

Fig. 2. The sequence alignment between TGF- β 2 and NGF. The two sequences are aligned according to their structural alignment. The TGF- β 2 numbering is used.

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TGF- $\beta$ 2  ALDAAYCFRNVQDN10CLRP20LYI30DFKRD40LGW50...K
NGF      V10DSVSVWVG20D30KT...TATDIKGKEV40

TGF- $\beta$ 2  WIHE...PKGYNANF40CA...GAL...50PYLWSSDTQHS
NGF      TVLAENVINRQ.YFFETK40CRASNPVESG50RG60I...

TGF- $\beta$ 2  RVLSLYNTINPEASASPC60CVSQDLEPLT70I80VY...IGKTFK
NGF      ...DSKH...WNSY60CTTT70HTFVK80ATTDEK...QAA

TGF- $\beta$ 2  IEQLSNMIVKS100CK110CK120CS
NGF      WRFI100.RIDT110.AC120VC130

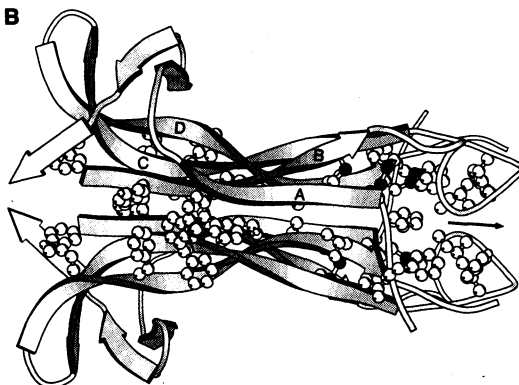
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A



Fig. 3. The dimers of TGF- β 2 and NGF. The cystine residues and those residues located in the dimer interface are represented by white spheres. The sulfur atoms of the disulfides are shown as dark spheres. The four corresponding β strands are labeled as A, B, C, and D in each structure. (A) The TGF- β 2 dimer with its dyad axis labeled at the center and pointing into the page. (B) The NGF dimer with the arrow pointing along its dyad axis. Both drawings are made with the program MOLSCRIPT (9).

B



et al. in which a Z score is calculated to be -11.7 when the 67 best aligned NGF residues are used to fit the profile derived from TGF- β 2 dimer (2, 6) (a negative Z

score means the two structures are incompatible in the context of the dimer).

There are also differences in the proposed receptor recognition sites. The pro-

posed type II receptor binding site for TGF- β 2 has been localized to the surface residues within the region 40 to 80 (7), which is at the back of the heel of the hand. Conversely, the putative receptor binding site for NGF is located around the three-hairpin loop region that includes residues 29 to 35, 43 to 48, and 92 to 98; TGF- β 2 lacks two of these loops, 29 to 35 and 43 to 48.

In summary, the topology of the four central β strands together with the three pairs of disulfides is conserved between the TGF- β and NGF families despite the low sequence homology and their very different roles in mediating the dimer formation. These common features may represent a more general structural motif that could be used as a common building block for other cysteine-rich growth factors.

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Silica-Carbonate Isotopic Temperature Calibration

A. Shemesh *et al.* (1) use the oxygen isotope fractionation between biogenic silica and foraminiferal carbonate in deep-sea sediments to determine variations in both the temperature of deposition and the isotopic composition of seawater over the last glacial cycle. It appears that they have overestimated the sensitivity of the silica-carbonate isotopic thermometer by a factor of 6 and that their results may therefore be invalid.

Shemesh *et al.* deduce the silica-carbonate fractionation curve by combining data

from the silica-water fractionation and the carbonate-water fractionation. The latter can be found in studies by S. Epstein *et al.* (2) on biogenic calcite and by R. N. Clayton (3) on inorganically exchanged calcite. For biogenic silica, L. D. Labeyrie (4) showed that isotopic fractionation between biogenic silica and water follows closely the fractionation between crystalline quartz and water measured in higher temperature laboratory experiments (5). Similar agreement was found for amorphous silica precipitated in geothermal wells (6). The temperature

dependence for deposition of silica by diatoms has been redetermined with the use of new analytical techniques (7), and results are in agreement with earlier findings, although the data are rather scattered.

Previous studies lead to the conclusion that quartz-calcite is a good approximation to diatom-foraminifera for the purposes of isotopic fractionation. The quartz-calcite isotopic fractionation is well known experimentally and theoretically at all temperatures (8). At ocean temperatures, the temperature coefficient of the quartz-calcite isotopic fractionation is -0.04 per mil per degrees Celsius. For an analytical precision of ± 0.15 per mil, the paleotemperature

uncertainty is $\pm 4^\circ\text{C}$. For most oceanographic and climatological purposes, such a large uncertainty would be unacceptable.

Shemesh *et al.* derived a silica-carbonate isotopic temperature calibration with a temperature coefficient of -0.26 per mil per degrees Celsius, with a corresponding paleotemperature uncertainty of only $\pm 0.6^\circ\text{C}$. How was this accomplished? From the data of A. Juillet-Leclerc and L. Labeyrie (7), Shemesh *et al.* selected 6 of the 18 data points spanning a small fraction of the temperature range and extracted a silica-water temperature coefficient that is incompatible with other data. Thus their conclusions appear to be invalidated.

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Response: In our report (1), we demonstrated the use of oxygen isotopes in deep-sea biogenic silica for paleoceanographic studies and concluded that (i) opal retains its isotopic composition for about 80,000 years, (ii) opal can be measured with reproducibility sufficient for paleoceanographic studies, and (iii) it is possible to differentiate between the temperature and ice volume effects by comparing the oxygen isotopic composition of foraminifera calcite ($\delta^{18}\text{O}_\text{C}$) and diatoms retrieved from the same samples. The first two conclusions are not in debate; Clayton argues only against the third. We reject his assertion that the results are invalid, and we think the isotopic composition of opal will contribute to the paleoceanographic community important information like isotopic records in regions void of carbonates and a new field of isotopic stratigraphy of the Southern Ocean.

The differentiation between the effects of temperature and isotopic composition of seawater ($\delta^{18}\text{O}_\text{w}$) is based on the difference between the carbonate-water and silica-water fractionations. Clayton suggests that the high-temperature (magmatic) calibration of quartz-water can be accurately extrapolated to low temperatures. He refers to a 1974 study (2) in which L. D. Labeyrie analyzed diatoms and concluded that, within the

Table 1. Compilation of $\delta^{18}\text{O}_\text{Si}$ and $\delta^{18}\text{O}_\text{C}$ from Holocene core tops. All $\delta^{18}\text{O}_\text{Si}$ and $\delta^{18}\text{O}_\text{w}$ are from (3) and reported versus SMOW. RC13-271 from (1). Data for $\delta^{18}\text{O}_\text{C}$ (plotted against Pee Dee belemnite) are from (1, 5). Temperature is represented by *t*.

| Core | Location | | $\delta^{18}\text{O}_\text{w}$ | <i>t</i> ($^\circ\text{C}$) | $\delta^{18}\text{O}_\text{Si}$ | $\delta^{18}\text{O}_\text{C}$ | Ref. |
|----------|----------|----------|--------------------------------|-------------------------------|---------------------------------|--------------------------------|------|
| MD80304 | 51°00'S | 67°44'E | -0.3 | 4 | 44.03 | 2.91 | (5) |
| MD73025 | 43°49'S | 51°19'E | 0 | 11 | 42.79 | 2.20 | (6) |
| MD73026 | 44°59'S | 53°17'E | 0 | 11 | 43.59 | 2.00 | (5) |
| MD82424 | 54°05'S | 0°70'E | -0.3 | 1.5 | 45.00 | 3.59 | (5) |
| RC13-269 | 52°37'S | 0°07'W | -0.3 | 4 | 42.69 | 2.2 | (9) |
| RC13-259 | 53°52'S | 04°56'W | -0.3 | 1.5 | 43.75 | 2.8 | (7) |
| PLDS-72 | 01°08'N | 109°15'W | 0.2 | 24 | 38.96 | 0.35* | (8) |
| RC13-271 | 51°59'S | 04°31'E | | | 42.5 | 2.90 | (1) |

*Isotopic composition of the planktonic foraminifera *Neoglobobulimina dutertrei*.

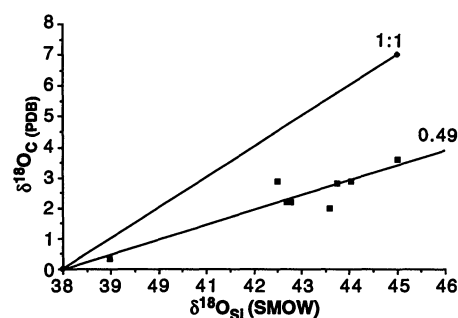


Fig. 1. Holocene core top diatoms and foraminifera isotopic compositions. The 1:1 line indicates the relationship expected if carbonate and opal have the same slopes. The 0.49 line indicates the best fit for the data. $Y = -18.63 + 0.49X$, $R^2 = 0.832$, PDB, Pee Dee belemnite; SMOW, standard mean ocean water.

limits of uncertainties, the diatom-water paleotemperature equation has the same slope as the carbonate paleotemperature equation. In this case, a calcite-opal isotopic thermometer cannot be applied (2).

In a 1987 study (3), A. Juillet-Leclerc and Labeyrie improved not only the analytical technique but also the core-top sampling of the main oceanic gradient. They determined the opal-water fractionation by analyzing marine diatoms and concluded that the slope of the opal paleotemperature equation was 2.4, about one-half that for carbonate, thus changing their earlier conclusions (2, 4). Although Shemesh *et al.* used only Antarctic samples for determining the cold water slope, the value obtained (2.03) was close to that determined by Juillet-Leclerc and Labeyrie (3), who used a larger data set; it is different from the slope of 4.3 determined for the carbonate paleotemperature equation.

Another line of evidence indicating that the opal slope is about half that for carbonate comes from the plot for oxygen isotopic composition of diatoms plotted against that for foraminifera ($\delta^{18}\text{O}_\text{Si}$ plotted against $\delta^{18}\text{O}_\text{C}$) (Fig. 1), in which we have combined all the core top samples for which both carbonate and opal data are available (Table 1). The $\delta^{18}\text{O}_\text{Si}$ plotted against $\delta^{18}\text{O}_\text{C}$ slope, 0.49, is close to that predicted

(2.4/4.3 = 0.56) from the opal-water slope in (3) and the well-established carbonate-water slope, which confirms that the slope for opal paleotemperature is different from that for carbonate. If the carbonate and opal slopes were identical, as suggested by Clayton's extrapolation, the expected slope in Fig. 1 would be 1.0. Moreover, if one does not account for the effect of seawater composition on the $\delta^{18}\text{O}_\text{Si}$ plotted against $\delta^{18}\text{O}_\text{C}$ slope, the data support the Juillet-Leclerc and Labeyrie opal-water slope and reflect the main oceanic thermal gradient from the equator to the Southern Ocean.

We are aware of the limitations of the opal-carbonate isotopic thermometer and of the fact that the opal-water system needs a better calibration. However, this calibration cannot be made by extrapolating from high-temperature crystalline quartz to low-temperature amorphous opal. Until new results are available, the indications we have suggest that at low temperatures the opal slope is different from that for the carbonate and that the diatom calibration, and not the high-temperature quartz calibration, should be used in determining the opal-calcite isotopic thermometer.

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