

conglomerates immunostained for SOD1 and ubiquitin were increasingly found. In spite of the prominent degeneration, none of the motor neurons showed nuclear changes (chromatin margination, pyknosis, karyorrhexis) suggestive of apoptosis. Although ISEL reveals nuclear DNA strand breaks well before the appearance of an apoptotic morphology, all motor neurons remained unlabeled, regardless of their degree of degeneration (Fig. 1a,b). High proteinase K concentrations only produced increased background staining of all nuclei in the section (not shown). Absence of neuronal staining was also found with antibodies to c-Jun/AP-1 (Fig. 1c), PCNA and activated caspase-3. By contrast, labeled cells were readily detected with all assays in the cerebellum of *weaver* mice (Fig. 1d).

Although we cannot definitely rule out that motor neuron death in mutant SOD1 mice occurs *via* apoptosis, the present data do not support this hypothesis. Motor neurons degenerate either by massive vacuolation or by formation of intracytoplasmic conglomerates. Whereas the former change appears to induce motor neuron destruction by a necrotic-like mechanism, it is unclear whether cytoplasmic inclusions, that cause dysfunction to motor neurons⁹, are also responsible for their death. However, the apoptotic machinery is not apparently recruited in either case. These results should be kept in mind when devising therapeutic strategies aimed at controlling cell death in human ALS.

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Italian changes are not surprising

To the editor—I am pleased to see that the ongoing process of change in Italian biomedical research policy is being brought to the attention of the international scientific community. In particular I am referring to Martina Ballmaier's *News* story in the August issue of *Nature Medicine* entitled "Institute surprise for Italian scientists." This is certainly proof that our scientists are accepted as peers by their European and American counterparts. However, with your permission, I would like to provide a few additional details that may clarify the situation and separate fact from fantasy.

The *News* story refers to a parliamentary decree that aims to transform Italy's Higher Institute of Public Health, Istituto Superiore della Sanità (ISS), into a more autonomous institute, separate from the Ministry of Health, and more focused on biomedical research. The decree was passed on 4 August 1999, and although it was most welcome, this change is far from being in itself revolutionary, as the article suggests. The new ISS will continue to carry out a wide range of public health regulatory, control and research functions. Therefore, the new entity will not be a pure research institution, as suggested in the news piece.

Moreover, you are right to state that "links between the ISS and the 31 national biomedical research institutes, Istituti di Ricovero e Cura a Carattere Scientifico (IRCCS), would be strengthened," but we definitely do not wish to create a closed "biomedical research network." In contrast, as Director General of the ISS, I advocate opening up the existing network—which is in fact an exclusive club—to the best institutions, irrespective of their nature—university departments, hospitals, public or private research institutes.

Furthermore, I believe that the fears voiced by the scientists interviewed, that the 'new ISS' will "receive and distribute a larger share of the government funds dedicated to biomedicine" and therefore "curtail the activities of the CNR [the Italian National Research Council]", as well as "foster serious conflicts

among different groups with interests in this field", are unfounded. We have never advocated and do not expect to receive one additional lira from the Italian government. On the contrary, we hope that by opening up the ISS-IRCCS closed network, the entire sum that is today taken from the National Health Fund (NHF) and given to the network—L500 billion—will become available to everyone.

Finally, in response to your argument that "the decree would place the new group in direct competition with the recently reformed CNR, which has hitherto been the country's only public biomedical research body," I honestly fail to see how the new development may hurt this organization. The new ISS will continue to compete for funds, as it does today, in the open market. It will have its own annual endowment, which I am afraid will not change; it will continue to bid for the NHF money, which could substantially increase the Institute's research capability; and will create, along with the CNR, a series of strategic research projects, such as the aging and cardiovascular diseases initiatives mentioned in the article. Creating joint strategic projects with the CNR will benefit those scientists working within the Council network. In theory, the only loser may be the IRCCS, which now have relatively large sums of money exclusively devoted to them: In 1998, more than 70% of the all NHF funding was granted to the IRCCS alone.

And far from worrying "that clinical research will become the dominant force and that rather than integrating this field with basic research, the decree would separate them further," Italian researchers can be assured that our aim is to join forces, not to create dominant or exclusive clubs. Our goal is to improve the quality of biomedical and public health research carried out in Italy.

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