 kDa whereas the predicted molecular masses for DEK and CAN proteins have been reported to be 43 and 220 kDa, respectively.

The evidence presented above leads us to conclude that nup-36 is present in the human genome. Dr. Wistow’s concern about yeast contamination of a cDNA library is always warranted, but seems not to apply in the current situation.

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**References**