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aspartate mutations generated by Galvan *et al.* and Graham *et al.* are indeed having their effect on the neurodegenerative diseases by preventing caspase action, this implies that cleavage of APP and Htt is downstream of some event that activates a cellular response to stress; that is, caspase cleavage and the subsequent pathological events are components of disease progression.

It is notable that the D664A mutation in APP did not affect the generation of Aβ42 or amyloid deposition. Perhaps the generation of Aβ42 induces a stress signal that results in caspase activation and its pathological consequences. Similarly, caspase-6 cleavage of Htt might also be in response to some stress signal, presumably polyQ-mutant Htt. To understand Huntington's disease fully, this initiating event will need to be identified. Alternatively, caspase-6 might not be the initiating protease for Huntington's disease *in vivo*, in which case identification of this crucial protease would be of paramount concern. It will therefore be essential to examine whether manipulating caspase-6 activity in the brain alters disease progression in YAC128 mice. Interestingly, lowering caspase-6 activity in cell-culture models of Huntington's disease does protect neurons from degeneration[6].

Caspase-6 has a unique set of substrate specificities that does not overlap with those of other caspases. So selective inhibitors of caspase-6 might block the symptoms of Huntington's disease. Other caspases also interact with APP and Htt, suggesting that blocking such interactions might be beneficial therapeutically[4,6]. Specific caspase inhibitors are being developed by pharmaceutical companies, but much work needs to be done before we know whether they are suitable for clinical use. The studies of Graham *et al.*[1] and Galvan *et al.*[2] do, however, validate caspases *in vivo* as potential therapeutic targets for Alzheimer's and Huntington's disease. ■

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50 & 100 YEARS AGO

50 YEARS AGO

"European Brewery Convention" — The idea of science infiltrating into brewing still frequently produces a reaction from the layman on the grounds that, first, beer has been brewed for more than six thousand years, so there can be little still to learn; second, the less the scientist has to do with it the better because it used to be better than it is (in fact, it is even hinted that nowadays "beer is made from chemicals"); third (triumphantly), brewing is an art and not a science. The first two points are born of ignorance of the real position, and the truth of the third depends on the sense of the word 'art': in so far as it refers to experience and skill in 'know how' it may be correct.

From *Nature* 11 August 1956.

100 YEARS AGO

Poverty and Hereditary Genius; a Criticism of Mr. Francis Galton's Theory of Hereditary Genius — The criticism which Mr. Constable brings forward in this book is that reputation is not a test of ability, and as Galton's theory of hereditary genius is based on this assumption, it has to be discarded. The statistical evidence given in "Hereditary Genius" has to be explained away, and Mr. Constable attempts to do this by what he calls the "swamping effect of poverty." We quite agree with Mr. Constable that it is harder for a poor man with uninfluential parents to achieve success as a judge than for a rich one with influence, but this does not seem to us to justify Mr. Constable in discarding the conclusions of "Hereditary Genius," for if the social conditions of both parents and offspring are relatively about the same, it seems as if the omission of the ability in poverty-stricken parents and their children is rather like leaving out of account the addition of numbers to both the numerator and denominator of a fraction.

From *Nature* 9 August 1906.

MICROSCOPY

Nanotomography comes of age

David Attwood

The use of X-rays to construct three-dimensional tomographic images is well established in medicine. The same principle is being extended to the nanoscale, bringing us startlingly accurate pictures of tiny objects.

Writing in *Applied Physics Letters*, Yin and colleagues[1] report an X-ray microscopy technique of broad potential for three-dimensional imaging in the physical and life sciences. By tuning high-energy X-rays, the authors manipulate the contributions of specific chemical elements to a series of two-dimensional images. They then use tomographic methods to combine images taken at different incident X-ray angles, allowing internal structures and — given sufficient spectral resolution — chemical bondings to be discerned with a spatial resolution of around 60 nanometres.

In essence, this technique is a nanometre-scale version of medical computed tomographic (CT) imaging of humans. The high spatial resolution of the new system[1] is largely determined by the 50-nm width of the outermost transmitting zone of its zone plate lens. This lens is a circular diffraction grating consisting of alternate transparent and opaque concentric rings[2,3] and is used to focus the X-ray photons. Higher doses of radiation are required for nanoscale imaging, so radiation-sensitive samples such as biological tissue can require cryogenic or other 'fixation' techniques that limit structural damage to them.

For their experiments, the authors use photons at wavelengths of between 0.11 and 0.15 nanometres; as a photon's wavelength is inversely proportional to its energy, this is equivalent to photon energies of between 11 and 8 kiloelectronvolts. Such high-energy X-rays are known as hard X-rays. At the 'absorption edges' of a chemical element, photons have enough energy to lift an electron out of a particular atomic orbital, and can therefore be absorbed. Thus, by tuning the X-ray energy to just above or below a prominent absorption edge, the contributions of specific chemical elements to the image can be enhanced or diminished.

Yin *et al.* tested their set-up on a thinned portion of a silicon computer chip containing copper–aluminium wires and an array of tungsten plugs. These plugs are used as electrical interconnects between the typically eight or nine layers of a computer chip. Such plugs