bers of the reticulon gene family, which are expressed in neurons mainly at intracellular sites[10,11]. The carboxy-terminal tail contains a consensus sequence that may serve as an endoplasmic-reticulum retention signal.

From its sequence, Nogo may be a membrane-associated protein consisting of a putative large extracellular domain of 1,024 residues with seven predicted *N*-linked glycosylation sites (N-X-S/T), two or three transmembrane domains and a short carboxy-terminal region of 43 residues, but experimental mapping will be needed to determine its exact orientation in the membrane.

To investigate whether human Nogo inhibits neurite outgrowth like its bovine homologue[9], we developed a soluble version of its largest isoform (relative molecular mass 220K). The extracellular region of this protein was prepared as a bivalent chimaeric protein using the CD33 signal sequence and human IgG Fc sequences. The purified protein was assayed *in vitro* for neurite-inhibitory activity. We allowed dissociated cerebellar granule neurons to adhere to substrate and then treated the cells with control Fc protein (SIRP-Fc), MAG-Fc or Nogo-Fc (Fig. 1b). We found that the control protein had no effect on neurite outgrowth, whereas myelin-associated glycoprotein (MAG) and Nogo were equally potent as dose-dependent inhibitors of nerve growth (Fig. 1c). The relative number of neurons present in each randomly selected field was similar for all the proteins tested, suggesting that the observed inhibition was not due to a failure of cell adhesion or indirect effects on cell survival.

Our results show that recombinant soluble Nogo produced as a bivalent Fc fragment is a potent neurite-outgrowth inhibitor. The availability of these active recombinant Nogo isoforms should enable their relative importance to be assessed in inhibiting neurite outgrowth at different anatomical loci and help in the identification of their receptor(s). Such definition is critical for the development of pharmacological treatments that will allow repair of lesions of the central nervous system.

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Materials

Creating the narrowest carbon nanotubes

The properties of carbon nanotubes[1] depend on their diameter and on the two integers (m,n) that describe their roll-up vector[2]. The smallest nanotube reported previously had a diameter of 0.7 nm, the same as that of a C_{60} structure[3], although nanotubes with a diameter of 0.4 nm have been predicted[4]. Here we report that simple improvements in the electric-arc technique can create a carbon nanotube with a diameter of 0.5 nm — the same as a C_{36} molecule[5].

We used the same apparatus and conditions as described in ref. 6, except for the anode. This was prepared by boring a 3-mm-diameter hole in a 6-mm-diameter graphite rod. We filled these holes with a mixture of cobalt metal powder (~ 5% at. metal) and the inner black core of a cathode deposit. This deposit was prepared using a graphite anode, and consisted of carbon nanotubes and other amorphous carbonaceous materials. We used a high-resolution transmission electron microscope (HRTEM, JEM 200-cx, operated at 200 kV) to characterize the morphologies and microstructures of the products. The specimens for HRTEM analysis were prepared by dissolving the black deposit in ethanol. After ultrasonic treatment, a drop of the liquid was sprayed onto a holey carbon copper grid.

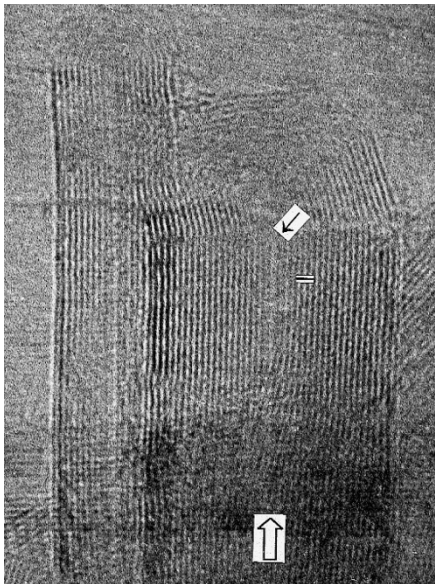

Figure 1 HRTEM image of two nanotubes with outer diameters of 6 nm and 16 nm, respectively. The hollow arrow points to the innermost tube in the right nanotube, which has a diameter of 0.5 nm. The other arrow points to the tip of this tube, which we believe to be closed with half a C_{36} cage. Scale bar, 1 nm.

Figure 1 shows an HRTEM image of the carbon nanotubes found in our experiment. This shows a uniform intershell spacing of 0.34 nm. The open arrow in Fig. 1 indicates the innermost nanotube, with a diameter of about 0.5 nm. Although the entire tip is not clearly imaged, this innermost nanotube is closed at the end by a half circle, as indicated in Fig. 1. We suspect that it is closed by half a C_{36} cage. Theoretical results predict that a zigzag nanotube with this diameter might have an (m,n) value of (6,0) and a diameter of 0.47 nm or (7,0)(0.55 nm).

It has been suggested that carbon nanotubes are built up from atoms or atomic ions[7]. If this is true, anodes filled with graphite or carbon nanotubes should give the same results. Our results indicate that in the discharge the nanotubes could grow from carbon fragments. We propose that the carbon fragments within the arc have two forms before they begin to join up: curved (nanotube-filled anodes) and flat (graphite-filled anodes). Curved fragments will require less energy to form carbon nanotubes than flat ones. Use of a catalyst — cobalt, in our case — will result in curved fragments forming carbon nanotubes of the smallest diameter (0.5 nm in our experiment).

C_{60} has quite different properties from C_{36}: for example it is soluble in toluene, whereas C_{36} is not[5], and the high curvature and increased strain energy of this smallest nanotube might lead to many unusual properties. These tubes are in the form of the innermost shell of multiwall nanotubes. An important question that remains is whether these small-diameter nanotubes could occur as single-wall nanotubes.

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