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Alzheimer's prevention role discovered for prions

A role for prion proteins, the much debated agents of mad cow disease and vCJD, has been identified. It appears that the normal prions produced by the body help to prevent the plaques that build up in the brain to cause Alzheimer's disease. The possible function for the mysterious proteins was discovered by a team of scientists led by Medical Research Council funded scientist Professor Nigel Hooper of the University of Leeds.

Alzheimer's and diseases like variant Creutzfeldt-Jakob Disease follow similar patterns of disease progression and in some forms of prion disease share genetic features. These parallels prompted Professor Hooper's team to look for a link between the different conditions. They found an apparent role for normal prion proteins in preventing Alzheimer's disease.

''Our experiments have shown that the normal prion proteins found in brain cells reduce the formation of beta-amyloid, a protein that binds with others to build plaques in the brain that are found in Alzheimer's disease,'' explains Professor Hooper.

He continues: ''In vCJD, the normal version of prion protein, PrPc, found naturally in the brain is corrupted by infectious prions to cause disease. The normal function of PrPc has been unclear.''

Using cells grown in the lab, the team looked at the effect of high and low levels of normal prion protein on the successful formation of beta amyloid, the source of Alzheimer's plaques. They found that beta amyloid did not form in cells with higher than usual levels of PrPc. In comparison, when the level of PrPc was low or absent, beta amyloid formation was found to go back up again.

Mice genetically engineered to lack PrPc were also studied. Again, this revealed that in its absence, the harmful beta-amyloid proteins were able to form.

It appears that PrPc, the normal prion protein, exerts its beneficial effect by stopping an enzyme called beta-secretase from cutting up amyloid protein into the smaller beta-amyloid fragments needed to build plaques.

Further evidence for the protective role of normal prion proteins is provided by mutated versions that are linked to genetic forms of prion disease because beta-amyloid fragments are able to form when the normal prion protein is corrupted by genetic mutation.

Professor Hooper concludes: ''Until now, the normal function of prion proteins has remained unclear, but our findings clearly identify a role for normal prion proteins in regulating the production of beta-amyloid and in doing so preventing formation of Alzheimer's plaques. Whether this function is lost as a result of the normal ageing process, or if some people are more susceptible to it than others we don't know yet.''

''The next step for our research will be to look in more detail at how the prion protein controls beta amyloid, knowledge that could be used to design anti-Alzheimer's drugs. Theoretically, if we can find a way of mimicking the prion's function we should be able to halt the progress of Alzheimer's. However, there's still a lot of work to be done in looking at levels of prions in the human system and how these may alter as we age.''

Notes to editors

For a copy of the research paper or to arrange an interview with Professor Nigel Hooper please contact the Medical Research Council press office on 020 7637 6011 or press.office@headoffice.mrc.ac.uk, out of office hours call 07818 428 297.

'Cellular prion protein regulates ß- secretase cleavage of the Alzheimer's amyloid precursor protein' is published in the Proceedings of the National Academy of Sciences USA.

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